



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.



Contents lists available at SciVerse ScienceDirect

## International Journal of Infectious Diseases

journal homepage: [www.elsevier.com/locate/ijid](http://www.elsevier.com/locate/ijid)Highlights from ProMED ([www.promedmail.org](http://www.promedmail.org))

## Latest outbreak news from ProMED-mail Novel coronavirus – Middle East<sup>☆</sup>

Marjorie P. Pollack<sup>a,\*</sup>, Craig Pringle<sup>b</sup>, Lawrence C. Madoff<sup>c</sup>, Ziad A. Memish<sup>d</sup><sup>a</sup> Deputy Editor, ProMED-mail, Epidemiology & Surveillance Moderator, ProMED-mail (Mod.MPP), Independent Consultant Medical Epidemiologist, New York City, New York, USA<sup>b</sup> ProMED-mail Viral Diseases Moderator (Mod.CP), Emeritus Professor Biological Sciences Department, University of Warwick, Formerly at the Medical Research Council Virology Unit, Glasgow, and the Animal International Committee on Taxonomy of Viruses, Coventry, England, United Kingdom<sup>c</sup> Editor, ProMED-mail, ISID (Mod.LM), Professor of Medicine, Division of Infectious Diseases and Immunology, University of Massachusetts Medical School, Worcester, Massachusetts, USA<sup>d</sup> Deputy Minister for Public Health, Director WHO Collaborating Center for Mass Gathering Medicine, Ministry of Health, Professor, College of Medicine, Alfaisal University, Riyadh 11176, Kingdom of Saudi Arabia

## ARTICLE INFO

## Article history:

Received 3 December 2012

Accepted 3 December 2012

On 20 September 2012, ProMED-mail posted a report on the identification of a novel coronavirus (nCoV) isolated from sputum from a fatal case of a severe respiratory illness (SARI) with renal failure in a 60 year old citizen of Saudi Arabia.<sup>1,2</sup>

The illness had occurred in June 2012. Three days later (23 September 2012) ProMED-mail posted on a second case of SARI also associated with renal failure in a 49 year old Qatari citizen in critical condition in a hospital in the United Kingdom (UK), having been transferred to the UK for intensive care. The second case had been tested for the nCoV after the clinicians in the UK read the ProMED-mail report on the first case.<sup>3</sup>

Comparison of sequencing of the 2 isolates was done revealing 99.5% match with one nucleotide mismatch over the regions compared.<sup>4–6</sup> The nCoV was identified as a new member of the beta group of CoVs, closely related to a bat CoV identified in 2008 in the Netherlands.<sup>7</sup> These two cases were not epidemiologically linked. Epidemiologic and laboratory investigations of known contacts of these two cases did not reveal secondary cases. (13 close contact healthcare workers in the UK gave a history of mild self-limiting respiratory symptoms 10 of whom were tested for the nCoV and were found to be negative).<sup>8</sup> The conclusion at that time was that the virus did not exhibit person to person transmission. Both cases had a history of exposure to animals in the period preceding the onset of their illnesses.

On 25 September 2012, an astute ProMED-mail subscriber, Dr. Irene Lai, requested information on a report of an undiagnosed

outbreak of SARI in an ICU in Zarga, Jordan in April 2012.<sup>9</sup> The outbreak involved 11 individuals including seven nurses, one doctor and a brother of one of the nurses, with one death in a nurse with “underlying medical conditions”. On 30 November 2012, WHO reported that testing of specimens from two of the cases in this cluster were positive for this nCoV – both of these cases had fatal outcomes, presumably one was the nurse mentioned in the reports in April 2012 and the other was the original patient admitted to the ICU with SARI.<sup>10</sup>

In response to the first two confirmed cases in late September 2012, a case definition for heightened surveillance was developed by WHO.<sup>11,12</sup> The WHO definition of a “Patient under investigation” included “a person with an acute respiratory infection AND suspicion of pulmonary parenchymal disease based on clinical or radiological evidence of consolidation AND travel to or residence in an area where infection with nCoV has recently been reported or where transmission could have occurred AND is not already explained by any other infection or aetiology”.<sup>12</sup>

On 4 November 2012, the Ministry of Health (MoH) of the Kingdom of Saudi Arabia (KSA) issued a press release and report for ProMED-mail announcing a new case of SARI associated with infection with the nCoV in a Saudi Arabian citizen, resident of Riyadh, with a history of visit to a farm one week preceding onset of his illness – the third confirmed case.<sup>13,14</sup>

On 21 November 2012 ProMED-mail posted a machine translation of a Saudi Arabian newswire containing a KSA MoH press release announcing a fourth case of SARI associated with infection with the nCoV.<sup>15</sup> Epidemiologic findings associated with the fourth case was not available at that time.

