



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Fabrizio Bruschi
 Department of Translational Research on New Technologies
 in Medicine and Surgery, University of Pisa, Italy

Valentina Giuffra
 Division of Paleopathology, Department of Translational
 Research on New Technologies in Medicine and Surgery,
 University of Pisa, Italy

*Corresponding author. Department of Translational
 Research on New Technologies in Medicine and Surgery, Via
 Roma 57, 56126 Pisa, Italy. Fax: +39 050 992706.
 E-mail address: gaeta-raffaele@libero.it (R. Gaeta)

Accepted 2 February 2017

<http://dx.doi.org/10.1016/j.jinf.2017.02.002>

© 2017 The British Infection Association. Published by Elsevier Ltd.
 All rights reserved.

**The impact of co-infection of influenza A
 virus on the severity of Middle East
 Respiratory Syndrome Coronavirus**



KEYWORDS

Middle East Respiratory
 Syndrome Coronavirus;
 MERS-CoV;
 Influenza;
 Co-infection

Ho and colleagues recently drew attention to the consequences of co-infection with Influenza and HIV.¹ We present four cases of combined infection with influenza and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection. Nasopharyngeal swabs or tracheal aspirates were tested for MERS-CoV using real-time reverse-transcription polymerase chain reaction (RT-PCR).^{2,3} Samples were tested for Influenza A, B and H1N1 by rapid molecular test (GenEXper for detection of flu A, B and 2009 H1N1, Cepheid).

Case 1

In the first case, a 39 year-old male, health care worker, an engineer who became ill seven days before admission. He had fever >38 °C, cough and sore throat. He had no nausea, vomiting, diarrhoea or shortness of breath (SOB). He denied history of travel or contact with positive case or camels. He was febrile with a temperature of 39.5 °C. Chest X-ray showed non-homogenous opacity at the lower right lung zone. A nasopharyngeal swab was positive for MERS-CoV with Ct value *upE* gene 34, and ORF1A 34 (Table 1). The test was negative for influenza but a repeat swab after 48 h was negative for MERS-CoV and positive for H1N1. The patient

Table 1 A summary of the four cases of co-infection of MERS-CoV and influenza.

#	Age	Gender	Symptoms	Comorbidity	Sample type	Viral load CT value (<i>upE</i> gene)	Co-infection	CXR	Intensive care	Outcome	Days ill before hospitalisation	Oxygen requirement
1	39	Male	Fever, cough, sore throat	None	NPS	34	H1N1	Non-homogenous opacity in lower right lung zone.	No	Discharged home	7	Nil
2	61	Female	Productive cough, SOB	DM, hypothyroidism	NPS	35	H1N1	Patchy opacities involving middle and lower zones of both lung fields	Yes	Discharged home	3	Ventilator for 13 days
3	29	Female	Fever, cough	None	NPS	32	H1N1	Normal	No	Discharged home	2	Nil
4	73	Female	SOB, productive cough	CHF, hypothyroidism	NPS	36	Influenza A	Bilateral diffuse infiltrate	No	Discharged home	4	Nasal cannula

NPS = nasopharyngeal swab; DM = diabetes mellitus; SOB = shortness of breath; CHF = congestive heart failure.

received azithromycin, ceftriaxone and oseltamivir. The patient was discharged home after two negative swabs of MERS-CoV and being asymptomatic for 48 h.

Case 2

In the second case, a 61 year-old female with diabetes mellitus and dyslipidemia was admitted with a three-day history of shortness of breath and productive cough. She had no nausea, vomiting, or diarrhoea. She denied history of travel or contact with positive case or camels. She was afebrile with a temperature of 37 °C. Chest X-ray showed patchy opacities involving middle and lower zones of both lung fields.

A nasopharyngeal swab was positive for MERS-CoV with Ct value *upE* gene 34, ORF1A 35 and negative for influenza. A repeat swab after 48 h was negative for MERS-CoV but positive for H1N1. She required BIPAP and she was subsequently intubated and was started on mechanical ventilation. She was extubated after 13 days. The patient received piperacillin–tazobactam, and erythromycin. The patient was discharged home after she had 2 negative swabs of MERS-CoV and being asymptomatic for 48 h.

