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### RESEARCH ARTICLE

#### MIDDLE EAST RESPIRATORY SYNDROME CORONAVIRUS (MERS-COV) TRANSMISSION AMONG HEALTHCARE WORKERS: A LITERATURE REVIEW.

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#### Abstract

Healthcare workers (HCWs) have been frequently infected with Middle East respiratory syndrome coronavirus (MERS-CoV), yet little attention has been paid to how HCWs are acquiring the infection. Therefore, this review highlighted the global distribution of HCWs cases and the latest available data about how they are acquiring the infection. Ninety-eight English articles published from September 2012 to July 2016 on PubMed and Google Scholar, and 252 case reports from WHO website were reviewed. The current review estimated 1,810 MERS-CoV cases reported globally across 27 countries, including 356 (20%) HCWs distributed across 8 countries. Among these, 24% were in close contact with confirmed cases and 13% were not. However, most cases (63%) were undocumented. HCWs were mainly infected in the emergency department. According to documented data, working in high-risk departments, being in close contact with confirmed cases and non-adherence to infection control precautions are the most probable factors of transmission.

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#### Introduction:-

Middle East respiratory syndrome (MERS) is a novel respiratory disease caused by Middle East respiratory syndrome coronavirus (MERS-CoV) that belongs to the C lineage of the genus Betacoronavirus.<sup>1, 2</sup> All available data supports that it is a zoonotic virus, and dromedary camels are a confirmed reservoir for MERS-CoV. The virus was originally acquired by humans in the Arabian Peninsula. However, most of human-to-human transmission has occurred in healthcare settings.<sup>3, 4</sup>

The virus was first isolated in June 2012 from a 60 year old man in Jeddah, Saudi Arabia who died from respiratory and renal failure.<sup>5</sup> B. Hijawi et al. reported that in Zarqa, Jordan, an earlier outbreak was retrospectively identified in April 2012, where 2 confirmed cases deceased.<sup>6</sup> Since then, the infection has spread globally to involve the Middle East, Europe, Asia, North America and North Africa.<sup>7, 8</sup> As of August 10<sup>th</sup>, 2016, 1,791 laboratory confirmed cases of MERS-CoV have been reported to the World Health Organization (WHO) in 27 countries, including 640 related fatalities (case-fatality rate of 36%), which is higher than the previously known outbreak of Severe Acute Respiratory Syndrome (SARS) in 2003 (10%).<sup>9, 10</sup> The majority of the reported MERS-CoV cases were from Saudi Arabia, in which 1,445 cases were confirmed with 610 deaths (42%).<sup>11</sup> Moreover, reported cases from outside the

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Arabian Peninsula have been traced back to it.<sup>7</sup>

The occurrence of most MERS-CoV outbreaks in healthcare settings has substantially increased the total number of cases since 2013.<sup>12</sup> Two of the largest outbreaks reported in Saudi Arabia were in healthcare settings. In Jeddah, 2014, the total number of cases was 255 with 93 deaths and in Riyadh, in 2015, 130 cases were reported with 51 deaths.<sup>13,14</sup> The largest outbreak beyond the virus's endemic area occurred in South Korea in 2015, where 186 cases were detected and 36 died.<sup>12</sup> Most recently, MERS-CoV was reported in Bahrain in April 2016.<sup>15</sup>

A healthcare worker (HCW) is defined as any person who works in a healthcare facility, whose activities involve exposure to infectious materials (e.g., body fluids and contaminated environment), regardless of whether he/she is paid or not.<sup>16</sup> Al-Tawfiq et al. reported that 35% of the secondary MERS-CoV cases worldwide were HCWs.<sup>17</sup> As of June 2016, HCWs cases reported to WHO reached 23% of global MERS-CoV cases.<sup>18</sup> In 2015, Al-Tawfiq et al. and Suwantararat et al. separately studied global HCWs cases and each reported a wide range of percentages from total MERS-CoV cases, 2%-67% and 1%-27% respectively.<sup>1,7</sup>

Yet, little attention has been paid to how HCWs are acquiring the infection. Therefore, in this review, we highlight the current distribution of HCWs cases globally, and the latest available data on how and where they are acquiring the infection.

