Journal of Human Environment and Health Promotion
Print ISSN: 2476-5481 Online ISSN: 2476-549X

Pulmonary Infection of *Lophomonas blattarum* as a Co-infection with COVID-19 in Patients with Severe Pneumonia

Azam Heidari [a, b] | **Samad Ghodrati** [c] | **Ahmadreza Mobaien** [d] | **Asghar Fazaeli** [b *]

a. Social Determinants of Health Research Center, Health and Metabolic Diseases Research Institute, Zanjan University of Medical Sciences, Zanjan, Iran.
b. Department of Medical Parasitology & Mycology, Medical School, Zanjan University of Medical Sciences, Zanjan, Iran.
c. Department of Internal Medicine, Medical School, Zanjan University of Medical Sciences, Zanjan, Iran.
d. Department of Infectious Diseases, Medical School, Zanjan University of Medical Sciences, Zanjan, Iran.

***Corresponding author:** Department of Medical Parasitology & Mycology, School of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran. Postal Code: 4513956111. E-mail: fazaeli@zums.ac.ir

ARTICLE INFO

Article type:
Original article

Article history:
Received: 14 March 2024
Revised: 3 April 2024
Accepted: 20 April 2024

https://doi.org/10.61186/jhehp.10.2.79

Keywords:

Lophomonas blattarum
COVID-19
Pulmonary Infection
Co-infection
Severe pneumonia

ABSTRACT

Background: *Lophomonas blattarum* is a newly reported opportunistic protozoan parasite that may cause pulmonary infections. Co-morbidity of this parasite and pulmonary viral infections, such as COVID-19 may exacerbate their pathological effects. This study aimed to evaluate the prevalence of *L. blattarum* infection in patients with COVID-19 infection.

Methods: In this study, mini bronchoalveolar lavage (mini-BAL) samples were taken from 93 patients with acute pneumonia due to COVID-19 infection in 2021. The samples were subjected to microscopic examination for the presence of *L. blattarum*, following smear preparation and staining with two specific methods of Giemsa and Papanicolao.

Results: The patients included 49 males and 44 females with a mean age of 68.8 ± 14.8 years. Of the specimens studied after staining, only one specimen (1.08%) was positive for *L. blattarum*. It was found in a patient with diabetic underlying disease.

Conclusion: It was concluded that the infection of *L. blattarum* in patients with severe COVID-19 pneumonia was low. However, the presence of this parasite in this group of patients should not be neglected. This is the first report of pulmonary infection with this protozoan parasite in Zanjan Province.

1. Introduction

A report of pneumonia with unknown cause was recorded as an emerging disease in a group of patients in Wuhan, Hubei Province, China, on December 30, 2019. Analysis of samples taken from the lower respiratory tract of these patients revealed a novel coronavirus that was named coronavirus 2019 or COVID-19 by the World Health Organization (Song et al., 2020). This infection is associated with viral pneumonia in most debilitated individuals, some elderly and underlying patients. It causes acute respiratory distress syndrome (ARDS), organ dysfunction, and eventual death. However, this infection is asymptomatic in many cases (Singhal, 2020). Underlying diseases, such as diabetes, hypertension, and cardiovascular disease, have been reported as risk factors associated with disease severity and death (Gebrecherkos et al., 2021). Despite extensive research conducted on various aspects of the COVID-19 pandemic, including clinical features, diagnostic methodologies, vaccine development, and evaluation of various anti-covid compounds, only limited investigations have been performed on the co-infection of SARC-COV-2 with other pathogens, including parasites (Zhu et al., 2020). Such co-infections may alter the immune response to SARS-COV-2 infection by directly modulating host immune responses (Gebrecherkos et al., 2021). *Lophomonas blattarum* is an

How to cite: Heidari A, Ghodrati S, Mobayen A, Fazaeli A. Pulmonary Infection of *Lophomonas blattarum* as a Co-infection with COVID-19 in Patients with Severe Pneumonia. *J Hum Environ Health Promot.* 2024; 10(2): 79-82.

