IJMS 2021 8(1): 88 - 100

International Journal of Multidisciplinary Studies (IJMS)
Volume 8, Issue 1, 2021

Legionella pneumonia as a cause of atypical pneumonia in a tertiary care hospital in Sri Lanka

Kottahachchi J[1 *], Dissanayake D.M.B.T[1], Athukorala D[1,2], Kottahachchi S.P[3], Fernando S.S.N[1], Weerasekara M.M[1], Gunasekara C[1], Nalaka M.J[1,4], Sudusinghe D[5], Marasinghe C[5]

[1]Department of Microbiology, Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka

[2]Department of Microbiology, University Hospitals of Coventry and Warwickshire NHS Trust, Clifford Bridge Road, Coventry, United Kingdom CV2 2DX (current working place)

[3]General Operating Theatre, Lady Ridgeway Hospital for Children, Colombo 10, Sri Lanka

[4]Out Patient Department, Base Hospital Medirigiriya, Sri Lanka (current working place)

[5]Department of Medicine, Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka

ABSTRACT

Atypical pneumonia which contributes to an important proportion of community acquired pneumonia and Legionella pneumophila is a noteworthy pathogen worldwide. Legionnaires' disease, the severe form of pneumonia is predominantly caused by Legionella pneumophila serogroup 1. This study was conducted to determine the presence of Legionella pneumophila as a pathogen and the associated risk factors among the patients admitted with atypical pneumonia to a tertiary care hospital in Sri Lanka. Seventy-five adult patients diagnosed with atypical pneumonia attending professorial medical unit of Colombo South Teaching Hospital, Sri Lanka were enrolled. Risk factors related to the disease was assessed by an interviewer administered questionnaire. Expectorated sputum was processed on supplemented buffered charcoal yeast extract medium and urine specimens were tested for Legionella pneumophila serogroup 1 antigen. Fifty-six percent of the patients were males and 91% were residing in urban areas. Smoking was admitted by 32% and that of alcohol consumption was in 25%. Composting and potting, distant travelling and frequent use of air conditioning was reported in 28%, 37% and 4% respectively. Majority of participants were not exposed to cooling towers, humidifiers or plumbing and not visited high risk areas. Among the study group, 21% had diabetes, 24% had ischaemic heart disease and 36% had chronic lung diseases. None of the sputum samples grew Legionella pneumophila, and all urine samples were negative for the antigen of Legionella pneumophila serogroup 1. It is concluded that, in this population of community acquired atypical pneumonia, Legionella pneumophila was not identified as a causative agent.

KEYWORDS: *Atypical pneumonia, community acquired pneumonia, Legionella pneumophila*

Corresponding author: Kottahachchi J, Email: jananie@sjp.ac.lk

1 INTRODUCTION

Atypical pneumonia accounts for about 30%-40% of cases of community acquired pneumonia (CAP) (Journal of the Association of Physicians of India 2013). *Mycoplasma pneumoniae, Legionella pneumophila, Chlamydophila pneumoniae, Chlamydophila psittaci, Coxiella burnetii* and viruses are recognised as common responsible pathogens. These organisms can cause infections alone or in combination with typical pathogens causing CAP (Esposito et al. 2002).

Legionella pneumophila has been increasingly recognized throughout the world as an important cause of sporadic and epidemic community-acquired pneumonia (Carratalà & Garcia-Vidal 2010). The severity of the disease varies from Pontiac fever, which is a mild febrile illness to Legionnaires' disease, a potentially fatal form of pneumonia which is mainly caused by *Legionella pneumophila* serogroup 1. This is the pathogen most frequently associated with early treatment failure caused by inappropriate empirical therapy for pneumonia (Roson et al. 2004). Moreover, it is known that clinical manifestations alone are unreliable in diagnosing Legionnaires' disease (Carratalà & Garcia-Vidal 2010).

The infection has been reported in all age groups and in both healthy and immunosuppressed hosts (Sopena et al. 2005). Transmission of the infection occurs when droplets or aerosols containing legionella bacteria are inhaled and deposited in the lungs on exposure to contaminated environmental source. Patients with legionella pneumonia are generally found in clusters and the infection does not transmit from person-to-person; however, can be related to exposure to the same source of infection. Severe legionella infections have been reported to occur as sporadic cases among previously healthy people, including young people without underlying disease or other known risk factors (Falguera et al. 2001). The mortality rate depends on the severity of the infection, mode of acquisition, late diagnosis and treatment and the presence of other risk factors (Fernandez et al. 2002, Edelstein & Roy 2015).

