

Case Study of Middle East Respiratory Syndrome (MERS-CoV) Outbreak in South Korea and Future Implications

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How to cite this paper: Lee, W.H., Ahn, D., Kim, K., Park, P.S., Moon, S.I., Lee, H.J., Park, D., Shin, H.S., Kang, E., Choo, D. and Chung, D.S. (2020) Case Study of Middle East Respiratory Syndrome (MERS-CoV) Outbreak in South Korea and Future Implications. *Advances in Infectious Diseases*, 10, 76-89.

<https://doi.org/10.4236/aid.2020.102007>

Received: December 11, 2019

Accepted: April 26, 2020

Published: April 29, 2020

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Abstract

The Middle East Respiratory Syndrome (MERS-CoV) is a potentially fatal respiratory viral infection that has had outbreaks in the Middle East and Asia region starting in 2012. As recent as 2015, MERS had outbreaks in South Korea, resulting in 36 deaths among 186 infected patients. The purpose of this thesis is to gain an in-depth understanding of how this viral infection behaves in outbreaks and how it is spread around the globe. To gain insight, real time analysis was performed under a case study methodology based on pooled data from the Ministry of Health & Welfare of South Korea. We calculated a striated mortality rate based on gender, age, and the presence of pre-existing health conditions ranging from heart, lung, and kidney diseases. We found that MERS outbreak follows the pattern of a point source outbreak, largely spurred by the patient-referral system under the universal healthcare system in South Korea. The purpose of this case is to discuss the benefits and challenges of such patient referral system, and to offer a possible solution in improving transparency between healthcare providers and the government under a universal healthcare system to prevent future outbreaks.

Keywords

Infectious Diseases, Respiratory Viral Infections, Public Health, Disease Prevention

1. Introduction

Viral respiratory infections have long affected mankind before modern understanding of their origins, diagnosis, and treatment. Viral respiratory diseases are now widely recognized as a substantial cause of hospitalizations and deaths around the world. Ranging from adenovirus infections and the common cold to influenza-like illnesses and coronaviruses, viral respiratory diseases are classified either by its virus, or more commonly, by its syndromes [1]. These diseases range significantly in their severity from mild to morbid, with the chance of developing into severe disease most likely among the elderly and infants. The causes of morbidity are both direct and indirect: while morbidity may be a direct result of the viral infection, it can also be caused by an aggravation of pre-existing cardiopulmonary conditions or bacterial infections in the lung, middle ear, and paranasal sinuses [1].

Early diagnosis for viral infections is crucial, as isolation of infected patients may inhibit further transmission of the infection and allows for early antiviral treatment. Current diagnostic tests for respiratory viral infections comprise of polymerase chain reaction (PCR) testing, cell culture, rapid antigen testing, and serologic tests [2]. According to Talbot, PCR, serologic test, and cell cultures are not effective methods of detection to be used for patient care since they are generally too slow, but are efficiently utilized to identify outbreaks as epidemiologic monitors.

Viral respiratory illness treatment is generally supportive: underlying causes of the diseases are not treated, but its symptoms are managed. Antibiotics can be used to treat secondary bacterial infections, but are not an appropriate method of treatment for the viral pathogen itself. Instead, antiviral drugs can be used to target the source of the illness [1].

1.1. Respiratory Viruses within South Korea

Over the past decade, there have been multiple outbreaks of respiratory diseases that have affected South Korea and the world; the most prominent cases being that of the Severe Acute Respiratory Syndrome (SARS), H1N1 virus, and the Middle East Respiratory Syndrome (MERS-CoV).

1.1.1. SARS

In 2002, SARS, caused by the SARS Coronavirus (SARS CoV), had a significant outbreak in China. The symptoms of SARS include coughing, fever, chills, chest pain, headache, diarrhea, and fatigue. SARS-CoV is highly transmissible, and like most other respiratory virus infections, is predominantly transmitted by respiratory droplets, direct contact with infectious secretions, or contact with contaminated fomites.

However, South Korea which is adjacent to China, did not suffer from the SARS outbreak even though it is highly transmissible. Insufficient information about the new disease and lack of preventive regimen appeared to increase the

emotional and physical stress of clinical nurses caring for SARS patients in China, especially following reports that several health personnel had died whilst taking care of SARS patients in China [3]. This insufficient knowledge from China caused the Korean government to become more alert and prepared. Initially, the Korean government placed restrictions and regulations on all forms of travel to any SARS suspected countries such as China and Canada. The government also utilized a computer-based thermometer system in Incheon International Airport to isolate any suspected patients with high body temperatures. Any suspected patients were forced to transfer to the isolation hospital where they were quarantined. Suspected patients had to remain until their body temperature dropped and any existing SARS symptoms, such as coughing, ceased. Through this effort, out of over 8,100 patients worldwide, South Korea only had 3 patients in total that needed treatment for SARS.

