Risk of Potential Invasive Non-Tuberculous Mycobacterial Infection in Major Cardiothoracic Surgeries

Maria Khan and Saba Khan

Department of Pathology, Peshawar Institute of Cardiology-MTI, Peshawar, Pakistan

ABSTRACT

Nontuberculous *Mycobacteria* (NTM) commonly colonise municipal water supplies and cause healthcare-associated outbreaks. Although the infections are rare, they are associated with high mortality. Aerosolization of NTM from colonised Heater cooler devices causes invasive infections in cardiac surgery patients. These units are widely used in open-chest heart surgery as an essential part of extracorporeal circulation but have been suggested as being a risk for infection. Water disinfection as well as effective engineering–related mitigation strategies should be designed to decrease the burden of NTM in the hospital water supply.

Key Words: *Nontuberculous Mycobacteria, Heater cooler devices, Endocarditis, Water, Cardiothoracic surgeries.*

How to cite this article: Khan M, Khan S. Risk of Potential Invasive Non-Tuberculous Mycobacterial Infection in Major Cardiothoracic Surgeries. *J Coll Physicians Surg Pak* 2024; **34(03)**:364-367.

Nontuberculous *Mycobacteria* (NTM) are robust environmental microbes dwell in water, dust, and especially in soil.[1] Frequently, NTM colonise water supply of municipal system,[2] including tap water of hospitals,[3] where they develop biofilms in water distribution networks.[4] Quite a few outbreaks of surgical site infections have been described exclusively with fast growing NTM subsequent to cardiac surgery. Namely, *Mycobacterium* (MO) *chelonae* contamination of an implant during manufacturing resulted in prosthetic valve endocarditis.[5] In addition to this, *Mycobacterium fortuitum* was linked to an outbreak among patients who underwent cardiac septum defect repair due to a single contaminated patch.[6] Recently, a single centre outbreak occurred due to heater cooler devices (HCD) where they were contaminated with *M. wolinskyi*.[7] Similarly, *Mycobacterium chimaera* and *Mycobacterium abscessus* infections were described in patients subsequent to cardiovascular surgery.[8] Likewise, *M. chimaera* is mostly involved in extrapulmonary infections like bloodstream infection and prosthetic valve endocarditis following open heart surgery in relation to an artificial heart valve implant and an annuloplasty ring.[9]

Although these infections are rare, they are associated with high mortality. Together the European Centre for Disease Prevention and Control (CDC) and the US Food and Drug Administration (FDA) have issued alerts.[10,11]

Correspondence to: Dr. Maria Khan, Department of Pathology, Peshawar Institute of Cardiology-MTI, Peshawar, Pakistan
E-mail: kmaria22@hotmail.com

Received: April 10, 2023; Revised: August 29, 2023; Accepted: December 07, 2023
DOI: https://doi.org/10.29271/jcpsp.2024.03.364

Outbreaks of rapidly growing mycobacteria are undistinguished and have been associated with colonised plumbing systems in commercial buildings and healthcare facilities.[12] More so, HCDs that are broadly utilised in open heart surgeries as an indispensable portion of extracorporeal circulation, have been proposed for being a risk factor for NTM infections in patients.[13] HCDs consist of water chambers which deliver temperature-controlled water to external heat exchangers or cooling/warming covers through sealed circuits. Even though the patient is not in direct contact with the water in the circuits, still there is a probability of aerosolization of contaminated water from exhaust of the device's vent into the surgical environment and potentially transmitting bacteria to the patient.[14]

Another European research, in 2016, illustrated an association relating to isolation of *M. chimaera* from HCDs and from clinical samples of several infected cardiothoracic patients, who underwent open cardiac surgery at the same time.[15] Evidently, *Mycobacterium abscessus* complex (*M. abscessus* subspecies *massiliense, M. abscessus* subspecies *abscessus*, and *M. abscessus* subspecies *bolletii*) are intrinsically resistant to most disinfectants and antibiotics.[16] Therefore, chlorhexidine and povidone-iodine that are commonly used pre-operative antiseptics, are effective against conventional viruses, Enterobacteriaceae, *Staphylococcus aureus*, and *Candida* species, have undocumented effectiveness for NTM, specifically, *Mycobacterium abscessus* complex.

Type of Surgery: Concurrently, an outbreak in North Carolina, USA, reported NTM infection among Lung transplant recipients (55%), recent cardiac surgery (13%), cancer (7%), and hematopoietic stem cell transplantation (7%), as well as multiple other patient categories (18%).[8] Another study recounted, a noticeably high rate of NTM-positive clinical samples among patients with cardiothoracic surgery than in patients undergone other more common general surgical procedures and

orthopaedic surgeries.[17] The odds of severe NTM infections increase with lengthier surgery timings i.e. use of HCD for more than 5 hours and overextended time on bypass i.e. greater than two hours.