Legionellae are ubiquitous in the environment and the major natural reservoir is water at temperatures ranging from 5° C to more than 50°C (Fields, Benson & Besser 2002). Rainfall is identified as a significant risk factor for sporadic infections (Garcia-Vidal et al. 2013). The bacteria are found in many different natural and artificial aquatic environments such as cooling towers, water systems in hotels, homes, ships and factories, respiratory therapy equipment, fountains, misting devices, and spa pools. Certain behavioral conditions such as smoking, alcoholism and recreational activities too are proven to favour the acquisition of the disease (Fields, Benson & Besser 2002, Nguyen et al. 2006, Straus et al. 1996, Edelstein & Roy, 2015).

Being a fastidious organism, *Legionella* does not grow on ordinary media used in routine diagnostic procedures and, on the contrary, requires special media for growth. Therefore, diagnostic laboratory

tests for legionella including culture in special media, urinary antigen test and molecular methods should be applied to all patients with atypical pneumonia for definitive diagnosis.

As a country with a considerably high rain fall, Sri Lanka can be considered as a high-risk area; however, there is a paucity of data on the prevalence of the legionella infection in relation to atypical pneumonia. In view of its notifiable presence found all over the world, as well as the high morbidity and mortality with suboptimal treatment (Roson et al. 2004), efforts to identify the pathogen and proper management of legionella pneumonia should remain a focus of major interest in Sri Lanka. The intention of this study was to determine the proportion of *Legionella pneumophila* and the associated risk factors among the patients admitted with atypical pneumonia to a tertiary care hospital in Sri Lanka.

2 MATERIALS AND METHODS

2.1 Patients and Study Setting

The study included 75 adult patients who were admitted to the professorial medical unit of Colombo South Teaching Hospital, Sri Lanka from January to October 2016. The patients were selected according to the clinical decisions made by the attending physicians. Previously healthy male and female patients who had signs, symptoms, and chest radiograph findings consistent with atypical pneumonia were considered eligible for inclusion. The exclusion criteria were typical pneumonia identified by isolation of the causative organisms, health care associated infections, immunosuppressed status (neutropenia, patient with splenectomy, use of systemic steroids, use of myelosuppressive drugs, solid organ transplantation or positive blood test for HIV) and use of antibiotics within 48 hours before admission.

Expectorated sputum and a urine sample each were collected from the patients within 24 hours of admission and the specimens were dispatched to the laboratory within 4 hours of collection. Processing of the specimens was carried out at Microbiology laboratory of the Department of Microbiology, Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka.

2.2 Questionnaire

An interviewer administered questionnaire was forwarded to participating patients to gather demographic data and to assess the risk factors related to legionella infection. Risk factors related to behavior, exposure, visiting crowded areas and underline comorbities were assessed.

2.3 Sputum Analysis

Good quality sputum specimens were selected according to Murray and Washington criteria and were processed on supplemented buffered charcoal yeast extract (BCYE) medium, the selective medium for Legionella. Plates were examined on the following day and they were incubated for up to 7 days observing daily for growth. Characteristic small, gray to white iridescent colonies which are catalase positive and oxidase negative and showing Gram negative, pleomorphic filamentous bacilli on Gram staining were

the morphological identification features of the expected growth. Colonies of *Legionella pneumophila* serogroup 1 were to be further diagnosed by co-agglutination with *Legionella pneumophila* serogroup 1 specific antisera (DRO 200 M) and other Legionella species were to be diagnosed by co-agglutination with *Legionella* specific antisera (DRO 220 M). All the media and reagents were quality controlled by a known strain of *Legionella* spp.

2.4 Urine Analysis

Urine specimens collected were tested for the presence of the *Legionella pneumophila* serogroup 1 antigen using a commercially available antigen detection kit (XPECT legionella R24680). Positive and negative controls were performed according to the manufacturer's instructions.

2.4 Data Analysis

Proportion of relevant information of the questionnaire was analyzed.

3 RESULTS & DISCUSSION

RESULTS

3.1 Patient Characteristics

In the study group, 56% (n=43) were males and mean age was 53 years (range 18-88 years). Sixty-four percent (n=48) of patients were not occupied. Permanent residence of 97% (n=73) was Western Province; 91% (n=68) being residing in urban areas.

