Characterization of *Mycobacterium chimaera* in a heater-cooler unit in Latvia

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To the Editor—Mycobacterium chimaera (*M. chimaera*) is an opportunistic environmental mycobacterium belonging to the *M. avium–M. intracellulare* complex. Transmission of *M. chimaera* from contaminated heater-cooler unit (HCU) water tanks to patients is a risk during open-heart surgery.[1] Specifically, investigations have revealed that the contaminated HCU devices (Stockert 3T) came from one particular manufacturing facility, LivaNova in Munich, Germany, and were a likely source for cardiothoracic surgery–related severe *M. chimaera* infections that occurred in Switzerland, Germany, The Netherlands, and the United Kingdom.[2] The importance of HCUs lies in their ability to regulate the body temperature of a patient during cardiac surgery. However, evidence suggests that the airborne transmission of aerosolized bacteria from the water tanks was responsible for these infections.[2] Currently, the extent of global outbreaks is unknown, but the burden of invasive *M. chimaera* was estimated to be 156–282 cases per year in 10 countries where most cardiac-valve replacements are performed.[3] We investigated the possible presence of *M. chimaera* in HCUs in the Cardiothoracic Department, Latvian Centre of Cardiology of Pauls Stradins Clinical University Hospital, Latvia. The water of HCUs was sampled before they underwent the routine disinfection procedure in May, 2017. Samples were cultured on Bactec MGIT 960 system (Becton Dickinson, Heidelberg, Germany). The growth of mycobacteria was observed in 2 samples. DNA was isolated and the *M. chimaera* was identified using a GenoType NTM-DR version 1.0 kit (Hain Lifescience, Nehren, Germany). Both isolates, designated LV-2017-1-HCU and LV-2017-2-HCU, were subjected to whole-genome sequencing with 150× coverage on an Ion Proton System (Thermo Fisher Scientific, Waltham, MA). For the bioinformatics analysis, reads in samples produced in this study were aligned to the *M. chimaera* reference genome JCM_14737 (ENA accession no. PRJNA324238) using the bwa MEM algorithm. Variants were called and marked based on the published criteria[4] using BCFtools. Sequences of both isolates were compared to strains ZUERICH-1 (DSM 101591) and ZUERICH-2 (DSM 101592), representatives of the major *M. chimaera* groups 1 and 2.[5]

For the phylogenetic analysis, raw sequencing reads of the isolates LV-2017-1-HCU and LV-2017-2-HCU were mapped against the *M. chimaera* type strain FI-01069 (DSM 44623)[6] and compared with strain ZUERICH-1 and 127 other publicly available data sets of *M. chimaera* isolates belonging to subgroup 1.1 and previously collected in Denmark, Germany, The Netherlands, the United Kindgom, Ireland, the United States, Australia, and New Zealand (available in the European Nucleotide Archive; http://www.ebi.ac.uk/ena).[4,5,7] The analysis was performed using CSI Phylogeny 1.4 software, Center of Genomic Epidemiology (https://cge.cbs.dtu.dk/services/CSIPhylogeny/), with default settings but including the reference in the final tree.[8] Molecular phylogenetic analysis was performed using the maximum likelihood method. The phylogenetic tree was built from 176 SNP positions of 130 *M. chimaera* isolates and was visualized in MEGA6.

Results

In total, 2,555,838 and 1,544,268 sequencing reads were generated for samples LV-2017-1-HCU and LV-2017-2-HCU, respectively. The sequencing reads were deposited in the European Nucleotide Archive (ENA) under study numbers ERS3734298 and ERS37 34299.

Molecular phylogenetic analysis revealed that both Latvian HCU's samples were closely related to the strain ZUERICH-1 (Fig. 1A). Specific SNP signatures[5] for subgroup 1.1. (substitutions of guanine (G) by adenine (A) at positions 113,518 and 209,278 of the DSM 44623T genome—GenBank accession no. LQOO00 000000) were found in both Latvian isolates. This result suggested that they belong to the subgroup 1.1 which contains most *M. chimaera* isolates from water systems or exhaust air of LivaNova HCUs in clinical use, isolates from HCUs sampled at the LivaNova production site, and isolates from related patients in different countries.[5]