NTM Cases: Significantly, higher chance of invasive NTM infection were observed during open heart surgery, that resulted in exposure to functioning HCD.[17] After initial exposure, patients who acquire this pathogen usually do not develop symptoms or signs of infection immediately, rather it takes months to years. Therefore, clinical criteria to suspect NTM infection in patients with medical or surgical history include; prosthetic vascular graft infection; prosthetic valve endocarditis; mediastinitis; sternotomy wound infection; bloodstream infection; disseminated infection, including immunologic and embolic and manifestations (e.g. bone marrow involvement with cytopenia, splenomegaly, osteomyelitis, arthritis, chorioretinitis, nephritis, lung involvement, myocarditis, hepatitis).[18] Typically, *M. abscessus* infections are problematic to diagnose and entail prolonged multiple antibiotics.[19] The US FDA pointed an increased risk of infection in patients receiving graft, heart valve, left ventricular assist device (LVAD), or any other prosthetic material or who had a heart transplant. Also, the FDA released health alerts to patients who underwent cardiopulmonary bypass (CPB), to be sentient of the probable signs and symptoms of NTM infection, like, fever, fatigue, redness, pain, muscle pain, night sweats, heat, joint pain, or pus at the surgical site, weight loss, abdominal pain, nausea, and vomiting.[14]

Common Clinical Samples: *Mycobacterium abscessus* is generally recovered from blood cultures (45%), pus from the sternal wound (23%), VAD driveline site (9%), pleural fluid (9%), lower respiratory tract samples (9%), and ascetic fluid (5%).[8] Subsequently, micro-aspiration of *M. abscessus* from tap water used for patient care activities has led to pulmonary colonisation or infection,[20] which was probably acquired *via* aerosols generated from colonised HCDs.[21] Furthermore, an outbreak at a Swiss hospital among cardiac surgery patients infected with *Mycobacterium chimaera* was genetically interrelated to colonised HCDs.[22] Additionally, hospitals in Pennsylvania, Iowa, and Europe, have also described *M. chimaera* infections in patients after cardiopulmonary bypass surgery.[23-25] Another study in 2015, published the potential for aerosolized NTM from CPB machines, that lead to infections in patients during cardiac surgery.[21] Usually, culture of samples for Mycobacteria are done by standard techniques using the mycobacteria growth indicator tube (MGIT) 960 system (Becton Dickinson Microbiology Systems, Maryland) or Middle brook 7H11 agar plates incubated at 37°C for 7 weeks or until positive.[21]

Samples from Field Surveillance: A hospital in the US reported, *M. abscessus* biofilm formation in more than half of the water pipes in multiple areas like faucets in patient room, water faucets in ICU hallway, in a shower head, water basin in a utility room, an OR scrub sink faucet and in one of the ice machine.[8] In addition, other factors including low residual disinfectant (chloramine) levels at multiple water outlets and slow flow rates of the water system were observed too. More so, as hot water system was a recirculating loop, so the water stored in tanks required a long flow time to reach the water outlets.[8]

Moreover, *M. chimaera* was isolated in samples of significant volume of air as well as also on sedimentation plates about 5 meters away from a HCD in a non-ventilated environment, resulting in contamination of implant devices used during the surgery.[21]

Interventions and Recommendations: Infections usually resolve after implementation of extra high potency disinfection protocols, like using sterile water for HCDs, daily water changes, disinfection with hydrogen peroxide daily in addition to bleach-based disinfection at regular intervals.[8] It is suggested to not use tap water for filling, rinsing, refilling or top-off water reservoir since this may host NTM organisms.[17] Contrarily, it is not recommended to use sterile and deionised water through reverse osmosis, as it may stimulate corrosion of the metallic components of the HCD.

To emphasise, the exposed patients should not use tap water, instead should use sterilised water for respiratory therapy, bathing, oral care, flushing the enteral tubes, consumption, and, until healing of the surgical sites.[20] Moreover, heart and lung transplant recipients should also avoid tap water in their early postoperative period after discharge.[8] The three primary water engineering-related interventions to reduce microbial load and proliferation rate are; water flushing through both the recirculating hot water systems and cold water system; removal or modification of water flow regulators, aerators, and hot water tanks not in working condition; and reducing the proportion of recirculating hot water that bypasses heat exchangers as well as 0.2 µm point-of-use filters should be installed at OR scrub sink faucets.[21] It was directed to immediately remove any heater-cooler devices, tubing, connectors, and all other devices tested positive for *M. chimaera* or have been associated with known NTM-infected patient in a healthcare setting. Emphasis was given regarding the use of new devices, accessories, tubing, and connectors to avoid recontamination while using another heater-cooler device. Awareness was raised regarding the possibility of device contamination from other means like environmental contamination or contact of the devices with the contaminated accessories.[14]