Table 1*: Level of education in study participants*

Level of Education	N	(%)
Graduated	2	3%
GCE A/L Passed	9	12%
GCE O/L Passed	24	32%
Grade 6-11	19	25%
Grade 1-5	16	21%
Never been to school	5	7%

Seven percent (n=5) of study subjects had never been to school while studying up to Grade 5, attending up to Grade 6-11, getting through GCE (Ordinary Level) and getting through GCE (Advanced Level) had been reported in 21% (n=16), 25% (n=19), 32% (n=24) and 12%(n=9) respectively. Only two of them were graduates (3%).

3.2 Assessing Risk Factors

***Table 2**: Activities engaged by study participants*

	Activities engaged						
	Smoking	**Alcohol**	**Spa pools**	**Thermal pools**	**Composting & potting**	**Distant travelling**	**A/C related activities**
Yes	24	19	0	0	21	28	3
No	51	56	75	75	54	47	72
Yes %	32%	25%	0%	0%	28%	37%	4%
No %	68%	75%	100%	100%	72%	63%	96%

In the study group, 32% were smokers while 25% consumed alcohol. None of the participants used spa pools or thermal pools. However, composting and potting, distant travelling and frequent use of air conditioning was admitted by 28%, 37% and 4% respectively.

***Table 3**: Frequency of exposure to risk factors by study participants*

	Frequency of risk factor exposure			
	A/C	**Cooling towers**	**Humidifiers**	**Plumbing**
Never	20	53	65	60
Rarely	25	8	8	9
Occasionally	15	6	0	5
Frequently	15	8	2	1
Never %	27%	71%	87%	80%
Rarely %	33%	11%	11%	12%
Occasionally %	20%	8%	0%	7%
Frequently %	20%	11%	3%	1%

Out of the study participants, 27%, 71%, 87% and 80% had never been exposed to air conditioning, cooling towers, humidifiers and plumbing respectively.

***Table 4**: Visited areas considered as risky by study participants*

	Visited areas								
	Industrial sites	**Shopping complexes**	**Air travel**	**Restaurants**	**Clubs**	**Leisure centres**	**Sports clubs**	**Salons**	**Cinema halls**
Yes	11	29	4	13	1	1	2	0	3
No	64	46	71	62	74	74	73	75	72
Yes %	15%	39%	5%	17%	1%	1%	3%	0%	4%
No %	85%	61%	95%	83%	99%	99%	97%	100%	96%

Majority of study subjects had not visited areas considered to be of high risk to acquire legionella disease whereas 39% of them visited shopping complexes.

***Table 5**: Comorbidities declared by study participants*

	Comorbidities								
	Diabetes	**IHD**	**Chronic lung disease**	**Chronic renal failure**	**Haematological malignancy**	**Cancer**	**Iron overload**	**Recent surgery**	**Organ transplnt**
Yes	16	18	27	2	0	1	1	5	0
No	58	57	48	73	75	74	74	70	75
Yes %	21%	24%	36%	3%	0%	1%	1%	7%	0%
No %	77%	76%	64%	97%	100%	99%	99%	93%	100%

Most of the patients denied having comorbidities; however, frequent findings were diabetes among 21%, ischaemic heart disease in 24% and chronic lung disease in 36% of them.

***Table 6**: Previous exposure to risk factors while admission to hospital*

	Comorbidities								
	Diabetes	**IHD**	**Chronic lung disease**	**Chronic renal failure**	**Haematological malignancy**	**Cancer**	**Iron overload**	**Recent surgery**	**Organ transplant**
Yes	16	18	27	2	0	1	1	5	0
No	58	57	48	73	75	74	74	70	75
Yes %	21%	24%	36%	3%	0%	1%	1%	7%	0%
No %	77%	76%	64%	97%	100%	99%	99%	93%	100%

Eight percent of the study population was ventilated earlier, while 60% had undergone nebulisation and 16% had history of treatment with respiratory devises.

3.2 Microbiological Investigations

Out of 75 good quality sputum samples processed on supplemented buffered charcoal yeast extract (BCYE) medium, none grew Legionella species irrespective of incubation of up to 7 days.
The urine specimens of all 75 patients gave negative results with the urinary antigen detection kit.

Although all the patients with atypical pneumonia admitted to the study setting during the study period from January to October 2016 were included (75), none of them were positive for legionella infections, hence zero prevalence in the study group was noticed.