#### **Search Strategy:-**

English language articles in PubMed and Google Scholar from September 2012 to July 2016 were searched using Medical Subject Heading (MeSH) and keywords of "Middle East Respiratory Syndrome Coronavirus, MERS-CoV, outbreaks, transmission, healthcare settings, healthcare workers, healthcare personnel and healthcare providers" which yielded a selection of 87 articles found to be relevant. The reference list of articles selected for inclusion were scanned for relevant studies and yielded 11 additional articles. The 98 full text articles were reviewed, along with 252 case reports from the websites of the WHO (Disease Outbreak News for Coronavirus Infections), Centers for Disease Control and Prevention (CDC), and Saudi Arabian Ministry of Health (MOH) for the most recent updates. The articles as well as the research team members were divided into two equal groups, each group being responsible for reviewing an equal number of articles and extracting the relevant information. The results of each team were reviewed by the other team and any discrepancies were resolved by consensus. Findings were summarized and analyzed for the generation of the final results.

#### **MERS-CoV in Healthcare Settings and its Global Impact:-**

In 2013, Van Doremalen N et al. found that MERS-CoV was more stable under low temperature and humidity conditions, which are similar to those in the hospital environment. In addition, the virus was still stable even after the process of aerosolization and remained viable after 48 hours.<sup>19</sup> This might contribute to the amplified transmission of MERS-CoV in healthcare settings, which is four times higher than that in the community.<sup>20</sup>

MERS-CoV poses a big challenge for infection control. Vaccine and chemoprophylaxis are still not available.<sup>21</sup> It has an incubation period ranging from 2 to 14 days (median of 5).<sup>22</sup> Evidence suggests it has prolonged viral shedding, however the exact period remains unknown and the mechanism of exposure as well as the mode and direction of transmission remain unclear.<sup>1,7,23</sup>

However, The most probable route of transmission is respiratory droplet.<sup>12</sup> Nonetheless, other routes of transmission including direct contact and airborne are possible. Symptoms vary from asymptomatic, mild or moderate to lethal MERS-CoV infections.<sup>1</sup> Asymptomatic HCWs pose a concealed threat, especially to their family members and most importantly to patients with comorbidities.<sup>24</sup> Notably, HCWs have been infected with the virus since it first appeared.<sup>6</sup> Increasing treatment expenses, absenteeism, and feelings of emotional distress and fear amongst HCWs burdens the healthcare system and negatively affects quality of care.<sup>25</sup> The alarming high number of nosocomial cases of MERS-CoV during outbreaks has led to increasing demands for airborne isolation rooms and the shutdown of hospitals.<sup>14,26</sup>

Public knowledge about this rapidly spreading virus has raised the awareness regarding precautionary measures, yet triggered high levels of concern and emotional stress.<sup>27</sup> The 2015 outbreak in South Korea led to school closures, a decline in tourism and economy, and cut-downs in social activity.<sup>12,28</sup>

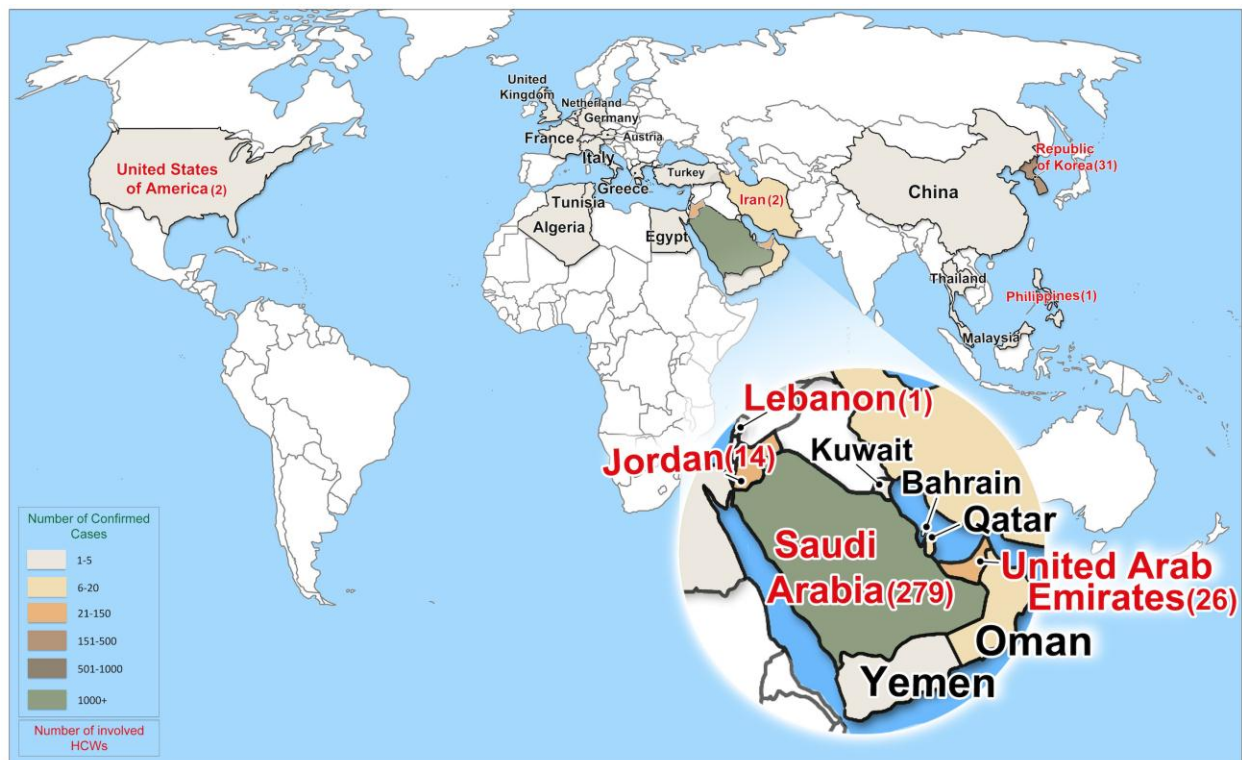
### Infection Control in Healthcare Settings:-

