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Legionellosis in health care facilities: state of the art in control and prevention in Italy

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Abstract

Background. *Nosocomial water systems may be contaminated by Legionella spp; therefore, health care facilities represent a potential health risk for patients and health care staff. Active, well-planned clinical and environmental surveillance in hospitals is the most important instrument of prevention.*
Aim and Methods. *The aim of the present article was to outline the state of the art in legionellosis control and prevention among Italian health care facilities by reporting some experiences in the field.*
Results. *Our results showed that Legionella spp. are largely reported as both hospital water system contaminants and etiological agents in water-related health care-associated infections (HCAI) in Italy. Among the numerous sources of HCAI, water is the most investigated, although it has been demonstrated that air sampling may provide additional information for risk assessment.*
Conclusions. *More appropriate risk assessment is needed, especially in large facilities. In addition, more sensitive diagnostic tests should be used and dedicated training courses should be implemented in health care facilities.*

Introduction

Legionellosis normally occurs after inhaling an aerosol containing *Legionella* produced from naturally or artificially contaminated water sources such as cooling towers, hot water systems, showers, whirlpool spas, and similar disseminators that draw upon a water supply (1, 2). Although possible person-to-person transmission has been reported (3), it is largely assumed that the environment is the main source of infection. The level of a person's susceptibility to the source of infection depends on individual factors and/or underling diseases (4).

Nosocomial water systems are often contaminated by *Legionella*; therefore, health care facilities represent a potential hazard for patients and health care staff, as high-risk health practices concerning airways (e.g., ventilation, aspiration, devices for artificial respiration, oxygen therapy, and dental tools) are largely carried out in these facilities (5-7).

Since epidemiological surveillance for legionellosis was established in 1983, a steady increase in both sporadic and epidemic cases has been reported in Italy. However, this upsurge seems likely owing more to improved detection and changes in

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clinical diagnostic methods than to an actual increase in infections (8).

In 2000, the Italian Institute of Health (Istituto Superiore di Sanità, ISS) issued its first guidelines for the prevention and control of legionellosis. This document was followed in 2005 by instructions targeted to microbiology laboratories, environmental control, tourist accommodation, and spas. Later, in 2015, all national recommendations, including those for hospitals, were included in a single updated document (9). This new document recommends measures to be adopted to avoid *Legionella* growth and diffusion in water systems. An active and well-designed clinical–environmental surveillance program in hospitals to verify the frequency of disease and identify the sources of infection is the most important instrument of prevention.

The aim of the present article is to outline the state of the art in control and prevention of legionellosis in Italian health care facilities, by reporting some experiences in this field.

Clinical surveillance

Clinicians who diagnose legionellosis must report the case according to the national mandatory notification system; moreover, the local health unit (LHU) must complete an additional surveillance form and send it to the ISS (6). Consequently, to identify the infection source, the LHU starts an epidemiological and environmental investigation by interviewing patients or relatives, and control measures are promptly adopted. The ISS is in charge of monitoring trends, studying the patients' characteristics, and looking for clustered cases not identifiable at local level.

The surveillance form includes patients' sociodemographic data (age, sex, residence), clinical data (symptom onset, hospitalization, outcome), risk factors, lifestyle before the disease onset (exposure to certain settings during the 10 day-incubation period preceding symptom onset, such as hospitals, dental outpatient clinics, prisons or barracks, hotels, campsites, spas, and swimming pools), laboratory diagnostic tests used, and whether an environmental investigation was carried out. According to the international case definition, cases are classified as confirmed or probable legionellosis and as community-, hospital-, or travel-associated legionellosis (6). The data from surveillance forms are entered in a specific database and analyzed, including data of cases reported by the European Centre for Disease Prevention and Control that occur among foreign travelers visiting Italy during the 10 days before disease onset (6, 10).

According to the latest national reports in 2017, legionellosis incidence in Italy is 33.2 cases per million inhabitants, showing a slight increase over the previous year (28.2/1,000,000). A North–South gradient is evident, with 50.1 cases per million in the North, 35.1 per million in Central Italy, and 9.7 per million in the South. The number of nosocomial cases in 2017 was 124 (6.2%), of which 50 (40.3%) were of certain nosocomial origin and 74 (59.7%) of probable nosocomial origin (11).

Apart from annual reports published by the ISS concerning legionellosis cases occurring in Italy and their features, in recent decades some authors have reported results from special surveillance programs for legionellosis in different geographic areas of Italy using different instruments (4, 12, 13). In particular, Trerotoli et al. (12) carried out a study among five large Italian hospitals, showing that presumed pneumonia imputable to *Legionella* represented 2.7% of all analyzed hospital discharge forms.

Seven cases of nosocomial Legionnaires' disease were diagnosed between 1999 and 2003 during a clinical–environmental surveillance in the Campania Region; in particular, two cases were caused by the persistence of a single clone of *L. pneumophila* serogroup (sg) 1 Philadelphia in the hospital environment (14).