DISCUSSION

This study was conducted to provide an insight to the presence of legionella pneumonia among patients with community acquired atypical pneumonia (CAAP) admitted to a tertiary care hospital; however, the infection was not detected among the study group.

Clinical diagnosis of atypical pneumonia is difficult despite it being contributing to nearly half of CAP (Marrie et al. 1996). Empirical therapy covering both typical and atypical pathogens for all hospitalized patients with CAP was recommended by Arnold FW et al.in 2007 (Arnold et al. 2007). One research in Korea detected atypical pathogens in 18.5% of patients requiring admission to hospital with CAP (Lee et al. 2002).

Studies conducted on CAP globally reported different frequencies of legionella infection which could be attributed to the different study population and the techniques used to diagnose the condition.

Although Legionnaires' disease contributes only to 1% to 5% of CAP, it still occurs both in sporadic and epidemic forms, sometimes involving a large number of victims (Castilla et al. 2008). In the UK, the infection accounts for about 3% of cases of CAPs each year with a case fatality rate of 10-15% exceeding 30% in certain risk groups (Lim et al. 2001). In United States, the proportion due to Legionnaires' disease has been reported ranging from 2 to 15% being the most important water-related pulmonary pathogens in the country (Butler & Breiman 1998, Edelstein & Roy 2015). Another prospective study conducted for 15 years revealed the infection in 5.4% of all cases of CAP (Viasus et al. 2013). A worldwide survey in 21 countries concluded a range of 3-9% of leigionella infection among 20-28% of atypical pneumonia cases (Arnold et al. 2007); further in Egypt 6% was demonstrated (Zaki & Goda 2009).

In Asia, community acquired pneumonia due to legionella infection is comparatively low. Accordingly, a Korean study did not reveal a single case (Lee et al. 2002). The same was found in Pakistan with no legionella infected cases reported out of 29% atypical pathogens which led to suggestion of modifying local guidelines to include anti-microbial coverage to consider atypical pathogens with less concern for legionella (Zubairi et al. 2012).

First isolation of *Legionella pneumophila* in Sri Lanka was from environmental water samples and revealed positive from 57.4% of selected hotels and 38.4% of selected cooling towers (Wahala & Wickramasinghe 2000). Further, a study enrolling 80 patients with CAP in a tertiary care hospital in the country did not reveal any case of legionella (Dissanayake et al. 2016). Similarly, the current study did not find a single case of legionella infection in the study group.

A characteristic epidemiological pattern in patients strongly relating to contact with compost (52%) and less frequently to travel (6·5%) was found from a 10-year survey in New Zealand (Graham et al. 2011). Although the current study did not diagnose legionella infected patients, 28% of the study group had been exposed to composting and potting, while 37% revealed distant travelling. Fields BS in 2002 reported that the organism is found at high concentration as 10^2 to 10^8 colony forming units /L in air conditioning cooling towers (Fields, Benson & Besser 2008). A large outbreak that occurred in France confirmed a strong association of cooling towers, smoking and staying outdoors (Nguyen et al. 2006) while another series detecting sporadic cases over 15 years discovered that 7.4% patients were travel-associated (Viasus et al. 2013). Despite confirming the relationship of the disease with cooling towers, water faucets and other activities associated with water in several publications (Straus et al. 1996) the current results deny those, reporting only 11% and 1% frequent association with cooling towers and plumbing respectively.

Several reports highlighted risk factors for community-acquired and travel-associated legionellosis as smoking, heavy alcohol consumption, immuno-suppression, and chronic respiratory or renal diseases

(Straus et al. 1996, El-Ebiary et al. 1997). Viasus et al. in 2013 concluded that at least a single comorbid factor was present in 55.6% patients with legionella infection, including chronic heart disease, diabetes mellitus, and chronic pulmonary disease, while the majority (72.8 %) being smokers (Viasus et al. 2013). Of note, smokers were more likely to develop pneumonia due to *Legionella* spp. (Straus et al. 1996). Among the patients in our research, however, a relative low rate of smoking (32%) was noted. This would have contributed to the absence of the pathogen in the population of the current study.