Case 3

In the third case, a 29 year-old housekeeper female was admitted with two days history of fever and cough. She had no nausea, vomiting, diarrhoea nor shortness of breathing. She had a history of contact with MERS-CoV positive case. She was afebrile with a temperature of 36.9 °C. Chest X-ray was normal. A nasopharyngeal swab collected upon presentation was positive for MERS-CoV with CT value *upE* gene 32 ORF1A 32. The swab was negative for influenza. A repeated swab after 48 h was positive MERS-CoV and positive for H1N1. The patient received oseltamivir, azithromycin and ceftriaxone. The patient was discharged home after she had 2 negative swab of MERS-CoV and being asymptomatic for 48 h.

Case 4

In the fourth case, the patient was a 73 year-old female with a history of hypothyroidism, heart failure, lymphoma, and lung fibrosis. She has no history of travel or contact with positive case or camels. Four days prior to her presentation, she had productive cough and shortness of breath. She had no fever, diarrhoea, vomiting or nausea. She was afebrile with a temperature of 36.7 °C. Chest X-ray showed bilateral diffuse infiltrate (Fig. 1). A nasopharyngeal swab was positive for MERS-CoV with Ct value *upE* gene 37; ORF1A 36 and negative for Influenza. A repeat swab after 3 days was negative for MERS-CoV but positive for influenza A. The patient was treated with piperacillin–tazobactam for six days and oseltamivir for 5 days. The patient was discharged home after two negative MERS-CoV and being asymptomatic for 48 h.

These patients highlight the co-infection with MERS-CoV and influenza. The exact reason to have a negative influenza test at the time of positive MERS-CoV is not completely understood. It is possible that the presence of MERS-CoV inhibits the PCR reaction for influenza virus. However, an



Figure 1 A chest radiograph showing bilateral diffuse opacities.

earlier case of MERS-CoV tested initially positive for influenza A(H1N1)pdm09.⁴ On the other hand, the positivity of nasal swabs for influenza is specimen type and technique dependent.⁵ Thus, initially negative influenza tests could be a false test result. Positive results for viral respiratory pathogens should not preclude testing for MERS-CoV because co-infection can occur.⁶ Only a small number of MERS cases had co-infection with influenza A, parainfluenza, herpes simplex, and *Streptococcus pneumoniae*.⁷ In one case, a co-infection with Herpes simplex virus type 1 DNA13 and rhinovirus RNA14 were detected by RT-PCR.⁸ The investigation of the first 47 cases showed no co-infection with MERS-CoV.² There is a controversy regarding the risk of increased or decreased severity of co-infections. For example co-infections with Respiratory Syncytial Virus (RSV) and human meta-pneumovirus (hMPV) causes more severe infection than either virus alone with longer hospitalization and oxygen requirement.⁹ Other studies did not demonstrate these effects.¹⁰ The association and the impact of co-infection with MERS-CoV and influenza viruses deserve further evaluation and studies.

Conflicts of interest

All authors have no conflict of interest to report.

References

1. Ho A, Aston SJ, Mitchell T, Alaerts M, Menyere M, Mallewa J, et al. The impact of HIV on the burden and severity of influenza illness in Malawian adults: the bash-flu study. *J Infect* 2015;71: 687–8. <http://dx.doi.org/10.1016/j.jinf.2015.09.030>.
2. 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;13:752–61. [http://dx.doi.org/10.1016/S1473-3099\(13\)70204-4](http://dx.doi.org/10.1016/S1473-3099(13)70204-4).

3. Corman VM, Müller MA, Costabel U, Timm J, Binger T, Meyer B, et al. Assays for laboratory confirmation of novel human coronavirus (hCoV-EMC) infections. *Euro Surveill* 2012;**17**:49.
4. Health Protection Agency (HPA) UK Novel Coronavirus Investigation team. Evidence of person-to-person transmission within a family cluster of novel coronavirus infections, United Kingdom, February 2013. *Euro Surveill* 2013;**18**:20427.
5. Cunha BA, Dumont M, Abruzzo E. An adult returned traveler from Dubai hospitalized with an influenza-like illness (ILI): Middle East Respiratory Syndrome (MERS) or influenza? Infection control implications from a near MERS case. *Infect Control Hosp Epidemiol* 2015;**36**:858–60. <http://dx.doi.org/10.1017/ice.2015.91>.
6. Saudi Ministry of Health. *Case definition and surveillance guidance for MERS-CoV testing in Saudi*. 2014. <http://www.moh.gov.sa/en/Documents/MoHCaseDefinitionMERSCoVVersionMay132014.pdf> [Accessed 17 January 2017].
7. World Health Organization. *WHO guidelines for investigation of cases of human infection with Middle East Respiratory Syndrome Coronavirus (MERS-CoV)*. 2013. http://www.who.int/csr/disease/coronavirus_infections/MERS_CoV_investigation_guideline_Jul13.pdf [Accessed 17 January 2017].
8. Drosten C, Seilmaier M, Corman VM, Hartmann W, Scheible G, Sack S, et al. Clinical features and virological analysis of a case of Middle East respiratory syndrome coronavirus infection. *Lancet Infect Dis* 2013;**13**:745–51. [http://dx.doi.org/10.1016/S1473-3099\(13\)70154-3](http://dx.doi.org/10.1016/S1473-3099(13)70154-3).
9. König B, König W, Arnold R, Werchau H, Ihorst G, Forster J. Prospective study of human metapneumovirus infection in children less than 3 years of age. *J Clin Microbiol* 2004;**42**:4632–5. <http://dx.doi.org/10.1128/JCM.42.10.4632-4635.2004>.
10. Debiaggi M, Canducci F, Ceresola ER, Clementi M. The role of infections and coinfections with newly identified and emerging respiratory viruses in children. *Viral J* 2012;**9**:247. <http://dx.doi.org/10.1186/1743-422X-9-247>.