From 2000 to 2002, a large hospital in Piedmont reported nine cases of legionellosis caused by *L. pneumophila* sg1. Molecular investigation by ribotyping demonstrated a nosocomial origin (15).

In a prospective surveillance program planned during 2001–2004 in Rome, only one case (2.3%) of legionellosis was identified among 43 cases of nosocomial pneumonia. This low incidence appeared to be associated with a low percentage (<20%) of positive water samples per semester and a low contamination level (<10^2 colony-forming units (cfu/L) (13).

During 10-year surveillance (2000–2009) in Apulia, 9 of 97 (9.3%) legionellosis cases were determined to be of nosocomial origin (4). In one particular case caused by *L. pneumophila* sg5, molecular investigation allowed for identification of the infection source by genotype comparison between the human strain and environmental strains from water samples collected in the two different hospital wards where the patient was hospitalized (4).

Although the scientific evidence emphasizes that legionellosis in Italy is increasing (8), the incidence of this disease remains underestimated; the reasons for this are as follow. First is the general lack of an etiological diagnosis for pneumonia; the patient often undergoes treatment before the microorganism has been identified. Second, there are some difficulties in the diagnosis of legionellosis; e.g., testing for this pathogen is not a routine laboratory practice, urine antigen testing is not constant over the time, and the antibody response is slow. Therefore, constant surveillance is necessary; in all pneumonia cases, not only legionellosis should be suspected but all specific laboratory tests should also be performed to clarify the causative agent. In fact, legionellosis cannot be excluded by a negative urine antigen test result or a single low antibody titer. Isolation and identification of the etiological agent is fundamental as this will permit identification of the precise source of infection so as to implement necessary disinfection measures, thereby limiting the spread of disease among both patients and health care staff (16).

Environmental surveillance

Water

Data concerning the water systems in Italy show widespread environmental contamination with *Legionella,* especially in hospital facilities where people are more susceptible to infections (17). Various guidelines, including Italian ones, recommend disinfection to be implemented according to the contamination threshold and/or percentage of positive samples (9). However, it is important to underscore that the presence of *Legionella* in the water system does not directly translate into an actual risk of developing the infection. In fact, it has been demonstrated that the bacterial load of *Legionella* spp. in hospital water systems is not constant over time. Therefore, preliminary risk assessment should be conducted to predict water contamination by *Legionella* (4).

Although *L. pneumophila s*g1 is reported in the literature as the most common isolate in humans, increasing cases of legionellosis have been attributed to other species and serogroups. Therefore, evaluation of environmental contamination by *L. non-pneumophila* sg1 should not be neglected. During a surveillance carried out in the Apulia region, *L. pneumophila* sg2–14 was the species most frequently isolated (54.8%) from hospital water systems, followed by *L. pneumophila* sg1 (31.3%) (4).

Another study carried out in five hospitals in Bologna (Emilia-Romagna Region) found *L. pneumophila* sg3 in 93.7% of positive water samples, two of which were associated with the simultaneous presence of *L. anisa* and *L. bozemanii* (18). In a large hospital in Rome, 18.7% of water samples were colonized by *L. pneumophila* and 50% belonged to sg1 (13).

In Sicily, the constant presence of *Legionella* was demonstrated in the water system of a large hospital of Messina during a period of 15 years (2004–2018) (1). Most water samples were positive for *L. pneumophila* sg 2–14 (72%) followed by *L. pneumophila* sg1 (18%) and *L non-pneumophila* (15%). The total percentage did not equal 100% because different *Legionella* serotypes were found in the same sample. Buildings with the largest positivity rates included those housing the intensive care unit and neurosurgery departments (77%), surgery and pneumology departments (76%), and the neonatal intensive care unit (71%) (1). Moreover, another study was conducted in the same hospital to evaluate *L. pneumophila* contamination using georeferential statistical analysis, to assess the possible sources of dispersion and, consequently, the risk of exposure for both health care staff and patients (19). *L. pneumophila* sg1 was the most frequently detected on both the ground floor (69%) and first floor (60%), followed by *L. pneumophila* sg2–14 (36% and 24%, respectively). This work showed that geostatistical methods applied to microbiological water analysis allow for better modeling of the object of study, better risk management, and a wider choice of prevention methods.

As simple water disinfection is insufficient to control infection risk, a comprehensive water safety plan (WSP) should be developed that includes system maintenance, staff training, and clinical surveillance system implementation aimed at early detection of cases (20). However, to maintain satisfactory results over time, any disinfection method must be adjusted or fine-tuned for individual hospitals (21).

Borella et al. (20) provided an update on the procedures for controlling environmental contamination during 15 years of activity. The performance ranking was highest for filters, followed by high-temperature boilers, monochloramine, and chlorine dioxide; the effectiveness of hyperchlorination was limited, and thermal shock was even less effective (20). After 5-year implementation of an integrated strategy of water disinfection and filtration aimed at controlling the presence of *Legionella* in a hospital water system, Orsi et al. concluded that thermal shock and continuous hyperchlorination achieve significant reduction of *Legionella*, especially in older buildings with no rational water system design (22).

