Journal of Taibah University Medical Sciences (2021) 16(4), 591–595

Taibah University

Journal of Taibah University Medical Sciences

www.sciencedirect.com

Original Article

Determining the correlation between comorbidities and MERS-CoV mortality in Saudi Arabia

Mohammad H. Alotaibi, MBBS [a,*] and Salman A. Bahammam, MBBS [b]

[a] *Department of Family Medicine, Joint Program of Postgraduate Studies of Family Medicine, Jeddah, KSA*
[b] *Department of Medicine, College of Medicine, King Saud University, Riyadh, KSA*

Received 28 September 2020; revised 8 February 2021; accepted 8 February 2021; Available online 12 March 2021

الملخص

أهداف البحث: هناك ٢٥١٩ حالة مؤكدة من متلازمة الشرق الأوسط التنفسية حتى يناير ٢٠٢٠، مع ٨٦٦ حالة وفاة من ٢٧ دولة. حدثت معظم هذه الحالات في السعودية (٢١٢١ حالة). منذ اكتشاف هذا المرض، دراسات قليلة تناولت الأمراض المصاحبة المرتبطة بالوفاة في حالات الإصابة بهذا الفيروس. الهدف من الدراسة هو تقدير العلاقة بين الأمراض المصاحبة والوفاة.

طرق البحث: هذه دراسة رجعية وصفية، درسنا فيها البيانات التي نشرتها منظمة الصحة العالمية بين يناير ٢٠١٧ ونوفمبر ٢٠١٩ وحللنا العلاقة بين الأمراض المصاحبة والوفيات.

النتائج: وجدنا ٥٧٢ حالة من حالات الإصابة بفيروس كورونا المسبب لمتلازمة الشرق الأوسط التنفسية التي أبلغت عنها المملكة العربية السعودية منظمة الصحة العالمية، منها ٣٨٧ حالة (٦٨٪) تعاني من أمراض مزمنة. ووجد أن معدل الوفيات يصل إلى ٢٥٪ بين الحالات. وكان داء السكري أكثر الأمراض المصاحبة انتشارا وبلغ معدل الوفيات ٣٢٪ مقارنة بـ ١٢٪ في المرضى غير المصابين بداء السكري. وكان ارتفاع ضغط الدم هو ثاني أكثر الأمراض المصاحبة، حيث بلغ معدل الوفيات ٣٥٪ مقارنة بـ ١٥٪ في غير المصابين بارتفاع ضغط الدم. وشهدت أمراض القلب والأوعية الدموية معدل وفيات ٣٩٪ مقارنة بـ ٢١٪ في الحالات التي ليس لها تاريخ في الإصابة بهذا المرض.

الاستنتاجات: فيروس متلازمة الشرق الأوسط التنفسية له معدل وفيات كبير في المصابين بأمراض مصاحبة. سيكون من المفيد دراسة هذا الفيروس في المستقبل لفحص تأثير تدابير مكافحة العدوى المجتمعية مثل التباعد الاجتماعي والكمامات، في سياق تدابير فيروس كورونا المستجد للحد من انتشار فيروس متلازمة الشرق الاوسط التنفسية ونتائجه السريرية.

الكلمات المفتاحية: متلازمة الشرق الأوسط التنفسية؛ انتشار المرض؛ الأمراض المصاحبة؛ عوامل الخطورة؛ معدل الوفيات؛ المملكة العربية السعودية

Abstract

Objective: As of January 2020, there were 2,519 confirmed Middle East respiratory syndrome coronavirus (MERS-CoV) cases with 866 deaths across 27 countries. Most of these cases (2,121) were reported in Saudi Arabia. Since the initial identification of MERS, few studies have investigated the role of comorbidities that could potentially lead to mortality in cases of the infectious disease. This study aimed to examine the association between comorbidities and MERS mortality in Saudi Arabia.