On 23 November 2012, WHO issued a report on the Global Outbreak Alert and Response (GAR) website detailing an additional four confirmed cases of SARI associated with infection with the nCoV. Of these four cases, three involved Saudi Arabian citizens (including two fatalities) and one Qatari citizen.<sup>16</sup> Of note was that the three newly confirmed cases in the KSA (including the two fatalities) were epidemiologically linked – family members living in the same household. An additional family member had similar symptoms, but his laboratory studies ultimately proved negative for infection with the nCoV.<sup>16,10</sup>

<sup>☆</sup> ProMED-mail is a program of the (International Society for Infectious Diseases) <http://www.isid.org>, Novel coronavirus – Middle East.

\* Corresponding author.

E-mail address: [pollack@promedmail.org](mailto:pollack@promedmail.org) (M.P. Pollack).

**Table 1**

Cases of novel Corona virus infection reported as of 2 Dec 2012

Case number	Month of onset	Outcome	Location of onset	Clinical features	Notes
1	April 2012	fatal	Jordan*	Renal failure	
2	April 2012	fatal	Jordan	Unknown	Nurse, linked to case 1, suggests H2H
3	June 2012	fatal	Saudi Arabia	Renal failure	First reported case: Animal contact
4	Sept 2012		Qatar**	Renal failure	UK hosp
5	Nov 2012		Saudi Arabia	Transient renal failure	Animal contact
6	Nov 2012	fatal	Saudi Arabia	Renal failure	Linked case 8 and case 9
7	Nov 2012		Qatar	Unknown	Germany hosp
8	Nov 2012		Saudi Arabia	No renal failure	Linked case 6 and case 9
9	Nov 2012	fatal	Saudi Arabia	Renal failure	Linked (family member) case 8 and case 6

\* An additional 9 cases of respiratory illness in this cluster – at present unknown how many had specimens tested for nCoV.

\*\* 13 health care workers with mild respiratory symptoms; 10 tested and were negative for nCoV.

In summary, as of 30 November 2012, there have been nine confirmed cases of SARI associated with infection with the nCoV of which five were fatal (a case fatality rate of 56%). Of the nine confirmed cases, five were in Saudi Arabian citizens, two in Qatari citizens and two in Jordanian citizens (Table 1). The nine confirmed cases involve two identified clusters – one among family members sharing the same household in Saudi Arabia and the other involving healthcare workers in an ICU where a case of SARI had been treated.

The virus has been identified by nucleotide sequencing to be a close genetic relative of a bat coronavirus. Sequencing of a fraction of the E gene and the ORF 1B gene, amplified by PCR using published primers,<sup>17</sup> produced identical reads for the first Saudi Arabian case and for the Qatari patient (hospitalised in the UK). These sequences could be aligned with published sequences of a human beta coronavirus.<sup>18</sup>

A phylogenetic analysis of available complete coronavirus genomes showed that Qatar and Saudi Arabian isolates are closely related and that these viruses form a distinct clade that is related to HKU4 and HKU5, two bat coronaviruses isolated from bats in Hong Kong. Further analyses indicated that their closest relative was another bat coronavirus isolated in Hong Kong and sequenced in the Netherlands in 2008.

At present, there are more questions than answers about this nCoV. In describing an outbreak epidemiologically one usually begins with a description of “PPT” – person, place and time.

The persons thus far have included predominantly males living in Eastern Mediterranean countries (Saudi Arabia, Qatar and Jordan), have included isolated cases and have included family members and healthcare personnel treating cases.

But, have other SARI clinical cases that have not had etiologies determined elsewhere in the world been tested for the nCoV?