Given the fact that culture is the best method, it is remarkable that Bartlett and Mundy reporting even sophisticated laboratories missing organism detection in 32% instances despite using pure cultures (Bartlett & Mundy 1995). Murdoch DR described that legionella infection is under recognized and combination of urinary antigen tests, sputum culture, and PCR testing of lower respiratory tract samples favours the diagnosis (Murdoch 2003). An Indian study revealed 17.69% antigenuria, 27.43% seropositivity and no culture positivity (Javed et al. 2010). A recent Sri Lankan research too did not yield legionella from culture or urinary antigen (Dissanayake et al. 2016). Similarly, the current study did not find positive results in spite of combining culture with urinary antigen detection.

It is noteworthy that clinical features do not constantly distinguish legionella pneumonia from that caused by other bacteria (Edelstein & Roy 2015). Of the available investigations, sensitivity and specificity for culture, urinary antigen detection, immunofluorescent microscopy and molecular amplification methods are 20%-95% and 100%, 60%-95% and >99%, 20%-50% and 99% and 70%-95% and 90%-95% respectively. Center for Disease Control and Prevention recommends obtaining both sputum for culture and urine for the urinary antigen test concurrently (Center for Disease Control and Prevention). A prospective study involving 3934 cases concluded that sensitivity of urinary antigen detection is superior to culture or serologic testing (Viasus et al. 2013).

Nevertheless, regardless of testing both the culture and the urinary antigen detection, the current study did not detect *Legionella pneumophila* serogroups from the enrolled patients presented with CAAP. Accordingly, the importance of associated risk factors in this population could not be evaluated. The exact low prevalence of this population needs to be elucidated; however, we suggest that selecting patients from a single center during a limited time period would have contributed for the outcome.

4 CONCLUSIONS

Among the patients with CAAP, *Legionella pneumophila* serogroups were not identified in the selected study population, hence the proportion of the infection in Sri Lanka may be very low. However extensive studies involving many centers should be conducted to confirm the exact situation.

ACKNOWLEDGMENTS

The authors acknowledge the Medical Research Institute, Colombo, Sri Lanka for the research grant (Project No. 41/2014)**.** The assistance provided by the staff of the Colombo South Teaching Hospital is greatly appreciated.

REFERENCES

Arnold, FW, Summersgill, JT, LaJoie, A S, Peyrani P, Marrie TJ, Rossi P. et al. and the Community-Acquired Pneumonia Organization (CAPO) Investigators 2007, 'A Worldwide Perspective of Atypical Pathogens in Community-acquired Pneumonia', *American Journal of Respiratory and Critical Care Medicine*, vol.175, no.10, pp. 1086–1093. Available from: https://www.atsjournals.org/doi/full/10.1164/rccm.200603-350OC. [06 April 2021].

Atypical pneumonia, 2013, Supplement to *Journal of the association of physicians of India*, vol.61, pp.28-31. Available from: https://www.japi.org/oldwebsitecontent/july_special_issue_2013_community_acquired_pneumonia/10_atypical_pneumonia.pdf. [07April 2021].

Bartlett, JG, & Mundy, LM 1995, 'Community-acquired pneumonia', The *New England Journal of Medicine*, vol. 333, no. 24, pp. 1618-1634. Available from: https://www.nejm.org/doi/full/10.1056/NEJM199512143332408. [07April 2021].

Butler, J, & Breiman, RF 1998, 'Legionellosis', in Evans AS & Brachman PS (eds) *Bacterial infections in humans: epidemiology and control*. *3rd Ed.*, pp. 355–376. Plenum Medical Book Company, New York, N.Y.

Carratalà, J, Garcia-Vidal, C 2010, 'An update on Legionella', *Current Opinion in Infectious Diseases*, vol. 23, no. 2, pp. 152–157. Available from: https://pubmed.ncbi.nlm.nih.gov/20051846/. [07April 2021].

Castilla, J, Barricarte, A, Aldaz, J, Garcia Cenoz, M, Ferrer, T, Pelaz, C. et al. 2008, 'A large Legionnaires' disease outbreak in Pamplona, Spain: Early detection, rapid control and no case fatality', *Epidemiology and Infection*, vol. 136, no. 6, pp. 823-832. Available from: https://www.cambridge.org/core/journals/epidemiology-and-infection/article/large-legionnaires-disease-outbreak-in-pamplona-spain-early-detection-rapid-control-and-no-case-fatality/D33D97D9C5713A2B2EA5AF36AD9A12C3. [07April 2021].

Center for Disease Control and Prevention (CDC), 'Legionella (Legionnaires'Disease and Pontiac Fever)'. Available from: https://www.cdc.gov/legionella/clinicians/diagnostic-testing.html. [03 April 2020].