Methods: This is a retrospective descriptive study. We retrieved the data published by the World Health Organization (WHO) between January 2017 and November 2019, and analysed the association between comorbidities and mortality.

Results: We found 572 MERS-CoV cases reported by WHO in Saudi Arabia during the defined period. Of these, 387 (68%) had a history of chronic illness. The overall mortality rate was found to be 25%. Diabetes mellitus was the most prevalent comorbidity—the mortality rate in the diabetics was 32% as opposed to 12% in the non-diabetics (p-value <0.01). Hypertension was second, with a mortality rate of 35%, as opposed to 15% in the non-hypertensive patients (p-value <0.001). The mortality rate in cases with cardiovascular disease was 39% as opposed to 21% in those without cardiovascular disease (p-value <0.05).

* Corresponding address: Joint Program of Postgraduate Studies of Family Medicine, 27781, Jeddah, 21941, KSA.
E-mail: tech_m_hilal@hotmail.com (M.H. Alotaibi)

Peer review under responsibility of Taibah University.

Production and hosting by Elsevier

 https://doi.org/10.1016/j.jtumed.2021.02.003

Conclusion: Our study shows that MERS-CoV had a significant case fatality rate in patients with comorbidities. Thus, it will be beneficial if future clinical trials for MERS-CoV examine the impact of improved societal infection control measures such as social distancing and masks, in the context of the coronavirus disease 2019 pandemic, on the prevalence and incidence of MERS and its clinical outcomes.

Keywords: Comorbidities; KSA; Middle East respiratory syndrome; Mortality; Risk factors

Introduction

Public health concerns have been growing with the emergence of infectious diseases.[1] At the end of December 2019, a new human coronavirus disease called coronavirus disease of 2019 (COVID-19) emerged in Wuhan, China. Shortly after, the World Health Organization (WHO) declared it a pandemic with over 9.6 million confirmed cases and over 490,000 deaths worldwide (as of 27 June 2020).[2] During such outbreaks, reliable data collection and analysis is of utmost importance and aids the public health response to contain the spread.[3]

One example of an emerging infectious disease seen in the past 10 years is the Middle East respiratory syndrome (MERS).[4] Just like COVID-19, MERS is caused by a beta-coronavirus (MERS-CoV) and has varying presentations—from being asymptomatic to life-threatening conditions such as acute respiratory distress syndrome and organ failure.[4,5] It has also been associated with more nosocomial transmission compared with COVID-19 that has spread widely due to community-based transmission.[6] Although associated with zoonosis, mainly in dromedary camels,[7] MERS has also spread through human-to-human transmission.[8] Given the high mortality rate and difficulty in differentiating MERS from other life-threatening respiratory tract infections, its emergence in late 2012 caused major concern worldwide.[9]

The first case identified as MERS involved a 60-year-old man in KSA in 2012, who eventually died due to respiratory and renal failure.[10] As of January 2020, there were 2,519 confirmed cases and 866 deaths across 27 countries.[11] Most of these cases were seen in KSA (2,121).[11] However, there were other outbreaks elsewhere such as in South Korea in 2015, with 185 cases and 36 deaths.[12] The case fatality rate has differed depending on the time and location of the outbreak, ranging between 28 and 63%.[13]

Since the initial identification of MERS seven years ago, few studies have addressed the comorbidities associated with mortality in MERS cases.[14] Therefore, we hypothesized that MERS has a higher mortality rate in elderly patients with comorbidities. In our study, we looked at the data published by WHO between January 2017 and November 2019, and analysed the associated comorbidities and their relationship with case fatality. As per our knowledge, this is the largest retrospective study focusing on the association between comorbidities and mortality in MERS patients conducted across KSA in the last five years and the most recent one prior to the COVID-19 pandemic.