Enhancing the awareness of MERS-CoV and implementation of infection prevention and control measures is crucial to minimize the risk of spread in healthcare facilities. Early identification of patients with MERS-CoV is challenging because the symptoms usually are nonspecific. Therefore, it is vital that HCWs apply standard precautions at all times with all patients.<sup>3</sup> They are recommended to apply droplet precautions while caring for patients with acute respiratory symptoms. In the event of confirmed MERS-CoV cases, contact precautions and eye protection is advised. Moreover, airborne precautions should be considered during all aerosol-generating procedures (AGPs) since HCWs were commonly involved in these procedures.<sup>17,24</sup>

CDC recommends that healthcare facilities adhere to strict infection prevention and control measures and that HCWs comply with work restriction protocols for 14 days in case of exposure to confirmed cases, while monitoring for the appearance of symptoms.<sup>21</sup> Despite this, a HCW in Abu Dhabi, United Arab Emirates (UAE) reportedly acquired the infection after caring for a confirmed case while not wearing a gown, while another HCW was providing care while symptomatic and transmitted the infection to two hospitalized patients.<sup>29</sup> In fact, two large outbreaks reported in Saudi Arabia in 2014 and in the Republic of Korea in 2015 are thought to be due to poor compliance to adequate infection prevention and control procedures due to the limited knowledge concerning MERS-CoV at that time.<sup>3</sup> HCWs are among the high-risk groups for acquiring MERS-CoV infection since they are on the frontline of the healthcare system.<sup>23</sup> This is supported by the findings of Al-Tawfiq et al. (2015) which revealed an attack rate of 10% among exposed HCWs,<sup>26</sup> and by Hunter et al. (2016) which found an attack rate of 16% among HCWs in the Emergency Department (ED).<sup>29</sup> Nurses, physicians, and technicians appear to be at the highest risk among HCWs due to their direct contact with patients. Nurses in particular have been predominantly affected due to their frequent and close contact with patients.<sup>7</sup> While hospital administrative clerks and health-related cleaners are indirectly exposed in the workplace.<sup>30</sup>

### Summary of Findings:-

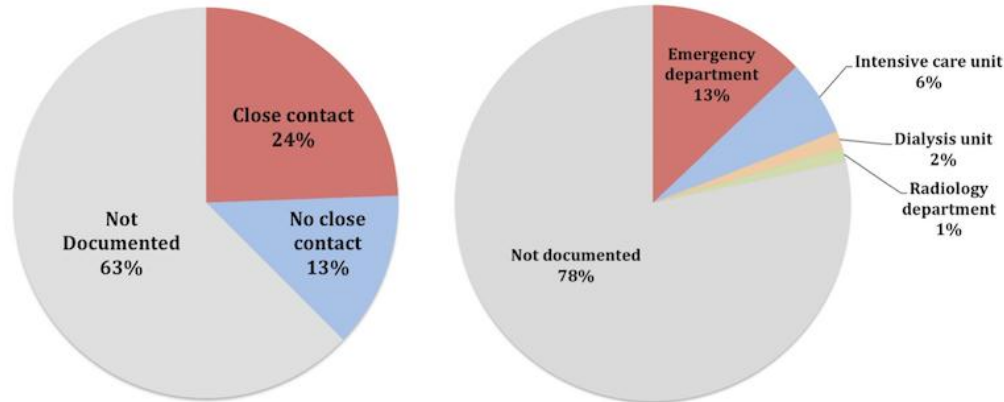
This review estimates that up to July 2016, there were 1,810 confirmed MERS-CoV cases globally, which included 356 (20%) HCWs.<sup>31</sup>



**Figure 1:-** Global distribution of total confirmed MERS-CoV cases across 27 countries and the involved HCWs cases in 8 countries up to July 2016.