During the phylogenetic analysis of the isolates LV-2017-1-HCU and LV-2017-2-HCU, the sequencing coverage was 92.3% and 78% of the reference genome, respectively. The percentage of the reference genome covered by all isolates was 43.8%. As expected, the isolates within the subgroup 1.1 showed little diversity, with a median pairwise distance of 2 SNPs (range, 0–40).[5] A median pairwise distance for the Latvian LV-2017-1-HCU and LV-2017-2-HCU isolates were 32 (range, 31–40) and 4 (range, 3–12) SNPs, respectively. The results showed that *M. chimaera* sequences from HCU in Latvia genetically clustered with the isolates from HCUs in The Netherlands, the United States, and Germany (samples 110, 128, 180, 187, 2015-22-15-01), as well as isolates from patients in The Netherlands (sample 198) and USA (samples 2015-22-63, 2015-22-79, 2015-22-80) (Fig. 1B).

Discussion

Overall, this is the first report of *M. chimaera* from HCUs in Latvia, which adds Latvia and the Baltic states to the global map of *M. chimaera* outbreaks associated with HCUs in hospitals. The presence of *M. chimaera* in the HCU in the university hospital in Latvia indicated the risk of exposure of patients that could lead to infection. Regular sampling of patients with chronic infections after cardiac surgery in Pauls Stradins Clinical University Hospital

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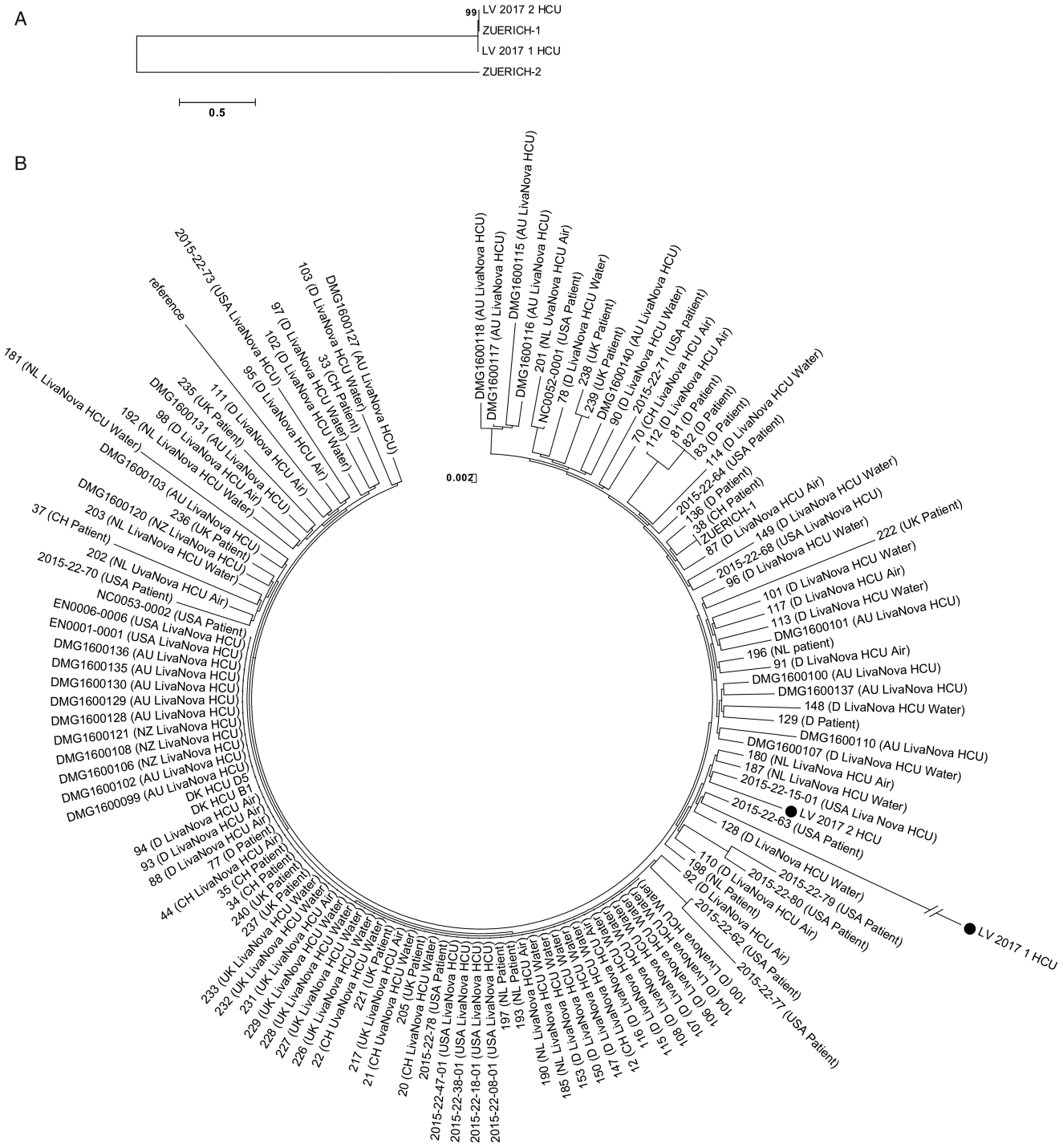