At the University Hospital of Zurich, all HCDs have been placed away from the surgical sites and their exhaust air was taken by a secondary housing and was directed to the operating room exhaust since 2014. All HCDs must be separated from air that can get access to sterile zones and instruments, and all such devices that create drafts should be removed from the operating room.[25] As source identification usually fails in most cases, NTM should be considered by clinicians when assessing patients with infections after cardiac surgery, particularly for atypical clinical presentation and extended incubation periods. Additionally, mycobacterial cultures, particularly for surgical specimens should be requested.[8]

According to the manufacturers' instructions and quality control program, proper maintenance schedules and regular cleaning and disinfection for HCDs should be carried out to reduce the risk of microbial growth. Any HCD, that shows discolouration or cloudiness in the fluid circuits/lines, which points towards any microbial (bacterial/fungal) growth should be immediately removed from the service. If HCD contamination is suspected, special considerations should be made to perform environmental, air, and water sampling.[14] Conversely, testing of HCDs to identify contamination with NTM presents technical challenges related to high rate of false negative tests, technicality in sample collection, and the prolonged culture time. Therefore, at the moment, FDA does not recommend it.[14] In other words, healthcare institutions should follow strict protocols for notifying and testing patients, if they suspect any infection related to HCDs. As evident, HCDs are important in patient care and the benefits of temperature control during cardiothoracic procedures generally prevail over the risk of infection transmission associated with these devices.[14]

CONCLUSION

The widespread presence of NTM in water supply of a healthcare facility, and elements that intensify their focus or stimulate aerosolisation onto susceptible patients, can give rise to an outbreak. Constant surveillance of NTM by a hospital is crucial for detection of an outbreak, but it is challenging and possibly perplexed due to endemic nature of the disease in communities with similar strains, nonconforming clinical manifestations, and prolonged incubation periods. Therefore, stratagems for minimising exposure of at risk groups of patients to waterborne NTM can effectively alleviate outbreaks; nevertheless, various other unanticipated scenarios of exposures may still need to be considered.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

MK: Contributed to the concept or design of the article.
SK: Drafted the article and revised it critically for important intellectual content.
The authors approved the final version of the manuscript to be published.

REFERENCES

1. Primm TP, Lucero CA, Falkinham JO 3rd. Health impacts of environmental mycobacteria. *Clin Microbiol Rev* 2004; **17(1)**:98-106. doi: 10.1128/CMR.17.1.98-106.2004.
2. Thomson R, Tolson C, Sidjabat H, Huygens F, Hargreaves M. *Mycobacterium abscessus* isolated from municipal water—a potential source of human infection. *BMC Infect Dis* 2013; **13**:241. doi: 10.1186/1471-2334-13-241.
3. Williams MM, Armbruster CR, Arduino MJ. Plumbing of hospital premises is a reservoir for opportunistically pathogenic microorganisms: A review. *Biofouling* 2013; **29(2)**:147-62. doi: 10.1080/08927014.2012.757308.
4. Wallace RJ Jr, Brown BA, Griffith DE. Nosocomial outbreaks/pseudo-outbreaks caused by nontuberculous mycobacteria. *Annu Rev Microbiol* 1998; **52**:453-90. doi: 10.1146/annurev.micro.52.1.453.
5. Strabelli TMV, Siciliano RF, Castelli JB, Demarchi LM, Leao SC, Viana-Niero C, *et al*. *Mycobacterium chelonae* valve endocarditis resulting from contaminated biological prostheses. *J Infect* 2010; **60(6)**:467-73. doi: 10.1016/j.jinf.2010.03.008.
6. Vukovic D, Parezanovic V, Savic B, Dakic I, Laban-Nestorovic S, Ilic S, *et al*. *Mycobacterium fortuitum* endocarditis associated with cardiac surgery, Serbia. *Emerg Infect Dis* 2013; **19(3)**:517-9. doi: 10.3201/eid1903. 120763.
7. Nagpal A, Wentink JE, Berbari EF, Aronhalt KC, Wright AJ, Krageschmidt DA, *et al*. A cluster of *Mycobacterium wolinskyi* surgical site infections at an academic medical center. *Infect Control Hosp Epidemiol* 2014; **35(9)**:1169-75. doi: 10.1086/677164.
8. Baker AW, Lewis SS, Alexander BD, Chen LF, Wallace Jr RJ, Brown-Elliott BA, *et al*. Two-phase hospital-associated outbreak of *Mycobacterium abscessus*: Investigation and mitigation. *Clin Infect Dis* 2017; **64(7)**:902-11. doi: 10.1093/cid/ciw877.
9. Achermann Y, Rossle M, Hoffmann M, Deggim V, Kuster S, Zimmermann DR, *et al*. Prosthetic valve endocarditis and bloodstream infection due to *Mycobacterium chimaera*. *J Clin Microbiol* 2013; **51(6)**:1769-73. doi: 10.1128/JCM.00435-13.
10. US Food and Drug Administration. Nontuberculous Mycobacterium infections associated with heater cooler devices: 2015. FDA Safety Communication.
11. European Centre for Disease Prevention and Control. Invasive cardiovascular infection by *Mycobacterium chimaera* potentially associated with heater cooler units used during cardiac surgery. 2015 Available at: http://www.ecdc.europa.eu/sites/default/ files/media/ en/ publications / Publications/mycobacteriumchimaera-infection-associated-with-heater-cooler-units-rapidrisk-assessment-30-April-2015.
12. Stout JE, Gadkowski LB, Rath S, Alspaugh JA, Miller MB, Cox GM. Pedicure associated rapidly growing mycobacterial infection: an endemic disease. *Clin Infect Dis* 2011; **53(8)**:787-92. doi: 10.1093/cid/cir539.
13. Weitkemper HH, Spilker A, Knobl HJ, Korfer R. The heater-cooler unit: A conceivable source of infection. *J Extra Corpor Technol* 2002; **34(4)**:276-80. doi:10.1051/ject/2002 344276.
14. US Food and Drug Administration. Update: *Mycobacterium chimaera* infections associated with LivaNova PLC (formerly Sorin Group Deutschland GmBH) Stöckert 3T Heater-Cooler System: FDA Safety Communication. October 13, 2016. Washington, DC: US Department of Health and Human Services. FDA Med Bull. 2016.
15. Haller S, Höller C, Jacobshagen A, Hamouda O, Sin MA, Monnet DL, *et al*. Contamination during production of heater-cooler units by *Mycobacterium chimaera* potential cause for invasive cardiovascular infections: Results of an outbreak investigation in Germany, April 2015 to February 2016. *Euro Surveill* 2016; **21(17)**. doi: 10.2807/1560-7917.ES.2016.21.17.30215.

