ORIGINAL ARTICLE 10.1111/1469-0691.12562

Screening for Middle East respiratory syndrome coronavirus infection in hospital patients and their healthcare worker and family contacts: a prospective descriptive study

Z. A. Memish[1,†], J. A. Al-Tawfiq[2,3,†], H. Q. Makhdoom[4,†], A. A. Al-Rabeeah[1], A. Assiri[1], R. F. Alhakeem[1], F. A. AlRabiah[5], S. Al Hajjar[5], A. Albarrak[6], H. Flemban[7], H. Balkhy[8], M. Barry[9], S. Alhassan[10], S. Alsubaie[11] and A. Zumla[1,12,13,†]

1) *Global Centre for Mass Gatherings Medicine (GCMGM), Ministry of Health, Riyadh,* 2) *Saudi Aramco Medical Services Organization, Saudi Aramco, Dhahran, Saudi Arabia,* 3) *Indiana University School of Medicine, Indianapolis, IN, USA,* 4) *Jeddah Regional Laboratory, Ministry of Health, Jeddah,* 5) *King Faisal Specialist Hospital,* 6) *Prince Sultan Military Medical City,* 7) *Alhada Military Hospital,* 8) *National Guard Hospital,* 9) *Adult infectious Diseases, King Saud University,* 10) *Security Forces Hospital, Ministry of Interior,* 11) *Paediatric Infectious Diseases, King Saud University, Riyadh, Saudi Arabia,* 12) *Division of Infection and Immunity, University College London and* 13) *NIHR, Biomedical Research Centre, UCL Hospitals NHS Foundation Trust, London, UK*

Abstract

The Saudi Arabian Ministry of Health implemented a pro-active surveillance programme for Middle East respiratory syndrome (MERS) coronavirus (MERS-CoV). We report MERS-CoV data from 5065 Kingdom of Saudi Arabia individuals who were screened for MERS-CoV over a 12-month period. From 1 October 2012 to 30 September 2013, demographic and clinical data were prospectively collected from all laboratory forms received at the Saudi Arabian Virology reference laboratory. Data were analysed by referral type, age, gender, and MERS-CoV real-time PCR test results. Five thousand and 65 individuals were screened for MER-CoV: hospitalized patients with suspected MERS-CoV infection (n = 2908, 57.4%), healthcare worker (HCW) contacts (n = 1695; 33.5%), and family contacts of laboratory-confirmed MERS cases (n = 462; 9.1%). Eleven per cent of persons tested were children (<17 years of age). There were 108 cases (99 adults and nine children) of MERS-CoV infection detected during the 12-month period (108/5065, 2% case detection rate). Of 108 cases, 45 were females (six children and 39 adults) and 63 were males (three children and 60 adults). Of the 99 adults with MERS-CoV infection, 70 were hospitalized patients, 19 were HCW contacts, and ten were family contacts. There were no significant increases in MERS-CoV detection rates over the 12-month period: 2.6% (19/731) in July 2013, 1.7% (19/1100) in August 2013, and 1.69% (21/1238) in September 2013. Male patients had a significantly higher MERS-CoV infection rate (63/2318, 2.7%) than females (45/2747, 1.6%) (p 0.013). MERS-CoV rates remain at low levels, with no significant increase over time. Pro-active surveillance for MERS-CoV in newly diagnosed patients and their contacts will continue.

Keywords: Clinical, coronavirus, demographic, diagnosis, MERS-CoV, Middle East, real-time PCR, sample type, SARS, screening, viral load
Original Submission: 29 December 2013; **Accepted:** 17 January 2014
Editor: M. Drancourt
Article published online: 24 January 2014
Clin Microbiol Infect

Corresponding author: Z. A. Memish, Collaborating Centre for Mass Gathering Medicine, Ministry of Health, Al-Faisal University, Riyadh 11176, Saudi Arabia
E-mail: zmemish@yahoo.com
[†]These authors contributed equally.