1.1.2. H1N1

A different respiratory outbreak occurred in 2009—the H1N1 virus, a subtype of the Influenza A virus widely known as swine flu. H1N1 can be transmitted through close contact with pigs, but not through consumption of pork that is properly handled or cooked. Between humans, H1N1 is spread similarly to the seasonal flu. Since H1N1 is airborne, it can be transmitted when a person coughs, sneezes, or speaks, and releases water droplets that contain strains of the virus. A person may also contract the virus by touching an object or surface that is already contaminated by the virus and subsequently touches his or her mouth, eyes, or nose [4]. Symptoms are like those of other flu strains, and include fever, cough, sore throat, runny nose, body aches, chills, diarrhea, and vomiting. Although most infected patients recover without complications, some patients develop pneumonia. Those that develop severe pneumonia can experience acute respiratory distress syndrome, multi-organ failure, and even death [5].

The virus spread, and on May 2nd of 2009, South Korea identified its first case [6]. Throughout the pandemic, health care workers contributed to the rapid spread of the H1N1 virus due to their exposure to many patients [7]. In Korea, only 3.89% of the H1N1 patients were 60 years and older, most of whom already had underlying medical conditions present, whereas 33.94% of reported patients were children 9 years and younger [8]. 94% of the patients were under 40 years old [5]. By the end of the pandemic, South Korea had the 3rd largest number of fatal cases in Northeast and South Asia, following India and China (mainland), but the most number of confirmed cases in all of Asia [9]. The majority of patients were from the capital area—716,922 from the Kyonggi Providence, 547,441 from Seoul, and 156,035 from Incheon—due to the high population density [8]. As a response to the pandemic, the Korean Health Authority distributed antiviral drugs. Since H1N1 is very similar to other influenza strains, an H1N1 vaccine was created relatively quickly and was readily distributed by early 2010 [10].

1.1.3. MERS

In June 2012, Middle East Respiratory Syndrome (MERS-CoV) was first reported in Jeddah of the Kingdom of Saudi Arabia, though the earliest outbreak is likely to have occurred in March or April 2012, a couple months prior to the first report. The initial symptoms entail flu-like symptoms such as coughing, fever, chills, arthralgia, and myalgia. When symptoms worsen, infected patients face respiratory difficulty and their conditions may progress to pneumonia [11]. Additionally, some infected patients may encounter problems with their gastrointestinal tract: 30% of patients have been reported to complain of diarrhea and vomiting [11]. MERS-CoV typically manifests as a nonspecific febrile respiratory tract infection, but it can either advance quickly to respiratory failure, or never become severe. MERS-CoV has a mortality rate of 35% - 50%, and an incubation period of anywhere from 2 - 14 days [12].

MERS-CoV, like SARS-CoV, is a corona-viral respiratory disease. Specifically, it is caused by a -coronavirus in lineage C, a different lineage from that of SARS-CoV, despite how similar MERS-CoV is to SARS-CoV in clinical presentation. Moreover, MERS-CoV taxonomically belongs to the same species as the Africa Neoromica capensis bat coronavirus (NeoCoV), having up to 95% homology for gene encoding structural proteins and 85% of its genome at the nucleotide scale [13].

Although sustained community transmission has not been observed, MERS-CoV, like SARS-CoV, is transmissible from person-to-person. As a result, health care workers are at the greatest risk for infection. Compared to SARS-CoV, MERS-CoV is less contagious but carries a higher fatality rate. Patients who contracted the virus through a secondary infection showed less severe cases and their mortality was lower than the index case [11]. Known transmission factors include consuming camel milk, eating undercooked camel meat, and respiratory exposure to camel secretions [14].