Materials and Methods

This is a retrospective descriptive study of MERS patients, as reported by WHO, in KSA between January 2017 and November 2019 (n = 572).[15] Samples were collected from WHO because all MERS cases detected in KSA are registered by the Saudi Ministry of Health and then reported to WHO periodically. Collected data included age, sex, region in KSA, year of diagnosis, history of chronic illness, history of contact with camels, history of camel milk consumption, history of contact with known MERS cases, healthcare workers, and mortality outcome.

The data was entered into a Microsoft Excel file after being transferred from coding sheets. Openepi was used, in conjunction with SPSS version 21, to calculate the P-value, odds ratio, and confidence interval.[16] Frequencies and percentages were used to represent qualitative variables after being categorized. The chi-square test, odds ratio, and 95% confidence interval were used to compare categorical variables. A P-value <0.05 was considered significant. Approval for the use of the data was obtained directly from WHO.

Due to unavailability of data on specific comorbidities from January 2017 to October 2018, we could only analyse that from November 2018 to November 2019—203 cases. No cases were excluded from the study in both of the mentioned periods.

Results

From January 2017 to November 2019, 572 MERS-CoV cases were reported by WHO in KSA—437 (76%) male patients and 135 (24%) female patients. Ages ranged between 10 and 94 with a mean of 52.5 ± 17.27 years. A majority of these patients were in the 41—60 age group (39%), followed closely by those in the >60 age group (34%). The number of patients in the <20 age group was the lowest, accounting for only 2% of the total cases. Regional incidences showed that close to half of the reported cases were detected in Riyadh—273 (47.7%)—followed by 58 (10%) in the Eastern province (Table A).

Annual distribution revealed 250 cases in 2017, which accounts for 44% of the total, 132 (23%) in 2018, and 190 (33%) in 2019. From the total, 387 (68%) had a history of chronic illness, 171 (30%) had had direct contact with camels, 122 (21%) had consumed camel milk, 202 (35%) had reported contact with known MERS-CoV cases, and 69 (12%) were healthcare workers diagnosed with MERS. The overall mortality rate in this time frame was found to be 25%, while the case fatality rate in 2017, 2018, and 2019 was 24%, 30%, and 24% respectively (Table B) (Figure A).

The 21—40 age group had the lowest mortality rate (11%) compared with its survivor rate (P-value <0.001). Only three from those in the <20 age group succumbed to MERS-CoV

(23%). The 41–60 age group had a mortality rate of 18% as opposed to a survivor rate of 82% (P-value <0.01), while the >60 age group had the highest case fatality rate—43% (P-value <0.001). Case fatality rate in the male patients was 28% (P-value<0.01) and in the female patients 16% (P-value<0.01) (Table C).

From November 2018 to November 2019, 203 cases were analysed to investigate the association between comorbidities and mortality. An examination of the associated comorbidities revealed that diabetes mellitus (DM) was the most prevalent, found in 44% of the cases—the mortality rate in the diabetics was 32% as opposed to 12% in the non-diabetics (P-value <0.01). Hypertension (HTN) was found to be the second-most prevalent comorbidity, detected in 39% of the cases—the mortality rate in the hypertensive patients was 35% as opposed to 15% in their non-hypertensive counterparts (P-value <0.001). A history of cardiovascular disease (CVD), which included ischemic heart disease and congestive heart failure, was reported in 14% of the MERS-CoV cases with a mortality rate of 39% as opposed to 21% in those with no history of CVD (P-value <0.05).

The other comorbidities considered were chronic renal failure, found in 20 patients (10% of the cases with a mortality rate of 45%); bronchial asthma, found in 11 patients (27% mortality rate); hypothyroidism, found in seven patients (29% mortality rate); chronic lung disease, found in two patients (100% mortality rate); leukaemia and lymphoma, found in three patients (67% mortality rate); and cerebrovascular accidents, observed in two patients (100% mortality rate). The comorbidities that had zero mortality in their groupings were malignancy, chronic liver disease, and epilepsy—however, there was only one case of each of these (Table D).