16. Cortesia C, Lopez GJ, de Waard JH, Takiff HE. The use of quaternary ammonium disinfectants selects for persisters at high frequency from some species of non-tuberculous mycobacteria and may be associated with outbreaks of soft tissue infections. *J Antimicrob Chemother* 2010; **65(12)**: 2574-81. doi: 10.1093/jac/dkq366.

17. Lyman MM, Grigg C, Kinsey CB, Keckler MS, Moulton-Meissner H, Cooper E, *et al*. Invasive nontuberculous mycobacterial infections among cardiothoracic surgical patients exposed to heater–cooler devices. *Emerg Infect Dis* 2017; **23(5)**:796-805. doi: 10.3201/eid2305.161899.

18. Centers for Disease Control and Prevention. Interim guide for the identification of possible cases of nontuberculous Mycobacterium infections associated with exposure to heater-cooler units.

19. Novosad SA, Beekmann SE, Polgreen PM, Mackey K, Winthrop KL; *M. abscessus* Study Team. Treatment of *Mycobacterium abscessus* infection. *Emerg Infect Dis* 2016; **22(3)**:511-4. doi: 10.3201/eid2203.150828.

20. Kanamori H, Weber DJ, Rutala WA. Healthcare outbreaks associated with a water reservoir and infection prevention strategies. *Clin Infect Dis* 2016; **62(11)**:1423-35. doi: 10.1093/cid/ciw122.

21. Sax H, Bloemberg G, Hasse B, Sommerstein R, Kohler P, Achermann Y, *et al*. Prolonged outbreak of Mycobacterium chimaera infection after open-chest heart surgery. *Clin Infect Dis* 2015; **61(1)**:67-75. doi: 10.1093/cid/civ198.

22. Kohler P, Kuster SP, Bloemberg G, Schulthess B, Frank M, Tanner FC, *et al*. Healthcare-associated prosthetic heart valve, aortic vascular graft, and disseminated Mycobacterium chimaera infections subsequent to open heart surgery. *Eur Heart J 2015*; **36(40)**:2745-53. doi: 10.1093/eurheartj/ehv342.

23. Well Span York Hospital Open Heart Surgery Infections. Frequently asked questions (FAQ) for physicians and APCs. Available from: http://www.wellspan. org/media/1243364/WYH-OpenHeart-FAQ-Providers.pdf (Accessed on 4 March 2016).

24. Milton S. Hershey Medical Center. Open-heart surgery: important information for medical professionals. Available from: http://www.pennstatehershey.org/web/guest/patientcare/open-heart/medical-professionals (Accessed on 4 March 2016).

25. University of Iowa Hospitals and Clinics. Potential infection risk in major heart and lung surgeries. Available from: http://uihc.org/news/potential-infection-riskmajor-heart-and-lung-surgeries (Accessed on 13 October 2016).