Finally, an aspect that should not be underestimated is the antibiotic susceptibility of environmental *Legionella* spp. strains. Attention is needed with regard to possible antibiotic resistance even among environmental *Legionella* strains, not only for epidemiological purposes but also for timely prediction of the onset of antibiotic resistance in the environment before it is evidenced in clinical specimens (23).

Air

Recommendations for the control and prevention of legionellosis include sampling procedures of different environmental matrices (e.g., water, fouling, deposits, among others), but not air. In addition, bioaerosol sampling is not considered reliable (11). Nevertheless, some authors state that air sampling can be combined with water systems surveillance to provide a useful tool in preventing legionellosis (24). However, the presence of *Legionella* in the air and its appropriate sampling modalities still represent problems that are largely debated (6, 25, 26).

Active and passive methods are generally used to evaluate microbial air contamination (10, 27-30), including by *Legionella* (25, 31), but no specific protocols have been developed to date. Laganà et al. (26) reported *Legionella* isolates in environmental samples (water and air) collected from the cardiology units of two hospitals in Messina during 2015–2016. Using air sampling via passive methods (settling plates), *L. pneumophila* sg1, sg3, and sg6 were detected in 8 of 25 samples (32%).

The low number of positive results for *Legionella* in the air using traditional samplers, i.e., the Surface Air System (SAS, PBI International, Milan, Italy) and passive sampling, has prompted studies (32) using an active air sampler with liquid medium (Coriolis®; Bertin Technologies, Montigny le Bretonneux, France), which can quantify *Legionella* in bioaerosols in both culture-based and molecular investigations. In an Italian national study evaluating air contamination, *Legionella* was found in 36.4% of enrolled health care facilities using at least one culture-based method; addition of the Coriolis sampler showed a higher sensitivity for *Legionella* when molecular-based methods were used (32, 33).

These results show that detection of *Legionella* in the air cannot replace water sampling. The absence of this microorganism in the air does not necessarily indicate its absence from water systems. At the same time, air sampling may provide additional information for risk assessment, and molecular investigations can serve as a useful support to future research in cases with negative culture-based results.

Discussion and Conclusions

Among the numerous sources of health care-associated infections (HCAI), water is among the most studied and discussed, partly owing to its controllability but also because water is used extensively in hospitals (34, 35). In particular, *Legionella* spp. are largely reported as both hospital water system contaminants and as etiological agents in water-related HCAI (8, 34). Therefore, water system disinfection is an effective preventive measure that should be implemented, although by itself, disinfection is insufficient for eliminating the risk of HCAI as no treatment has been identified that can definitively sterilize a water system.

Only adopting a multi-pronged approach of engineering and hygiene measures as well as surveillance and management of hospital water systems it is possible to reduce the risk of contracting hospital legionellosis. In this regard, the World Health Organization (WHO) suggests that the best approach is the development of a WSP, which is a useful operational tool for the systematic assessment or risk analysis of water delivery lines (1). Moreover, it is essential for health care personnel to be provided with adequate information, such as in educational interventions (36-38), so as to understand the reservoirs, risk factors, and transmission pathways of nosocomial infections (39-41), to be able to adopt the correct control and prevention measures of prevention.

As recently demonstrated by a national cross-sectional questionnaire survey carried out in 178 Italian hospitals, control and prevention measures for legionellosis are currently implemented but some critical aspects should be improved (7). More appropriate risk assessment is necessary, especially in large facilities. In addition, more sensitive diagnostic tests should be used, and dedicated training courses should be organized. Moreover, considering that *Legionella* emission from water systems is not necessarily constant over time, disinfection should be carried out, even with low levels of contamination (4).

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Riassunto

La legionellosi nelle strutture sanitarie: stato dell'arte su controllo e prevenzione in Italia

Premessa. Gli impianti idrici ospedalieri possono essere contaminati da *Legionella* spp; pertanto, le strutture sanitarie rappresentano un potenziale rischio clinico per la salute dei pazienti ed il personale sanitario. Una sorveglianza attiva clinico-ambientale ben disegnata negli ospedali è il più importante strumento di prevenzione.

Disegno dello studio e Metodi. Scopo di questo articolo è quello di esporre lo stato dell'arte nel controllo e prevenzione della legionellosi nelle strutture sanitarie italiane, riportando alcune esperienze in questo campo.

Risultati. I risultati evidenziano come la *Legionella* spp sia largamente riportata come contaminante degli impianti idrici ospedalieri e come agente eziologico nelle infezioni correlate all'assistenza (ICA) associate all'acqua. Tra le numerose sorgenti di ICA, l'acqua è una delle più studiate e discusse; nonostante questo, il campionamento dell'aria può fornire ulteriori informazioni per la stima del rischio.

Conclusioni. Sono necessarie valutazioni del rischio più appropriate, specialmente nei grandi ospedali, dovrebbero essere adottati test diagnostici più sensibili, e corsi di formazione dedicati dovrebbero essere implementati.

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