Dissanayake BN, Jayawardena, DE, Senevirathna, CG & Gamage, TM 2016, 'Community acquired pneumonia due to Legionella pneumophila in a tertiary care hospital', *Sri Lankan Journal of Infectious Diseases*, vol. 6, no. 2, pp. 101-105. Available from: https://sljid.sljol.info/articles/abstract/10.4038/sljid.v6i2.8112/. [07April 2021].

Edelstein, PH & Roy, CR 2015, 'Legionnaires' Disease and Pontiac Fever' in Bennett JE, Dolin R, Blaster MJ (eds), *Mandell, Douglas, and Bennett's principles and practice of infectious diseases. Vol.2. 8th Ed.,* pp. 2633- 2644. Elsevier Saunders. Philadelphia PA.

El-Ebiary, M, Sarmiento, X, Torres, A, Nogué, S, Mesalles, E, Bodí, M et al. 1997, 'Prognostic Factors of Severe Legionella Pneumonia Requiring Admission to ICU', *American Journal of Respiratory and Critical Care Medicine*, vol. 156, no. 5, pp. 1467–1472. Available from: https://pubmed.ncbi.nlm.nih.gov/9372662/. [07April 2021].

Esposito, S, Bosis, S, Cavagna, R, Faelli, N, Begliatti, E, Marchisio P. et al. 2002, 'Characteristics of *Streptococcus pneumoniae* and Atypical Bacterial Infections in Children 2–5 Years of Age with Community-Acquired Pneumonia', *Clinical Infectious Diseases*, vol. 35, no. 11, pp. 1345–52. Available from: https://academic.oup.com/cid/article/35/11/1345/428092. [07April 2021].

Falguera, M, Sacristan, O, Nogues, A, Ruiz-Gonzales, A, Garcia, M, Manonelles, A, et al. 2001, 'Nonsevere community-acquired pneumonia: correlation between cause and severity or comorbidity', *Archives of Internal Medicine*, vol. 161, no.15, pp.1866–1872. Available from: https://pubmed.ncbi.nlm.nih.gov/11493128/. [07April 2021].

Fernandez, J, Lopez, P, Oroxco, D & Merino, J 2002, 'Clinical study of an outbreak of Legionnaires' disease in Alcoy, Southeastern Spain' *European Journal of Clinical Microbiology and Infectious Diseases*, vol. 21, no. 10, pp.729–735. Available from: https://pubmed.ncbi.nlm.nih.gov/12415472/. [07April 2021].

Fields, BS, Benson, RF, Besser, RE 2002, 'Legionella and Legionnaires' disease: 25 years of investigation', *Clinical Microbiology Review*, vol. 15, no.3, pp. 506-526. Available from: https://cmr.asm.org/content/15/3/506. [07April 2021].

Garcia-Vidal, C, Labori, M, Viasus, D, Simonetti, A, Garcia-Somoza, D, Dorca J, et al. 2013, 'Rainfall Is a Risk Factor for Sporadic Cases of Legionella pneumophila Pneumonia', *PLOS ONE | www.plosone.org.*, vol. 8, no. 4, pp. e61036. Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0061036. [14 April 2021].

Graham, FF, White, PS, Harte, DJ & Kingham, SP 2012, 'Changing epidemiological trends of legionellosis in New Zealand, 1979-2009', *Epidemiology and Infection*, vol.140, no. 8, pp. 1481-96. Available from: https://www.cambridge.org/core/journals/epidemiology-and-infection/article/changing-epidemiological-trends-of-legionellosis-in-new-zealand-19792009/5A2612870D7C9ADDCC47661ACAE65E06. [07April 2021].

Javed, S, Chaudhry, R, Passi, K, Sharma, S, Padmaja, K, Dhawan, B, et al. 2010, 'Sero diagnosis of Legionella infection in community acquired pneumonia', *Indian Journal of Medical Research*, vol. 131, pp. 92-96. Available from: https://pubmed.ncbi.nlm.nih.gov/20167980/. [07April 2021].

Lee, SJ, Lee, MG, Jeon, MJ, Jung, KS, Lee, HK & Kishimoto, T 2002, 'Atypical pathogens in adult patients admitted with community acquired pneumonia in Korea', *Japanese Journal of Infectious Diseases*, vol. 55, no. 5, pp.157—159. Available from: https://pubmed.ncbi.nlm.nih.gov/12501255/. [07April 2021].