Is this virus just limited to exposure in these Eastern Mediterranean countries?

And while the cases in KSA and Qatar have occurred in males, the outbreak in Jordan involved female nurses. The first apparent outbreak occurred in late April 2012 in Jordan. Is there a travel history known for the index case in that outbreak?

What are the “PPT” details of the index case? Apparently five of the nine confirmed cases had a history of exposure to animals preceding the onset of illness. What were the animals?

Have there been studies of the animals to see if any of the animals have/had evidence of infection with this nCoV?

Have there been studies of bats in the areas of possible exposure of these cases to identify the prevalence of the nCoV infection in these bats?

As for the current laboratory testing for confirmation of cases there are questions. During the SARS outbreak in 2003, there were

a significant proportion of cases that were negative for infection with the SARS CoV by PCR testing. Does the absence of confirmation of nCoV infection in healthcare personnel with mild respiratory symptoms caring for the Qatari national treated in the UK definitively rule out the possibility of a milder form of clinical disease associated with this virus? And the individuals with more severe illness in Jordan that recovered, were they confirmed as having had nCoV infection? Some answers may be revealed by the development of specific serologic assays for nCoV infection.

It is clearly very early in our body of knowledge on the behavior of this nCoV. Information on the epidemiology of this organism including the host/reservoir, the geographic distribution and the clinical spectrum of disease is presently being identified – a sample of nine confirmed cases is too small to feel confident that we fully understand this novel virus.

## References

1. ProMED-mail, Novel coronavirus - Saudi Arabia: human isolate 2012; 20 Sep.
2. 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**:1814–20.
3. ProMED-mail, Novel coronavirus - Saudi Arabia (02): additional cases, RFI 2012; 23 Sep.
4. ProMED-mail, Novel coronavirus - Saudi Arabia (03): UK HPA, WHO, Qatar 2012; 23 Sep 2012.
5. ProMED-mail, Novel coronavirus - Saudi Arabia (05): WHO, case def., nomenclature 2012; 26 Sep.
6. Bermingham A, Chand M, Brown C, Aarons E, Tong C, Langrish C, et al. Severe respiratory illness caused by a novel coronavirus, in a patient transferred to the United Kingdom from the Middle East, September 2012. *Euro Surveill* 2012;**17**(40). doi:pii: 20290.
7. ProMED-mail, Novel coronavirus - Saudi Arabia (16): whole genome sequence 2012; 14 Nov.
8. ProMED-mail, Novel coronavirus - Saudi Arabia (11): clin. lab. & epi. investigations 2012; 4 Oct.
9. ProMED-mail, Novel coronavirus - Saudi Arabia (04):: RFI, Jordan, April 2012 2012; 25 Sep.
10. ProMED-mail, Novel coronavirus - Eastern Mediterranean: WHO, Jordan, conf., RFI 2012; 30 Nov 2012.
11. ProMED-mail, Novel coronavirus - Saudi Arabia (05): WHO, case def., nomenclature 2012; 26 Sep.
12. ProMED-mail, Novel coronavirus - Saudi Arabia (10): WHO, revised case def. 2012; 30 Sep.
13. Al Barrak AM, Stephens GM, Hewson R, Memish ZA. Recovery from severe novel coronavirus infection. *Saudi Med J* 2012;**33**:1265–9.
14. ProMED-mail, Novel coronavirus - Saudi Arabia (15): new case 2012; 4 Nov.
15. ProMED-mail, Novel coronavirus - Saudi Arabia (17): 4th case, RFI 2012; 21 Nov.
16. ProMED-mail, Novel coronavirus - Saudi Arabia (18): WHO, new cases, cluster 2012; 23 Nov 2012.
17. Corman VM, Eckerle I, Bleicker T, Zaki A, Landt O, Eschbach-Bludau M, et al. Detection of a novel human coronavirus by real-time reverse-transcription polymerase chain reaction. *Euro Surveill* 2012;**17**. pii: 20285.
18. Human betacoronavirus 2c EMC/2012, complete genome. GenBank: JX869059.2 Available from URL: <http://www.ncbi.nlm.nih.gov/nucore/JX869059>.