Sarah H. Alfaraj
Corona Center, Infectious Diseases Division, Department of Pediatric, Prince Mohamed Bin Abdulaziz Hospital, Ministry of Health, Riyadh, Saudi Arabia

Jaffar A. Al-Tawfiq
Johns Hopkins Aramco Healthcare, Dhahran, Saudi Arabia
Indiana University School of Medicine, Indianapolis, IN, USA

Nojoom A. Alzahrani
Corona Center Department, Prince Mohamed Bin Abdulaziz Hospital, Ministry of Health, Riyadh, Saudi Arabia

Talal A. Altwaijri
Department of Surgery, Prince Mohamed Bin Abdulaziz Hospital, Ministry of Health, Riyadh, Saudi Arabia

Ziad A. Memish*
School of Public Health, Emory University, Atlanta, GA, USA

Infectious Diseases Division, Department of Medicine, Prince Mohamed Bin Abdulaziz Hospital, Ministry of Health, Riyadh, Saudi Arabia

*Corresponding author.
E-mail address: zmemish@yahoo.com (Z.A. Memish)

Accepted 2 February 2017

<http://dx.doi.org/10.1016/j.jinf.2017.02.001>

© 2017 The British Infection Association. Published by Elsevier Ltd. All rights reserved.

Completeness of case ascertainment and availability of environmental data in Legionnaires' disease enhanced surveillance in England, 2012–2014



To the Editor,

Bai et al.¹ previously highlighted the importance of effective communicable disease surveillance in China for the detection of outbreaks to inform infectious disease prevention and control. To achieve similar aims with relation to the control of Legionnaires' disease in England a national enhanced surveillance scheme operates.

Surveillance data must be both complete and as timely as possible, as highlighted by Freeman et al. in this journal.² Therefore we sought to assess the completeness of case ascertainment in addition to the availability of environmental data reported to the national enhanced legionella surveillance scheme (NELSS) for residents in England. The value of environmental data is particularly important for Legionnaires' disease in order to inform the attribution of potential environmental sources of cases and clusters of this infection.

In England, the National Legionella Surveillance Team (NLST) leads on surveillance and control of Legionnaires' disease, while Field Epidemiology Services (FES) teams collect surveillance data and investigate sporadic cases, clusters and outbreaks in conjunction with local Health Protection Teams (HPTs). The NLST worked with the FES teams in the North West (NW) and West Midlands (WMids) regions of England to audit the reporting of Legionella cases with onset dates during each calendar year between 2012 and 2014, inclusive. Eligible cases were those cases of *Legionella* spp. infections resident in either of these regions in England, which were laboratory confirmed by urinary antigen testing, culture or serological testing. These cases were identified in the month of February following each calendar year by the NLST and were compared to those known by the FES teams for NW and WMids regions.

Completeness of case ascertainment was calculated as the proportion of cases recorded by FES teams for cases with onset of symptoms between 2012 and 2014 inclusive which were reported to the NLST. The availability of environmental data reported to the national enhanced surveillance scheme was calculated as the proportion of cases during the same time period with any environmental investigation data reported to the NLST.

The results are summarised in Table 1; in the NW region, a mean of 34 cases were reported per year between 2012 and 2014. In the WMids region, the mean number of cases per year was 46. Both regions reported 100% of cases to the NLST.

Mean availability of environmental data reported was 80.8% in the NW and 42.8% in WMids. However, there was a