Discussion

This study revealed that out of the 572 reported MERS-CoV cases in KSA, a history of comorbidities was found in 387 (68%), with an increase in the mortality rate across most comorbidities. As per our knowledge, ours is the largest study on comorbidities and mortality in MERS patients conducted across KSA in the last five years since Banik's research, which comprised 1,060 patients, from May 2013 to October 2015.[17] The most recently published study conducted in KSA - between April 2014 and March 2018- examining comorbidities and mortality in 314 MERS-CoV patients was done by Alfaraj et al. in 2019; it was confined to the central region of KSA.[14]

These findings confirm what was previously reported in other studies in KSA[18–20]—this includes noting a higher prevalence of DM in MERS-CoV cases.[18] This is likely a reflection of the increasing incidence of DM in the Saudi population, as it was found in 2016 that 32.8% of Saudis over the age of 30 had the ailment, and this number was expected to increase in the coming years.[21]

Assiri et al. had reported in 2013 that the MERS-CoV case fatality rate in KSA was 60%;[22] we, on the other hand, found the case fatality rate to be 25% between 2017 and 2019. Overall mortality in patients with comorbidities was higher in the study by Assiri et al. compared with that in ours—as per their analysis, 66% of the diabetics had fatal outcomes as opposed to the 32% in ours.[22] Other comorbidities followed a similar trend—for example, the case fatality rate of HTN was reported to be 81% in 2013,[22] while we found it to be 35% in the period 2017–19.

The study by Alfaraj et al., published in 2019, has reported one of the lower case fatality rates in KSA—24.8%; this is similar to ours.[14] However, as mentioned above, their April 2014–March 2018 study was confined to the country's central province—they noted that mortality increased with age, which is similar to our finding of highest mortality in the >60 age group (43%)—advancing age usually brings more comorbidities,[14,23] which has been reported in other studies on increased mortality.[24]

A meta-analysis by Badawi and Ryoo, where the majority of patients were from KSA, found that DM and HTN equally prevalent in close to 50% of the MERS-CoV cases they studied.[25] This too is close to our finding for DM (44%), though is higher than our finding for HTN (39%), as their mean age was close to ours (52 ± 3) as well. Their meta-analysis also reported finding comorbid CVD in 31% of the MERS-CoV cases analysed,[25] which is double of our finding for the same (14%). A higher incidence of MERS-CoV complications was noted in those with comorbid conditions, which our findings confirm as well.[25]

The reported mortality rate varied depending on the time and location of the outbreak, and ranged from 10% to 69.2%.[26] Our study shows a mortality rate closer to the lower end of the spectrum (25%) in Saudi MERS patients and is relatively close to the findings of Alfaraj et al. (24.8%)[14] and Alraddadi et al. (28%).[27]

Furthermore, our finding regarding gender discrepancy in mortality—the male patients having higher mortality than the female patients—agrees with what was reported by Banik et al., as 74.6% of their mortality sample was male because men were found to have more comorbidities than women.[17] Alghamdi et al. too reported that mortality was higher in men (52%) compared with women (23%).[20]

Currently, several studies are examining the relationship between COVID-19 and the presence of comorbidities. A recent meta-analysis of COVID-19 reported aggravation of the disease in patients with comorbidities, especially those with DM, HTN, and CVD,[28] similar to what has been described in our study for MERS-CoV.

Strengths and limitations

As per our knowledge, this is the largest retrospective study on the association between comorbidities and mortality in MERS patients conducted across KSA in the last five years. Because of its type, the study is highly dependent on accurate case reporting by KSA to WHO as there may well be many more MERS-CoV cases that have not been reported or diagnosed properly. It would have been beneficial to our study if specific comorbidities had been reported since the start of data collection in January 2017—in the absence of this data, we were forced to confine our analysis of the association between comorbidities and mortality to the period between November 2018 and November 2019.