Fig. 1. (A) Molecular phylogenetic analysis of the isolates in the present study using the maximum likelihood method. Both samples were closely related to the strain ZUERICH-1. (B) Maximum likelihood phylogenetic tree built from 176 SNP positions of 130 *M. chimaera* isolates mapped to the genome of *M. chimaera* type strain FI-01069. The 2 isolates in the present study are indicated by black circles. Codes of the samples belonging to group 1.1. correspond to those used by van Ingen et al (2017). Note. AU, Australia; D, Germany; NL, The Netherlands; NZ, New Zealand; LV, Latvia; UK, United Kingdom; CH, Switzerland; and DK, Denmark.

has failed to identify *M. chimaera*–related clinical cases. The HCU produced by LivaNova PLC was replaced with another device in 2018, and new cases of infection could occur over significant period.[9] HCUs are vulnerable to contamination from water sources, which may lead to infection by nontuberculous mycobacteria such as NTM, including *M. gordonae* and *M. paragordonae*, in addition to *M. chimaera*.[10] Thus, further investigations of mycobacterial infections in patients and related medical devices are warranted.

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Conflicts of interest. All authors report no conflicts of interest relevant to this article.

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Impact of the pandemic on antimicrobial consumption patterns

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To the Editor—Novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) impacts on economic, social, and healthcare systems. Uncertainties regarding coronavirus disease (COVID-19) promote concerns in choosing the best therapeutic strategy. Several drugs with antiviral effects were prescribed to treat COVID-19, but scientific evidence is not conclusive regarding benefit.

Unnecessary antimicrobial use may cause an increase in multidrug-resistant organisms.[1,2] It is necessary to consider actions to prevent consequences that SARS-CoV-2 may have on antimicrobial use.[1,2] Antibiotic stewardship is a strategy to promote the optimal use of antibiotics. SARS-CoV-2 probably changes the antibiotic consumption profile, and it is necessary to measure this difference.

Thus, our goal was to evaluate the impact of the pandemic on antimicrobial usage patterns comparing cohorts of SARS-CoV-2–positive and SARS-CoV-2–negative patients admitted in specific hospital locations.

Methods

Setting

Hospital de Clínicas de Porto Alegre, a 845-bed university, tertiary-care, public hospital is located in the city of Porto Alegre, southern Brazil. On March 20, 2020, Brazil declared recognition of community-based coronavirus transmission across the country. It is the local reference for hospitalization of patients with suspected or confirmed COVID-19. At the pandemic moment, areas for COVID-19 isolation were created in the intensive care unit (ICU), the emergency department, and clinical wards.

Study design

A cross-sectional study was performed and data on antimicrobial consumption of May 2020 was included in our analysis. We adopted a "days of therapy" (DOT) methodology to measure antimicrobial consumption.[3]

Data collection

All hospital antimicrobial data from administrative databases were included, except antibiotics that are not audited by the infection control committee. We conducted an overall analysis and cluster analysis in COVID-19 and non–COVID-19 ICU, emergency department, and clinical ward. We selected the most used antimicrobial drugs in each cluster. Units were coupled per similarity to compare COVID-19 and non–COVID-19 antibiotics consumption.

Statistical analysis

We calculated antibiotics consumption based on DOT and adjusted per patient days (PD). We then compared this person–time rate with point estimates and confidence intervals for the incidence rate ratio considering Poisson distribution. The analysis was performed using Stata version 15.1 software (StataCorp, College Station, TX).

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