In the summer of 2015, South Korea had an outbreak of MERS. The outbreak began when a 68-year-old man from South Korea traveled to Bahrain, United Arab Emirates, the Kingdom of Saudi Arabia, and Qatar and returned to South Korea on May 4th [11]. On May 11th, he began to show symptoms of MERS but he was not officially diagnosed with the viral disease until his fourth hospital visit on May 20th, and he was finally hospitalized on June 12th. While visiting 2 outpatient clinics and 2 hospitals during his initial visitation medical centers, he initiated chains of transmission that involved 126 MERS cases and 11 deaths as of June 10th. The Ministry of Health and Welfare investigated records on which hospitals the first patient visited and found that during his first visit to ASAN-Seoul Hospital, one other patient was confirmed to have been infected with MERS [11]. Next, he was admitted to Pyeongtaek Sungmo hospital during the dates of May 15th-17th and spread the virus to a total of 36 admitted patients including his wife. Still not diagnosed with the virus, he then visited Seoul Yeolin clinic on May 17th, where he infected one other patient. He was finally diagnosed with MERS after being admitted to Samsung Medical Centre on May 20th. A second-

ary patient from Pyeongtaek Hospital was then transferred to Samsung Medical Centre, where he infected 18 tertiary patients [11]. Furthermore, another secondary patient from Pyeongtaek hospital visited two other clinics in DaeJeon, where chains of transmission continued to grow in different regions of South Korea. This resulted in a significant increase in the number of diagnosed MERS patients at the Samsung Medical Centre in Seoul, which treated almost 50% of total MERS cases.

As of August 3rd, 2015, the MERS outbreak was considered to be over as two maximum incubation periods, or 28 days, had passed since the last laboratory confirmed diagnosis. The outbreak resulted in the infection of a total of 186 patients and the deaths of 36 individuals.

The objective of this study is to centralize information pertinent to the Middle Eastern Respiratory Syndrome Coronavirus and its outbreak in South Korea. Additionally, we will look at the potential reasons that the MERS-CoV outbreak occurred within this nation that is often heralded as having a proficient health-care system. After analyzing these underlying causes, we offer suggestions that will prevent a future outbreak like MERS in the South Korean peninsula as well as propose methods and protocols that can be utilized by other nations to prevent a MERS outbreak, or a respiratory virus similar to it.

2. Methodology

Our study specifically observed the Middle East Respiratory Syndrome as it occurred in real time within South Korea. As such, our study placed emphasis on searching for sources that reported specific numbers and statistics about the MERS outbreak within South Korea. We expanded our search of information to include news articles that reported about the condition of MERS patients in South Korea to gain information and increase the amount of data available. Additionally, we chose to include news articles within our research to gain a real time understanding of the outbreak as it occurred within the months of June and July of 2015. Our study began on July 3rd, 2015, and concluded once the MERS outbreak was officially over on August 3rd, 2015.

This epidemic consisted of the Korean government quarantining 16,993 individuals over a 14-day period to control the outbreak [15]. Our data is based on pooled information made publicly available by the Ministry of Health & Welfare of South Korea. Specifically, we were interested in the 186 confirmed cases of MERS-CoV as confirmed by the Ministry. We collected data such as the movement of the index case, number of diagnoses by date, and the mortality rate. We also gained insight based on follow-up radiographs in 36 individuals after recovery from MERS-CoV. This literature serves as a review on the epidemiology of pandemic MERS-CoV of the 2015 MERS-CoV outbreak in Korea.

3. Results

From the data gathered, we observe several facts that are important and inter-

esting. From **Figure 1**, we observe that the greatest number of incident cases arose on June 7th, 2015, with a total of 23 cases. We can also reasonably see that the graph follows the patterns of a point source outbreak, which is true of the MERS outbreak in South Korea. Knowing that the incubation period of MERS range from 2 - 14 days, we can also see that the date at which the outbreak was over is August 3rd, as the most recent diagnosis was made on July 6th, and a period of maximal incubation is needed to determine an outbreak to be over.

Figure 2 allows us to observe the rate at which the diagnosis of MERS took place within South Korea during the outbreak. We also observe that the last