emerging hypermastigote protozoan that, although rare, is one of the important causes of pulmonary respiratory infections, especially in immunocompromised individuals. This protozoan has multiple flagella and lives in the midgut of arthropods such as termites and cockroaches. It has two biological stages: cyst and trophozoite. the former is infectious and transmissible to humans, while the latter causes clinical damage in the lungs (Martinez-Girón & van Woerden, 2013). The common laboratory diagnostic method of this protozoan is based on microscopic observation of the organism in stained smears (Alam-Eldin & Abdulaziz, 2015). In recent years, infections of the upper and lower respiratory tract caused by *Lophomonas* have emerged from various parts of the world, notably China and Iran, with the latter reporting a relatively higher incidence (Nakhaei et al., 2021). This discrepancy may, however, be attributed to the widespread presence of the German beetle (*Blatella germanica*) in houses throughout Iran, which is also a carrier of *L. blattarum* (Fakhar et al., 2021). However, the accuracy of this hypothesis remains uncertain due to the limited number of studies and populations surveyed for *L. blattarum* investigation, with published studies mostly including case reports. Furthermore, apart from a single case report (Nakhaei et al., 2021), no information is available on the co-occurrence of this parasitic infection with COVID-19 pneumonia. Therefore, this study was designed to evaluate the prevalence of *L. blattarum* in patients admitted to the intensive care units (ICU) with severe pneumonia due to COVID-19 infection.

2. Materials and Methods

2.1 Participants

In this descriptive cross-sectional study, a total of 93 patients admitted to the ICUs of Vali-e-Asr Hospital in Zanjan due to acute pneumonia caused by COVID-19 infection were subjected to the study. This hospital was selected as the major medical center for COVID-19 patients in Zanjan province, given the high number of admissions and hospitalizations since the disease epidemic in February 2020. Demographic data, including sex, age, history of underlying diseases, and clinical characteristics of the patients were recorded in a special questionnaire for every individual.

2.2 Sample collection

After coordination with the relevant hospital officials, a pulmonologist obtained mini-BAL specimens from the patients. The samples were collected in Falcon tubes and transferred to the laboratory under controlled conditions and specialized packaging.

2.3 Laboratory examination

To prepare the samples, an equal volume of sterile saline was added to each sample in a Falcon tube. The mixture was then vortexed and centrifuged at 3000 rpm for 15 min. Consequently, the supernatant solution was gently discarded in a detergent container containing 10% sodium hypochlorite, and the remaining sediment was spread onto glass slides by a disposable micro-pipette. The smears were dried under the hood and fixed with methanol, followed by Giemsa and Papanicolao staining using kits purchased from Bahar Afshan Company (Iran). The staining methods were performed according to the manufacturer's instructions. All sample processing steps were performed under a safety hood. The stained samples were examined under a light microscope, using emersion oil with × 1000 magnification, to detect *L. blattarum* trophozoites.

3. Results and Discussion

The participants of the study included 49 males and 44 females with a mean age of 68.8 ± 14.8 years, 66 and 71 years for males and females, respectively. The age group distribution is mentioned in Table 1.

Table 1. Sex and age group distribution of the COVID-19 patients surveyed for *L. blattarum* co-infection

Sex Age (year)	Male	Female	Total
	No	No	No
20-30	2	1	3
31-40	1	0	1
41-50	7	0	7
51-60	8	7	15
61-70	9	13	22
> 70	22	23	45
Total	49 (52.7%)	44 (47.3%)	93 (100%)

The proportions of underlying diseases among the studied COVID-19 patients are mentioned in Figure 1. Heart disease and hypertension were the most frequent ones (29 out of 93 cases), followed by diabetes in 21, lung disease in 13, cancer in 4, kidney transplant in 2, and other diseases (i.e. thyroid, stroke, and physiological problems) in 9 cases. Fifteen patients had no history of underlying diseases.

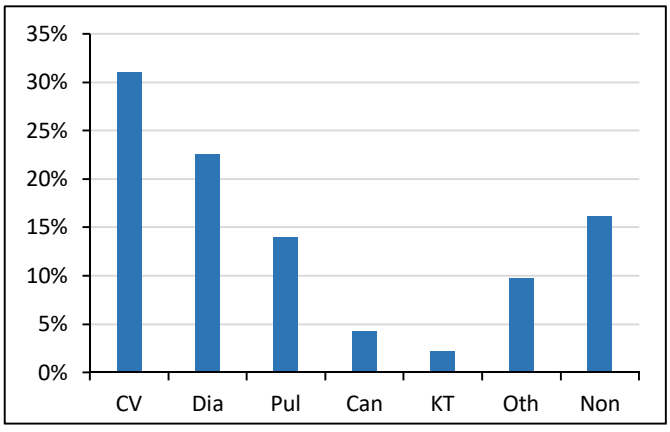

Figure 1. The percentage of underlying diseases associated with COVID-19 in patients surveyed for *L. blattarum* detection. CV: cardiovascular diseases; Dia: diabetes; Pul: pulmonary disease; Can: cancer; KT: kidney transplant; Oth: other underlying diseases; Non: non-underlying diseases