Introduction

Understanding the natural history, epidemiology and clinical presentation of new killer infectious diseases is dependent on, and influenced by, the WHO recommended surveillance strategies for case detection, which largely focus on severe

illness and microbiological testing, coupled with details from case studies. Contact-tracing activities allow for the detection of confirmed cases with a broader spectrum of illness. For infectious diseases caused by viruses, confirmed cases include only those with a positive PCR test result for viral genetic material, in accordance with the laboratory guidelines. Since the first case report of the novel Middle East respiratory syndrome (MERS) coronavirus (MERS-CoV) in September 2012 [1], the Kingdom of Saudi Arabia (KSA) Ministry of Health (KSA-MoH) has been working closely with international collaborators and the WHO to better understand and define the epidemiological, demographic, clinical and laboratory features of the new disease. A molecular real-time PCR diagnostic test was rapidly developed after the first case, and was subsequently the method recommended by the WHO for detecting the presence of the MERS-CoV infection [2,3]. This test was used in a retrospective analysis on biobanked samples to confirm two cases of MERS from an earlier outbreak of respiratory infection in Jordan in April, 2012 [4].

Important steps for the surveillance and control of MERS-CoV infection are the early detection and isolation of patients with active MERS-CoV disease, and screening of their contacts. Surveillance studies also help in defining and monitoring transmission rates, case load, and epidemic risk assessment, and assist in instituting infection control measures with new diagnostic methods and treatments. Although MERS-CoV case detection is critically dependent on the degree of awareness of the attending physician, accurate laboratory testing is also essential in making a diagnosis. Soon after the detection of the first case of MERS in Jeddah in September 2012 [1], the KSA-MoH put in place a proactive surveillance and screening programme for inpatients admitted with respiratory illness suspected of being caused by MERS-CoV. It also included active screening of contacts of confirmed MERS cases. KSA-MoH recommendations for MERS-CoV screening are based on the WHO guidelines on case definition, detection, and contact investigations [5–7]. This led to an increase in the numbers of requests for MERS-CoV screening from hospitals throughout the KSA. We report these laboratory data on the use of real-time PCR tests on clinical samples received from 5065 individuals screened for MERS-CoV during a 12-month period, commencing from the first case detection in September 2012.

Methods

Selection of individuals for MERS-CoV screening

The KSA-MoH has implemented a pro-active early case detection and surveillance system for MERS-CoV. It recommends sending respiratory tract samples from critically ill patients admitted to hospitals with fever and lower respiratory tract infection symptoms. Screening for MERS-CoV is also recommended for family and healthcare worker (HCW) contacts of proven cases of MERS-CoV infection. All samples are transported to and are processed by the KSA-MoH virology laboratory in Jeddah, which is accredited and regulated by the Central Board for Accreditation of Health Care Institute. Quality assurance and control for all diagnostic tests is monitored through Internal Policy Procedures and by external quality assurance schemes.

Collection of clinical specimens

Respiratory specimens collected from patients and contacts were: sputum samples; nose and throat (N + T) swabs; nasopharyngeal (NP) swabs; and tracheal aspirate samples. Sputum was collected directly into a sterile, leak-proof, screw-capped sputum collection sterile container; NP swabs and N + T swabs were collected with sterile synthetic tip Dacron flocked swabs. For NP specimens, the swabs were inserted through the nostril, parallel to the palate, into the nasopharynx. Swabs were left in place for a few seconds to absorb secretions. For N + T swabs, both nostrils and the throat were swabbed with separate swabs. All swabs were placed immediately into sterile tubes containing 2–3 mL of viral transport medium. For inpatients, lower respiratory tract samples—2–3 mL of bronchoalveolar lavage fluid and tracheal aspirate—were obtained and placed into sterile, leak-proof, screw-capped sterile dry containers.

Labelling, storage and transportation of specimens

When there were short periods of transportation (≤48 h) of specimens to the laboratory, specimens were held in a refrigerator at 2–8°C rather than frozen; for periods exceeding 48 h, specimens were shipped on dry ice at −70°C as soon as possible after collection. Each specimen container was labelled with the patient's ID number, the specimen type, and the date on which the sample was collected. All specimens were pre-packed to prevent breakage and spillage. Specimen containers were sealed with parafilm and placed in zip-lock bags. Absorbent material to absorb the entire contents of the secondary container (containing the primary container) was placed to separate the primary containers (containing specimen) to prevent breakage.

RNA extraction

Extraction of RNA was performed with Roche MagNa Pure LC (RNA Viral isolation Kit). Sputum samples were pretreated with 2 × lysis buffer for 30 min in a shaking incubator. Swabs were placed in lysis buffer. Two hundred microlitres of each sample was added to the MagNA Pure LC plate, which contains