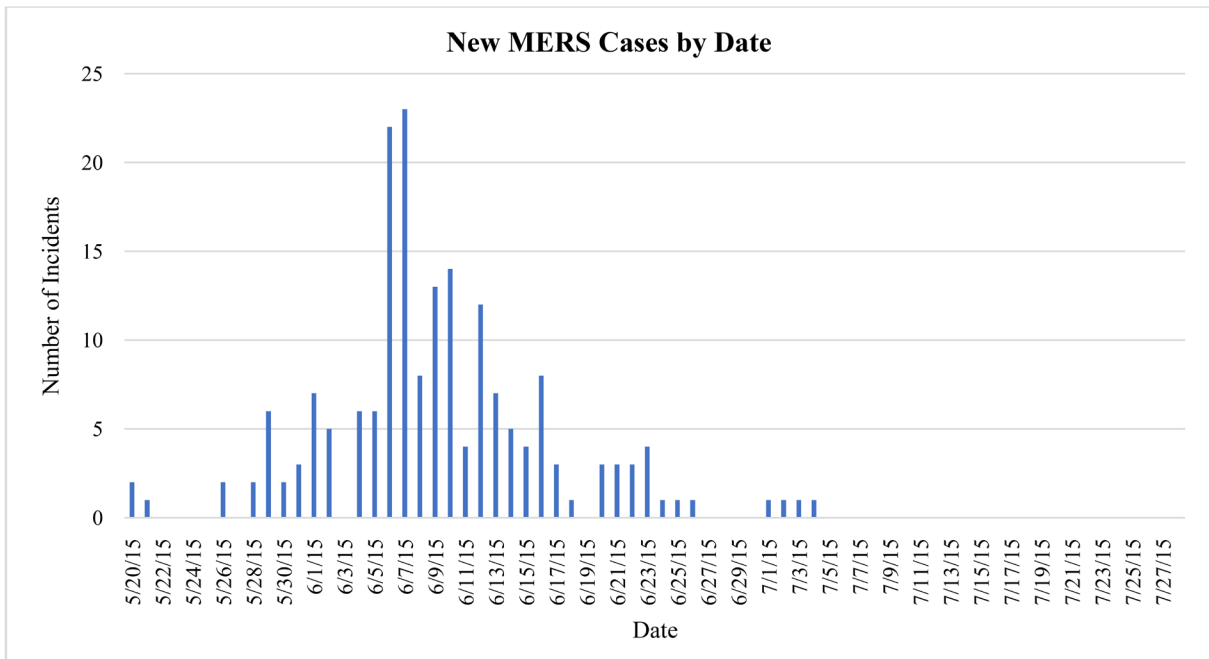


Figure 1. New MERS incident cases in south Korea by date.

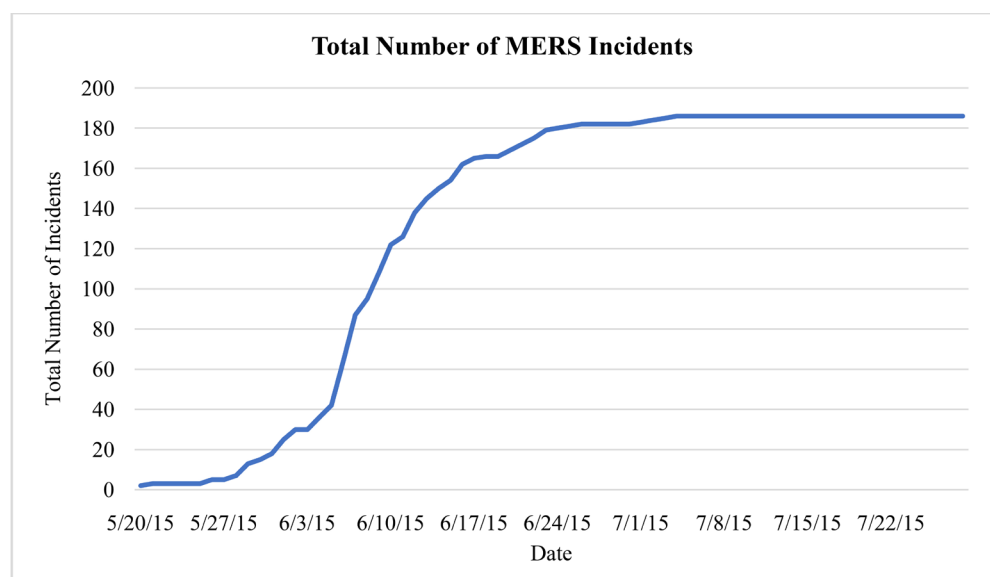


Figure 2. Total number of mers cases by date.

diagnosed MERS case was on July 6th, 2015, with the number of confirmed cases remaining at 186 after that date.

Figure 3 allows us to see the distribution of MERS infections by patient relation to the hospital. We can see that 82 of the 186 total infections (44.1%) arose from hospital inpatients, or patients that were staying within the hospital. 65 of the infections (34.9%) arose from MERS patients' family members, caretakers, or visitors to the hospitals. The final 39 MERS patients (21.0%) were from hospital workers. Amongst these hospital workers were 8 doctors, 15 nurses, 2 radiologists, 1 patient transporter, 2 ambulance workers, 8 caregivers, 2 security personnel, and 1 computer worker (as shown in **Figure 4**). From this data, we note that the populations most susceptible to contracting the disease consisted of those whose occupations had clinical characteristics of repetitive and continuous direct contact with patients. Nurses and caregivers who have the most contact with the patients were the most susceptible.