Examination of the stained smears provided from mini-BAL specimens under a light microscope resulted in the detection of one case of *L. blattarum* (1.08%) in COVID-19 patients (Figure 2). The positive specimen belonged to a patient with a history of diabetes. This is the first report of pulmonary infection with this protozoan parasite in Zanjan Province. Meanwhile, findings of the present study indicate that infection with *L. blattarum* is not high in Covid-19 patients.

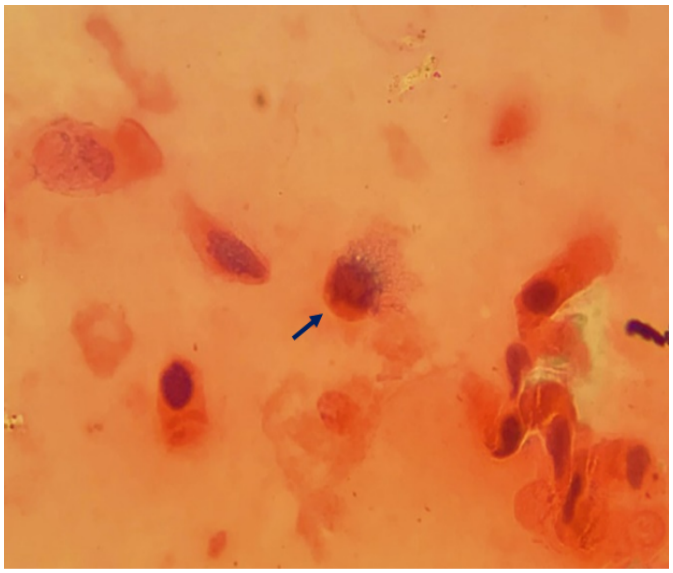

Figure 2. A positive microscopic slide was obtained from a mini-BAL specimen of a COVID-19 patient and stained with Papanicolao for the detection of *L. blattarum*. The arrow shows a trophozoite of *L. blattarum*. (× 1000)

Although the first article on *Lophomonas* was published in 1933, little is known about this parasite and its clinical consequences to most researchers and physicians around the world (Keighobadi et al., 2021). Some studies have been performed in groups of patients with pulmonary disorders other than COVID-19 in some areas during the last two decades. Most cases have been reported from China (Xue et al., 2014). A retrospective survey reported a total of 53 *L. blattarum* cases that were recorded in the Beijing Children′s Hospital from July 2014 through December 2016 (Ding & Shen, 2021). This infection has also been reported in Iran by some researchers since 2014. A case of sinusitis presented with *L. blattarum* infection was reported by Berenji *et al.* (2016a). Other cases were patients with different pulmonary problems, including a high rate of *L. blattarum* (35%) in patients with respiratory disorders admitted to hospitals in Mashhad, southwest Iran (Berenji et al., 2016b). In 40 asthmatic patients, using Geimsa-stained smears of sputum, this infection was 10% (Mirzazadeh et al., 2017). In 156 BAL specimens of children with respiratory symptoms, it was about 40% as reported in north east of Iran (Ghafarian et al., 2018). *L. blattarum* is one of the opportunistic organisms, probably more frequent in immunocompromised individuals (Li & Gao, 2016). Because the clinical signs of lophomoniasis such as fever, cough, shortness of breath, pulmonary obstruction (Martinez-Girón & van Woerden, 2013), and decreased CD4 + lymphocytes (Wang et al., 2006) are similar to the common symptoms of COVID-19 infection, it could be proposed that the combination of these two infections can be effective in the severity of COVID-19 disease and the deterioration of the patients' clinical condition. Some researchers have shown that 20 to 50 percent of patients with COVID-19 are diabetic, and diabetic patients are considered a high-risk group due to increased virus entry into their cells and decreased immunity (Agrawal et al., 2020). In our study, the patient with *L. blattarum* infection had a history of diabetes. As the diabetic factor can be a cause of a severely weakened immune system, the patient may have been susceptible to infection with unusual protozoa such as *L. blattarum*, although this cannot be a definite conclusion due to the small number of infections. It has been found that the plasma level of proinflammatory cytokines in COVID-19 patients admitted to the ICU is higher than that in normal individuals and even in COVID-19 patients admitted to non-ICU wards (Huang et al., 2020). Also, an increase in serum levels of IL-6 and a sharp decrease in the number of lymphocytes had a significant relationship with morbidity and mortality in these patients (Zhou et al., 2020). Metronidazole is the drug of choice for the treatment of *L. blattarum* infection; it can reduce the level of inflammatory cytokines such as IL-6 and, with its lymphocyte proliferation property, increase the number of circulating lymphocytes and strengthen the immune system (Gharebaghi et al., 2020). Therefore, early detection and specific treatment of *Lophomonas* infection can play a vital role in the treatment management of patients with acute pneumonia. So far, except for a few reported cases of co-infection of *L. blattarum* and COVID-19, no extensive study has been performed on these patients. Nakhaei *et al.* (2021) detected the parasite in a 33-year-old woman with severe COVID-19 infection. Sharifpour *et al.* (2021) detected another case of *Lophomonas* infection in the BAL sample of an Iranian patient with a history of heart disease and diabetes, who was hospitalized with recurrent symptoms of COVID-19. In our study, the rate of this parasitic infection in COVID-19 patients was 1.08%. This infection rate may be underestimated due to the use of microscopic detection-based techniques that are less sensitive than molecular methods.