Conclusion

Our retrospective study reveals that MERS-CoV had a significant case fatality rate in patients with comorbidities, which confirms what has been described in related literature. It also found an increase in mortality rate with advancing age and in the male patients.

Recommendations

We believe that with the emergence of COVID-19, it will be beneficial to study MERS-CoV again to examine the impact of improved societal infection control measures such as social distancing and wearing of masks on the prevalence and incidence of MERS and its clinical outcomes. As this study shows, as of November 2019, MERS is still present and prevalent in KSA; therefore, further studies are needed to assess its progression with better community awareness in regard to the currently applied infection control measures, especially for patients with comorbidities. Furthermore, taking strict precautionary measures for the high-risk population with comorbidities may aid governments and health organizations significantly in reducing the number of comorbidities as well as mortality in regard to diseases caused by coronaviruses, such as MERS, COVID-19, or any other that may emerge in the future.

Source of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors have no conflict of interest to declare.

Ethical approval

The study [344336] was approved by the World Health Organization on June 29, 2020.

Authors' contributions

MHA and SAB conceived and designed the study, conducted research, and reviewed the literature. MHA collected, analysed, and interpreted the data. SAB wrote the initial and final drafts of the manuscript. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

Acknowledgment

We would like to thank the World Health Organization for authorizing our request to publish their material and data in this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jtumed.2021.02.003.

References

1. Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, et al. Global trends in emerging infectious diseases. **Nature 2008**; 451(7181): 990–993.
2. *Coronavirus disease (COVID-19) situation report-159*. World Health Organization; 2020 [cited 27th June, 2020]. Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200627-covid-19-sitrep-159.pdf?sfvrsn=93e027f6_2.
3. Morens DM, Folkers GK, Fauci AS. The challenge of emerging and re-emerging infectious diseases. **Nature 2004**; 430(6996): 242–249.
4. Al-Tawfiq J, Memish Z. Drivers of MERS-CoV transmission: what do we know? **Expet Rev Respir Med 2016**; 10(3): 331–338.
5. Arabi YM, Arifi AA, Balkhy HH, Najm H, Aldawood AS, Ghabashi A, et al. Clinical course and outcomes of critically ill patients with Middle East respiratory syndrome coronavirus infection. **Ann Intern Med 2014**; 160(6): 389–397.
6. Munster VJ, Koopmans M, van Doremalen N, van Riel D, de Wit E. A novel coronavirus emerging in China - key questions for impact assessment. **N Engl J Med 2020**; 382(8): 692–694.
7. Memish ZA, Cotten M, Meyer B, Watson SJ, Alsahafi AJ, Al Rabeeah AA, et al. Human infection with MERS coronavirus after exposure to infected camels, Saudi Arabia, 2013. **Emerg Infect Dis 2014**; 20(6): 1012–1015.
8. Al-Tawfiq JA, Assiri A, Memish ZA. Middle East respiratory syndrome novel corona MERS-CoV infection. Epidemiology and outcome update. **Saudi Med J 2013**; 34(10): 991–994.
9. Garbati MA, Fagbo SF, Fang VJ, Skakni L, Joseph M, Wani TA, et al. A comparative study of clinical presentation and risk factors for adverse outcome in patients hospitalised with acute respiratory disease due to MERS coronavirus or other causes. **PloS One 2016**; 11(11):e0165978.
10. Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus AD, Fouchier RA. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. **N Engl J Med 2012**; 367(19): 1814–1820.
11. *MERS situation update*. World Health Organization; January 2020. 2020 [cited 14 June 2020]. Available from: http://www.emro.who.int/pandemic-epidemic-diseases/mers-cov/mers-situation-update-january-2020.html.
12. World Health Organization. *Middle East respiratory syndrome coronavirus (MERS-CoV) – Republic of Korea*; 2020 [cited 26 September 2020]. Available from: https://www.who.int/csr/don/14-july-2015-mers-korea/en/.
13. Nam HS, Park JW, Ki M, Yeon MY, Kim J, Kim SW. High fatality rates and associated factors in two hospital outbreaks of MERS in Daejeon, the Republic of Korea. **Int J Infect Dis 2017**; 58: 37–42.
14. Alfaraj SH, Al-Tawfiq JA, Assiri AY, Alzahrani NA, Alanazi AA, Memish ZA. Clinical predictors of mortality of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection: a cohort study. **Trav Med Infect Dis 2019**; 29: 48–50.
15. *MERS-CoV*. World Health Organization; 2020 [cited 15 June 2020]. Available from: https://www.who.int/csr/don/archive/disease/coronavirus_infections/en/.
16. *OpenEpi menu*. Openepi.com; 2020 [cited 26 September 2020]. Available from: http://www.openepi.com/Menu/OE_Menu.htm.
17. Banik GR, Alqahtani AS, Booy R, Rashid H. Risk factors for severity and mortality in patients with MERS-CoV: analysis of publicly available data from Saudi Arabia. **Virol Sin 2016**; 31(1): 81–84.
18. Alsahafi AJ, Cheng AC. The epidemiology of Middle East respiratory syndrome coronavirus in the Kingdom of Saudi Arabia, 2012-2015. **Int J Infect Dis 2016**; 45: 1–4.