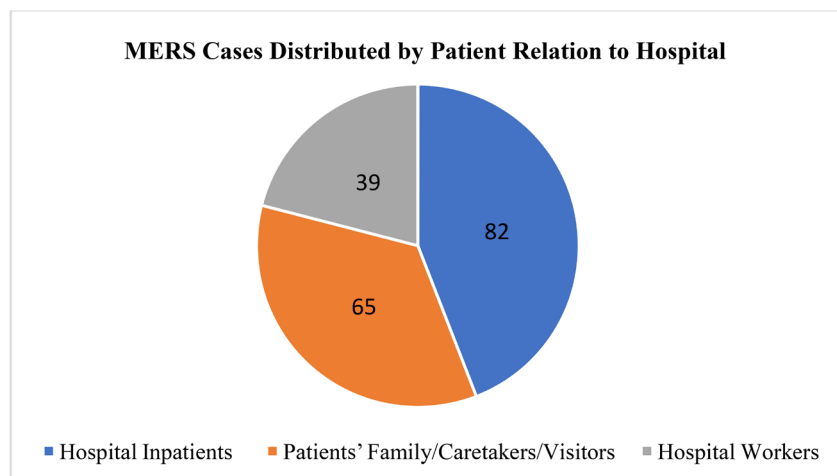


Figure 3. MERS cases distributed by patient relation to the hospital.

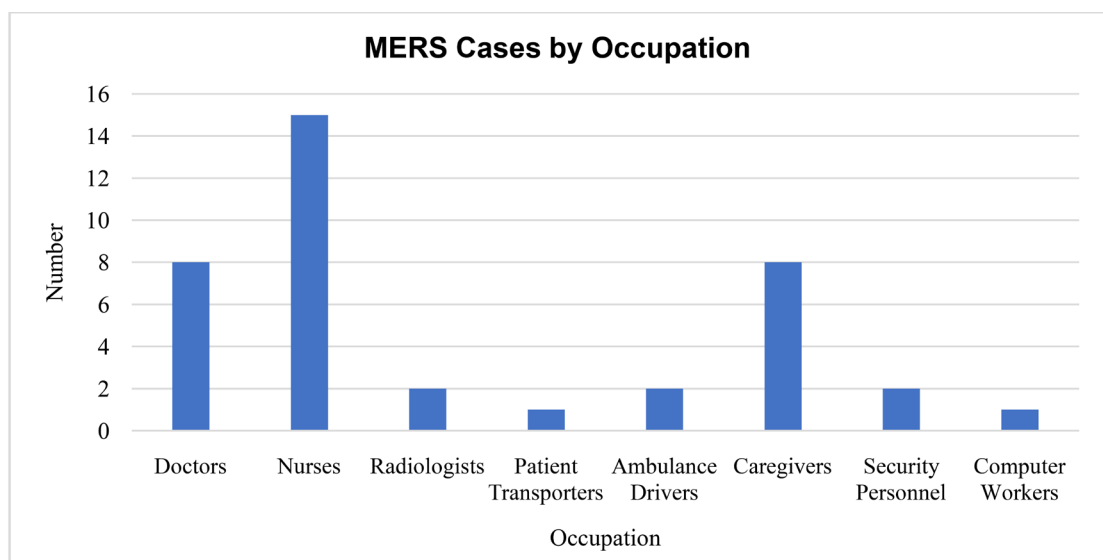


Figure 4. MERS diagnoses distribution of hospital workers by occupation.

In **Figure 5** and **Figure 6**, we examine the number of MERS cases and subsequent deaths of MERS patients by age groups. Patients aged 50 - 59 had the highest number of infections. However, the age groups of 60 - 69 and 70 - 79 had the highest number of deaths among those infected with MERS at 11 each. Furthermore, out of 40 patients that had contracted MERS under the age of 40, none passed away. Within patients aged 40 - 49, a total of 29 individuals were infected, with only 1 resulting in death. However, patients aged 80 - 89 had the highest rate of death as 7 out of 9 patients (77.8%) who had contracted MERS within this age category passed away.