Lim, WS, Macfarlane, JT, Boswell, TC, Harrison, TG, Rose, D, Leinonem, M, et al. 2001, 'Study of community acquired pneumonia aetiology (SCAPA) in adults admitted to hospital: implications for management guidelines' *Thorax*, vol. 56, pp. 296–301. Available from: https://thorax.bmj.com/content/56/4/296. [07April 2021].

Marrie, TJ, Peeling, RW, Fine, MJ, Singer, DE, Coley, CM & Kapoor, WN 1996, 'Ambulatory patients with community-acquired pneumonia: the frequency of atypical agents and clinical course', *The American Journal of Medicine*, vol. 101, no. 5, pp. 508—515. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0002934396002550. [07April 2021].

Murdoch, DR 2003, 'Diagnosis of Legionella infection', *Clinical Infectious Diseases*, vol. 36, no.1, pp. 64-69. Available from: https://academic.oup.com/cid/article/36/1/64/283769. [07April 2021].

Nguyen, TMN, Ilef, D, Jarraud, S, Rouil, L, Campese, C, Che, D, et.al. 2006, 'A Community-Wide Outbreak of Legionnaires Disease Linked to Industrial Cooling Towers— How Far Can Contaminated Aerosols Spread?', *The Journal of Infectious Diseases*, vol. 193, no.1, pp. 102–111. Available from: https://academic.oup.com/jid/article/193/1/102/863674. [07April 2021].

Roson, B, Carratala, J, Fernandez-Sabe, N, Tubau, F, Manresa, F & Gudiol, F 2004, 'Causes and factors associated with early failure in hospitalized patients with community-acquired pneumonia', *Archives of Internal Medicine*, vol. 164, no. 5, pp. 502–508. Available from: https://www.researchgate.net/publication/7748062_Causes_and_Factors_Associated_With_Early_Failure_in_Hospitalized_Patients_With_Community-Acquired_Pneumonia. [07April 2021].

Sopena, N, Pedro-Botet, L, Mateu, L, Tolschinsky, G, Rey-Joly, C & Sabria, M 2007, 'Community-acquired legionella pneumonia in elderly patients: characteristics and outcome', *Journal of the American Geriatrics Society*, vol. 55, no. 1, pp. 114–119. Available from: https://pubmed.ncbi.nlm.nih.gov/17233694/. [07April 2021].

Straus, WL, Plouffe, JF, File Jr, TM, Lipman, HB, Hackman, BH, Salstrom, SJ, et al. 1996, 'Risk factors for domestic acquisition of legionnaires disease. Ohio Legionnaires Disease Group', *Archives of Internal Medicine*, vol. 156, no. 15, pp. 1685-1692. Available from: https://pubmed.ncbi.nlm.nih.gov/8694667/. [07April 2021].

Viasus, D, Yacovo, SD, Garcia-Vidal, C, Verdaguer, R, Manresa, F, Dorca, J, et al. 2013, 'Community-Acquired Legionella pneumophila Pneumonia. A Single-Center Experience With 214 Hospitalized Sporadic Cases Over 15 Years', *Medicine (Baltimore)*, vol. 92, no. 1, pp. 51-60. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5348137/. [07April 2021].

Wahala, WM & Wickramasinghe, RS 2000, 'First isolation of Legionella pneumophila in Sri Lanka', *Ceylon Medical Journal*, vol. 45, no. 4, pp.171-172. Available from: file:///C:/Users/FMS_Desk/Downloads/6724-23764-1-PB.pdf. [07April 2021].

Zaki, MES & Goda, T 2009, 'Clinico-pathological study of atypical pathogens in community-acquired pneumonia: a prospective study', *Journal of Infection in Developing Countries*, vol. 3, no. 3, pp. 199-205. Available from: https://jidc.org/index.php/journal/article/view/19759475. [07April 2021].

Zubairi, ABS, Zafar, A, Salahuddin, N, Haque, AS, Waheed, S & Khan JA 2012, 'Atypical pathogens causing community-acquired pneumonia in adults', *Journal of the Pakistan Medical Association*, vol. 62, no. 7, pp. 653-656. Available from: https://ecommons.aku.edu/cgi/viewcontent.cgi?article=1296&context=pakistan_fhs_mc_med_med. [07April 2021].