value of this comparison would be >0.05. However, just by looking at the P value one cannot state that ribavirin was not effective in the treatment of CCHF. The lack of the statistical significance could be related to small sample size. Therefore, before making such a statement, a sufficient sample size must be achieved. Obviously, we prefer to stay on the safer side when treating our patients. Accordingly, the comment of Hayran and Aşçıoğlu regarding the lack of statistical inference in this example is not relevant in clinical practice, particularly for the example of CCHF; rather, it might mislead practitioners.

The positions of World Health Organization and the European Center for Disease Control and Prevention are clear regarding the beneficial use of ribavirin, and it would be unethical to perform a placebo-controlled, randomized study [4]. Moreover, recent studies have supported the beneficial use of ribavirin, particularly during the early phase of the disease [5]. Besides the small sample size, potential confounders and biases should be controlled precisely in studies on CCHF; these factors have been described in detail elsewhere [4].

In conclusion, ribavirin was found to be effective in vitro and to be beneficial in clinical studies, although the statistical significance of this benefit has not yet been reached [6]. As we stressed in our manuscript 5 years ago, additional studies are necessary.

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Önder Ergönül,1 Aysel Çelikbaş,2 Başak Dokuzoğlu,2 Şehnem Eren,2 Nurcan Baykam,2 and Harika Esener2
1Marmara University, School of Medicine, Infectious Diseases and Clinical Microbiology Department, Altunizade, Istanbul, and 2Ankara Numune Education and Research Hospital, Infectious Diseases and Clinical Microbiology Clinic, Ankara, Turkey

References


Subclinical Infection with the Novel Influenza A (H1N1) Virus

To the Editor—On 15 May 2009, an 18-year-old woman was admitted to the Beijing Ditan Hospital because of fever, headache, dyspnea, and a sore throat. The patient is an undergraduate student in the United States, and she arrived in Beijing on 11 May. Two days before admission, the patient developed fever, with temperatures ≤39.4°C. At admission, the temperature was 37.7°C, the blood pressure 110/65 mm Hg, and the pulse 86 beats/minute. A nasopharyngeal swab specimen from the patient was obtained, and real-time reverse-transcriptase polymerase chain reaction (RT-PCR) assay confirmed the infection of novel influenza A (H1N1) virus.

On the basis of the local strategy for prevention and control of H1N1 virus infection, the mother of the patient, who had accompanied the patient since her arrival, was quarantined for medical observation. On 17 May, the nasopharyngeal swab specimen from the mother produced positive results for H1N1 by RT-PCR assay. But examination of the mother revealed a temperature of 36.6°C, a blood pressure of 127/80 mm Hg, and a pulse of 72 beats/minute. Moreover, no respiratory symptoms were observed in the mother during the subsequent 1-week medical observation.

Two strains of H1N1 viruses, A/Beijing/01/2009 and A/Beijing/02/2009, were isolated from specimens obtained from the patient and her mother, respectively. Whole-genome sequencing of the 2 isolates revealed that the genomes of the 2 viruses are exactly identical in all segments (GenBank accessions, GQ183617–GQ183632). The result corroborated the epidemiologic evidence that the virus was directly transmitted from the patient to her mother. Furthermore, it’s particularly intriguing that the same virus induced severe respiratory symptoms in the patient but caused only inapparent infection in the mother.

More than 70,000 cases of H1N1 virus infection have been confirmed worldwide to date, but very few cases of subclinical infection have been reported. However, a recent statistical study estimated that 23,000 individuals had been infected by the H1N1 virus in Mexico by late April, which doubles the number of cases publicly reported, implying a >50% rate of mild or subclinical infection in the 2009 H1N1 pandemic [1]. The prolonged unawareness of the large proportion of asymptomatic infection is not surprising, because clinical evidence for asymptomatic infection is extremely scarce, and medical resources and surveillance always focus on severe cases in the initial stage of a pandemic. Nevertheless, this unawareness could be detrimental to global disease control. On the one hand, it hampers the reliable assessment, based on public statistics, of the transmissibility of the H1N1 virus and the severity of the pandemic, as exemplified by Fraser et al [1]. On the other hand, the effectiveness of nonphar-
maceutical interventions, such as health screening and case patient isolation, is severely diminished when a substantial proportion of transmission occurs via asymptomatic infection [2]. Indeed, although little is known about the effect of transmission through subclinical infection during pandemics, a simulation study suggests that asymptomatic infection plays an important role in a disease outbreak [3]. Therefore, further studies focused on subclinical infection are required for better understanding and control of the 2009 H1N1 pandemic.

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Jian Yang,1,a Fan Yang,1,a Fang Huang,2,a Jianwei Wang,1 and Qi Jin1
1State Key Laboratory for Molecular Virology and Genetic Engineering, Institute of Pathogen Biology, Chinese Academy of Medical Sciences, and 2Beijing Centers for Disease Control and Prevention, Beijing, China

References


a J.Y., F.Y., and F.H. contributed equally to this letter.

Reprints or correspondence: Dr Qi Jin, State Key Laboratory for Molecular Virology and Genetic Engineering, 8 Rongjing Eastern Street, BDA, Beijing 100176, China (zdsys@sina.com).

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