Figure 7 allows us to see the MERS cases and deaths by gender. We can easily see that out of the total number of MERS patients, males had a much higher number. Out of 186 MERS cases, 111 (59.7%) were male, and 75 (40.3%) were female. Out of 36 cases of death, 24 (66.7%) were male and 12 (33.3%) were female. It is also important to note that out of 36 cases of death, 33 patients (91.7%) had pre-existing health conditions that ranged from heart, lung, and kidney diseases, as well as cases of diabetes, cancer, and other co-morbidities. Furthermore, calculating a mortality rate striated for gender resulted in a male

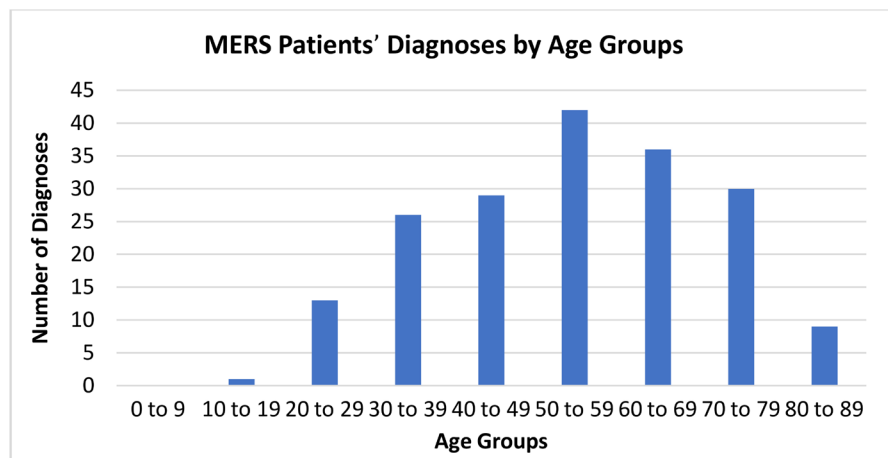


Figure 5. MERS diagnoses distributed by age groups.

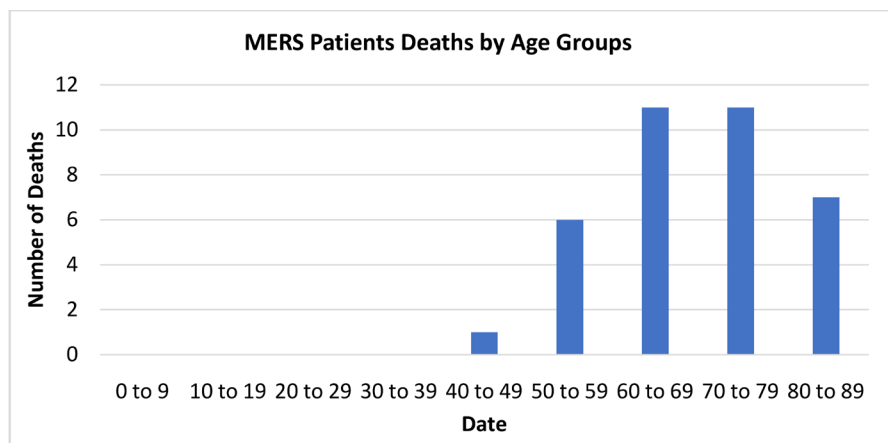


Figure 6. MERS patients' deaths by age groups.

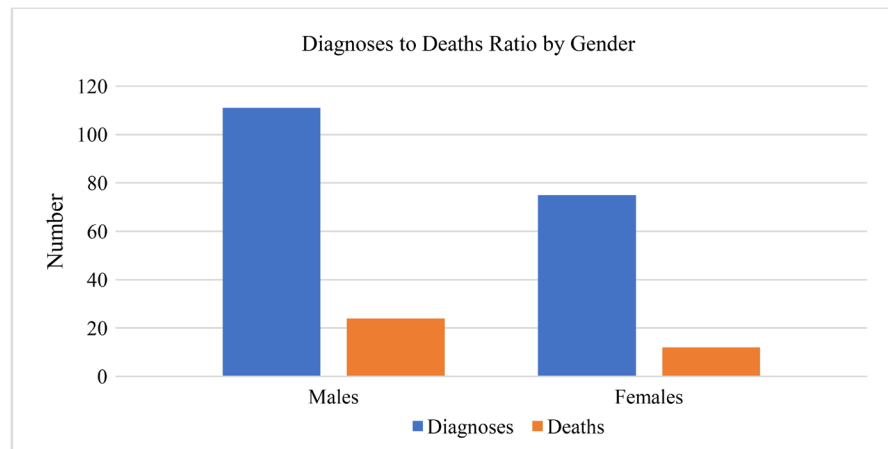


Figure 7. MERS diagnoses to deaths ratio distributed by gender.

patient mortality rate of 21.6% (24 male deaths out of 111 total male cases) and a female patient mortality rate of 16% (12 female deaths out of 75 total female cases).