4. Conclusion

It was concluded that the rate of co-infection of *L. blattarum* in patients with severe COVID-19 pneumonia in the study region was low. However, the presence of this parasite in this group of patients should not be neglected. Particularly in the cases that do not respond to conventional therapies and antibiotics, unusual protozoan infections such as *L. blattarum* should be considered and diagnostic measures and appropriate treatment should be used. Given the low rate of *Lophomonas* infection in this study, it is worth noting that microscopic examination may not be sufficiently sensitive, and using complementary DNA-based diagnostic methods would be suggested.

Authors' Contributions

Azam Heidari: Data curation; Investigation and Writing-original draft. Samad Ghodrati: Investigation & Resources. Ahmadreza Mobaien: Investigation & Resources. Asghar Fazaeli: Conceptualization; Supervision and Writing-review & editing.

Funding

This study is part of MSc thesis of A. Heidari. The proposal was approved and funded by the Research Council at Zanjan University of Medical Sciences. (code number: A-12-245-11).

Conflicts of Interest

There is no conflict of interest concerning this publication.

Acknowledgements

The authors greatly appreciate scientific and administrative supports provided by the Social Determinants of Health Research Center, Zanjan University of Medical Sciences, Zanjan, Iran. Our thanks also extended to the authorities of Zanjan Vali-e-Asr Hospital and COVID-19 ward who kindly facilitated this research.

Ethical considerations

This research project was confirmed by the Research Ethics Committee of Zanjan University of Medical Sciences. (Code number: IR.ZUMS.REC.1399.014).

References

1. Agrawal, D., Jaiswal, P., & Goyanka, B. (2020). Diabetes and covid-19: A review. *International Journal of Research in Pharmaceutical Sciences*, 376-379.

2. Alam-Eldin, Y. H., & Abdulaziz, A. M. (2015). Identification criteria of the rare multi-flagellate *Lophomonas blattarum*: comparison of different staining techniques. *Parasitology Research, 114*, 3309-3314.

3. Berenji, F., Parian, M., Fata, A., Bakhshaee, M., & Fattahi, F. (2016). First case report of sinusitis with *Lophomonas blattarum* from Iran. *Case Reports in Infectious Diseases*, 1-2.

4. Berenji, F., Fata, A., Vakili, V., Sayedi, S. J., Abdollahi, B., Imanfar, H., ... & Khorasani, S. R. (2016b). Unexpected high rate of *Lophomonas blattarum* in resistant upper and lower respiratory infection. *Health Sciences, 5*(9), 74-80.