19. Memish ZA, Zumla AI, Al-Hakeem RF, Al-Rabeeah AA, Stephens GM. Family cluster of Middle East respiratory syndrome coronavirus infections. **N Engl J Med 2013**; 368(26): 2487–2494.
20. Alghamdi IG, Hussain II , Almalki SS, Alghamdi MS, Alghamdi MM, El-Sheemy MA. The pattern of Middle East respiratory syndrome coronavirus in Saudi Arabia: a descriptive epidemiological analysis of data from the Saudi Ministry of Health. **Int J Gen Med 2014**; 7: 417–423.
21. Meo SA. Prevalence and future prediction of type 2 diabetes mellitus in the Kingdom of Saudi Arabia: a systematic review of published studies. **J Pakistan Med Assoc 2016**; 66(6): 722–725.
22. Assiri A, Al-Tawfiq JA, Al-Rabeeah AA, Al-Rabiah FA, Al-Hajjar S, Al-Barrak A, et al. Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study. **Lancet Infect Dis 2013**; 13(9): 752–761.
23. Saquib N, Saquib J, Alhadlag A, Albakour MA, Aljumah B, Sughayyir M, et al. Chronic disease prevalence among elderly Saudi men. **Int J Health Sci 2017**; 11(5): 11–16.
24. Saad M, Omrani AS, Baig K, Bahloul A, Elzein F, Matin MA, et al. Clinical aspects and outcomes of 70 patients with Middle East respiratory syndrome coronavirus infection: a single-center experience in Saudi Arabia. **Int J Infect Dis 2014**; 29: 301–306.
25. Badawi A, Ryoo SG. Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): a systematic review and meta-analysis. **Int J Infect Dis 2016**; 49: 129–133.
26. Park JE, Jung S, Kim A. MERS transmission and risk factors: a systematic review. **BMC Publ Health 2018**; 18(1): 574.
27. Alraddadi B, Bawareth N, Omar H, Alsalmi H, Alshukairi A, Qushmaq I, et al. Patient characteristics infected with Middle East respiratory syndrome coronavirus infection in a tertiary hospital. **Ann Thorac Med 2016**; 11(2): 128–131.
28. Wang B, Li R, Lu Z, Huang Y. Does comorbidity increase the risk of patients with COVID-19: evidence from meta-analysis. **Aging (N Y) 2020**; 12(7): 6049–6057.

How to cite this article: Alotaibi MH, Bahammam SA. Determining the correlation between comorbidities and MERS-CoV mortality in Saudi Arabia. J Taibah Univ Med Sc 2021;16(4):591–595.