4. Discussion

The Middle East Respiratory Syndrome's penetration of the South Korean peninsula alarmed and surprised many health care professionals within the nation. When the first case was diagnosed, some practitioners did not even know that the disease existed, much less the methods to diagnose it. Furthermore, the index case patient did not properly convey information that he had visited the nations of Bahrain, Saudi Arabia, Qatar, and the United Arab Emirates. This made difficult for health care professionals to suspect and identify MERS as the contracted disease as MERS's symptoms are quite like those of the common cold, which include coughs, fevers, and other flu-like symptoms. Additionally, MERS is a respiratory viral infection. As such, the way in which to identify MERS infected patients is to conduct proper laboratory testing through PCR, serologic tests, or other approved means [2]. Thus, more time and resources are needed to conduct tests to properly diagnose suspected MERS patients.

From the data, it is important to note that 33 out of 36 deaths (91.7%) of MERS patients had co-morbidities that ranged from heart disease, liver disease, diabetes, and various other health conditions. As a result, we deduce that patients with pre-existing health conditions have a much higher risk of mortality from MERS than patients with relatively healthy background with no pre-existing health conditions.

We also observe that males have a higher number of diagnoses as well as a higher number of overall death cases compared to females (59.7% male MERS diagnosis vs. 40.3% female diagnosis). Additionally, males have a higher mortality rate (21.6%) when compared to female mortality rate (16%). This may be due to the trend that males visit hospitals less frequently and thus visited hospitals to receive treatment when their conditions reach severe levels, whereas female pa-

tients often visit hospitals at an earlier point, allowing doctors to intervene at an early stage of the disease. However, it cannot be stated with certainty that males are more susceptible to the disease and mortality from MERS since we do not have exact statistics as to which gender had a higher proportion of patients with pre-existing health conditions.

The data also exhibits that within older age groups, there seems to be a higher mortality rate. However, this statistic may be because older individuals are more susceptible and more likely to be ailing from pre-existing health conditions, which would increase the likelihood of mortality as well as contraction of MERS due to a weakened immune system.

Another observed phenomenon is the way in which the index case patient moved between several different hospitals before being diagnosed. This not only arose due to the lack of an exact diagnosis of the index case patient, but also because of the patient referral system that exists within South Korea. Currently, South Korea offers universal health care to all its citizens. This allows patients a certain degree of freedom in moving from hospital to hospital with proper referrals. Through this referral process, many patients seek to receive their medical services within Seoul, the capital of South Korea and the most densely populated area of the nation. The most famous hospitals within Seoul are referred to as the Big 5: Asan Medical Center, Samsung Medical Center, Seoul National University Hospital, Severance Hospital, and Seoul Saint Mary's Hospital [16]. Because of the level of services and resources available at these facilities, many patients seek to receive medical attention at these centers. Thus, the high number of MERS patient cases that arose from the Samsung Medical Center may be explained and the cause of the difficulty in containing the MERS outbreak once it entered the country.

To investigate the treatment outcomes of patients after recovery, 36 patients with confirmed cases underwent follow-up chest radiographs after recovery [17]. Out of these patients 23 (64%) showed normal radiographs, suggesting full pulmonary recovery. Most notably, 12 patients (33%) showed signs of lung fibrosis, with increased ICU admission days (19 ± 8.7 days, P value = 0.001). These patients belonged in an older age group (50.6 ± 12.6 years, P value = 0.02), which was consistent with the findings in **Figure 5**, which demonstrated that the age group from 50 to 59 years of age was the most susceptible to contracting the virus.

The overall mortality rate of the MERS outbreak within South Korea was 19.4%, far lower than the expected 35% - 50% mortality rate of countries previously dealing with the virus [18]. Although, there is no definite reason as to why this trend occurred, and perhaps there are several reasons it can be attributed to. Korea is often respected in the world as a forerunner in medical practices and services. As such, the treatment given to MERS patients at hospitals may have prevented a higher number of MERS related deaths from occurring. Furthermore, once South Korean health care professionals realized that MERS had entered the country, they took proper practice in quarantining infected

school zones, work areas, and hospitals, as well as designating specific hospitals as specialized treatment centers for MERS.

5. Conclusions

5.1. Transparency

One factor that may prevent the spread of infectious diseases is the increase of transparency between healthcare providers & the government with the citizens of the nation. After the first South Korean MERS patient was diagnosed, the South Korean government utilized a non-disclosure policy that concealed the names of the hospitals that the index case patient visited. The action was eventually repealed on June 7th through the request of the National Union of Healthcare Workers, and the names of the 24 hospitals that had contact with MERS patients were released to the public [19].