Saudi Arabia had the highest incidence with a total number of 1,416 cases, including 279 HCWs (20%), followed by 186 cases in Republic of Korea, including 31 HCWs (17%), and 95 cases in UAE, including 26 HCWs (27%) (Figure 1).

Based on published articles addressing multiple outbreaks in Saudi Arabia, the estimated percentage of HCWs was ranging between 4% and 51%.<sup>3, 4, 13, 30, 32-39</sup>



**Figure 2:-** Distribution of HCWs by extent of contact to confirmed cases and department.

Figure 2 illustrates the 356 global MERS-CoV cases among HCWs, distributed according to the most probable factors of transmission. As evident, undocumented data represents the highest percentage.

HCWs were considered as having close contact with confirmed MERS-CoV cases if the HCWs provided direct care, or were in close proximity (2 meters) to a confirmed case for a prolonged period of time and were not wearing full personal protective equipment (PPE), or reported a direct contact with confirmed MERS-CoV secretions while not wearing full PPE, which is in line with the CDC definition of close contact.<sup>40</sup>

### Discussion:-

Saudi Arabia has had the highest count of MERS-CoV cases including HCWs. Accumulative data from the Saudi MOH since January 2015 concluded that 12% of cases in Saudi Arabia were HCWs.<sup>11</sup> In 2016, Al-Tawfiq et al. summarized in his recent review that 31% of the outbreak cases in Saudi Arabia were HCWs.<sup>26</sup> In this review of published articles on multiple MERS-CoV outbreaks in Saudi Arabia, the estimated percentage of infection in HCWs ranged between 4%-51%.<sup>3, 4, 13, 30, 32-39</sup>

The wide range between these percentages may be attributed to the overlap between multiple articles describing outbreaks in the same population at the same time period. Notably, multiple healthcare associated outbreaks in 2014 were reported in Jeddah, Saudi Arabia without mentioning the exact setting or the involvement of HCWs.<sup>13, 30, 32-34</sup>

Documented findings have revealed that HCWs are most likely to acquire MERS-CoV infection through their close contact with confirmed cases. For those who acquired the infection without close contact to confirmed cases, the virus might have been transmitted indirectly by fomite transmission. Studies have shown that HCWs in ED and Intensive Care Unit (ICU) have the highest risk of infection.<sup>41</sup> Despite the mentioned efforts, there has been incomplete reporting of the factors affecting transmission of MERS-CoV to HCWs, which is apparent from the high percentage of cases in which place and extent of contact were not documented (Figure 2). Other factors mentioned in the literature include overcrowding, late identification of cases, inappropriate triage system and utilization of AGPs.<sup>14, 32</sup> These factors are related to ED and ICU settings, which support our finding. More inclusive data need to be collected to understand the risk of transmission to HCWs.

These findings highlight that poor compliance to infection control precautions may be the most probable factor in MERS-CoV transmission to HCWs. Therefore, application of appropriate infection control measures was commonly declared in the literature, as being the single reasonable measure which can be applied in practice to help prevent disease transmission to HCWs.<sup>7, 17, 26, 29</sup>

Limitations of this study include, incomprehensive reporting of MERS-CoV cases, and the conditions in which transmission to HCWs occurred. That has led to inaccurate estimation and analysis of the factors affecting transmission.

### Conclusion:-

This review was undertaken to understand how HCWs are acquiring MERS-CoV infection in healthcare settings by highlighting the number of affected HCWs, and summarizing what is known about the risks of transmission. According to the documented data in the literature, working in high-risk departments, being in close contact with confirmed cases of MERS-CoV and non-adherence to infection control precautions are the most probable factors resulting in transmission of the virus to HCWs.

HCWs are advised to strictly follow the recommended infection control guidelines and to adhere to standard, contact, and airborne precautions when indicated. Comprehensive reporting of outbreaks and tracing of HCWs cases are of great value to reduce the spread of infection among HCWs.

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