The MERS crisis of South Korea showed the importance of government transparency. Due to the non-disclosure policy that was upheld by the government, it is impossible to tell the number of patients that were exposed as well as infected by MERS due to visitation to those hospitals. The non-disclosure policy was taken on because a private hospital in Gyeonggi province was falsely rumored to have a MERS patient on social media sites, and suffered financial hardships. The hospital later demanded that the Korean government compensate for the loss, blaming the lack of patient and hospital confidentiality upheld by the government for its hardships [19].

Kim Woo-Joo, the Joint Committee Head of the MERS Public and Private Joint Response Force and Chairman of the Board for the Korean Society of Infectious Diseases, pointed out at the Sejong Government Complex media briefing that, “As the names of perfectly safe hospitals who are diligently treating MERS patient, hospitals who have already been investigated, are divulged, the consequences of that public knowledge are considerably worrisome.” Kim expanded on his concern, saying, “If we put hospitals that are altruistically treating MERS patients on the chopping block, especially considering they were not designated to provide such a response, then the private sector may pledge to not deal with such infectious diseases in the future” [19]. Due to the low number of public hospitals that exist within South Korea, if the private sector does not actively seek to treat infectious diseases, then a proper and ready disease response will become essentially impossible within South Korea. Thus, transparency and progressive work towards preventative medicine and care is needed by both the private and public sector for adequate infectious diseases response in the future.

5.2. Proper Protocol

The entry of MERS into South Korea was a highly unpredictable event. Furthermore, the focus on the Ebola virus over the previous year and a half after the first diagnosis of MERS within Saudi Arabia diluted the influence and voice of MERS advocates. As such, the Korean government and healthcare providers did

not have a proper protocol and manual for dealing with suspected MERS patients or the outbreak when it occurred. However, the Myeongji Hospital organized its own team of 80 members and rehearsed proper protocols with its staff, predicting that MERS would enter the Korean peninsula [18]. They created their own manual and protocol for MERS regarding how to combat the disease and treat infected individuals while protecting medical staff. The protocols implemented by the hospital involved the following: organization of a Contagious Disease Response Team (CDRT) to prevent further infection in the hospital, planning of a one-minute route for the transportation of a MERS infected patient to a quarantine room with minimal exposure to the public, mastering skills of wearing and removing protective clothes for infectious diseases, and the designation of 20 medical staff to live with patients full-time in the Negative Pressure Isolation Facility where they were in charge of food delivery and dealing with the MERS infected patients [20]. The hospital also held the 80 members of the organization accountable for studying academic journals and papers about the disease when making treatment plans to offer patients the most comprehensive care available. Moreover, the hospital ran 10 practice drills and meetings amongst the medical staff about their created MERS protocol. This performance by the Myeongji Hospital resulted in the treatment and recovery of 5 patients and a zero-infection rate among the medical staff treating the patients.

From the example of Myeongji Hospital, we can see the importance of proper protocol and instruction being in place not only for the treatment of patients, but also for the safe keeping of the medical staff. Additionally, the practice of these protocols allowed for the staff members to properly deal with infected patients when they arrived. As such, patients could properly recover and infection rates kept to a minimum.

5.3. Further Research about MERS

The medical world still lacks proper information and research relating to the Middle East Respiratory Syndrome. The exact means of transmission are not exactly determined, and the symptoms which are very similar to those of the flu and the common cold are difficult to detect. Moreover, an antiviral or vaccine does not exist for this virus. However, progress has been made in therapeutic treatments, as it has been discovered in an experiment with Rhesus monkeys that treatment of MERS-CoV infected monkeys with interferon- α 2b and ribavirin improved outcomes by decreasing the replication rates of infected cells [21]. The experiment was also conducted upon human subjects and found positive results. However, the treatment had no positive effect on individuals that seemed to be in the later stages of the disease, suggesting that the interferon and ribavirin treatment affects MERS-CoV replication at an early stage [22]. Research such as the one by Al-Tawfiq needs to continue and be funded to produce results that may conclude in an effective treatment for MERS patients at all stages. However, it is also imperative to understand that the implementation of a proper public

health protocol to infectious diseases must be created, rehearsed, and properly utilized to contain exposure.

Acknowledgements

The authors acknowledge the Fuzbien Technology Institute and Youth with Talents for sponsoring this project (YWT-2017-6). We would like to thank the medical doctors and staffs in hospitals in Korea for their advice and assistance throughout this study.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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