5. Ding, Q., & Shen, K. (2021). Pulmonary infection with *Lophomonas blattarum*. *The Indian Journal of Pediatrics, 88*, 23-27.

6. Fakhar, M., Nakhaei, M., Sharifpour, A., Safanavaei, S., Abedi, S., Tabaripour, R., ... & Banimostafavi, E. S. (2021). Morphological and molecular identification of emerged *Lophomonas blattarum* infection in Mazandaran Province, northern Iran: first registry-based study. *Acta Parasitologica, 66*(4), 1510-1516.

7. Gebrecherkos, T., Gessesse, Z., Kebede, Y., Gebreegzabher, A., Tasew, G., Abdulkader, M., ... & Wolday, D. (2021). Effect of co-infection with parasites on severity of COVID-19. *MedRxiv*, 1-15.

8. Ghafarian, N., Bakhtiari, E., Berenji, F., Nakhaei, M., Nakhaei, B., Jamali-Behnam, F., & Sayedi, J. (2018). The study of *Lophomonas blattarum* infection in children with respiratory symptoms: a descriptive clinical study in north east of Iran. *International Journal of Pediatrics, 6*(6), 7797-7802.

9. Gharebaghi, R., Heidary, F., Moradi, M., & Parvizi, M. (2020). Metronidazole; a potential novel addition to the COVID-19 treatment regimen. *Archives of Academic Emergency Medicine, 8*(1), e40.

10. Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., ... & Cao, B. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet, 395*(10223), 497-506.

11. Keighobadi, M., Nakhaei, M., Sharifpour, A., Khasseh, A. A., Safanavaei, S., Tabaripour, R., ... & Fakhar, M. (2021). A bibliometric analysis of global research on *Lophomonas Spp.* in Scopus (1933-2019). *Infectious Disorders-Drug Targets (Formerly Current Drug Targets-Infectious Disorders), 21*(2), 230-237.

12. Li, R., & Gao, Z. C. (2016). *Lophomonas blattarum* infection or just the movement of ciliated epithelial cells?. *Chinese Medical Journal*, *129*(06), 739-742.

13. Martinez-Girón, R., & Cornelis van Woerden, H. (2013). *Lophomonas blattarum* and bronchopulmonary disease. *Journal of Medical Microbiology, 62*(11), 1641-1648.

14. Mirzazadeh, F., Berenji, F., Amini, M., Salehi, M., Shamsian, A., Fata, A., ... & Ghofraniha, L. (2017). *Lophomonas blattarum* in asthmatic patients and control group. *Journal of Research in Medical and Dental Science, 5*(5), 1-5.

15. Nakhaei, M., Fakhar, M., Sharifpour, A., Banimostafavi, E. S., Zakariaei, Z., Mehravaran, H., ... & Soleimani, M. (2022). First co-morbidity of *Lophomonas blattarum* and COVID-19 infections: confirmed using molecular approach. *Acta Parasitologica*, 1-4.

16. Sharifpour, A., Zakariaei, Z., Fakhar, M., Banimostafavi, E. S., Nakhaei, M., & Soleymani, M. (2021). Post-COVID-19 co-morbidity of emerged *Lophomonas* infection and invasive pulmonary aspergillosis: first case report. *Clinical Case Reports, 9*(9), e04822.

17. Singhal, T. (2020). A review of coronavirus disease-2019 (COVID-19). *The Indian Journal of Pediatrics, 87*(4), 281-286.

18. Song, F., Shi, N., Shan, F., Zhang, Z., Shen, J., Lu, H., ... & Shi, Y. (2020). Emerging 2019 novel coronavirus (2019-nCoV) pneumonia. *Radiology*, *295*(1), 210-217.

19. Wang, Y., Tang, Z., Ji, S., Zhang, Z., Chen, J., Cheng, Z., ... & Li, L. (2006). Pulmonary *Lophomonas blattarum* infection in patients with kidney allograft transplantation. *Transplant International, 19*(12), 1006-1013.

20. Xue, J., Li, Y. L., Yu, X. M., Li, D. K., Liu, M. F., Qiu, J. F., & Xue, J. J. (2014). Bronchopulmonary infection of *Lophomonas blattarum*: a case and literature review. *The Korean Journal of Parasitology, 52*(5), 521-525.

21. Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z., ... & Cao, B. (2020). Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet, 395*(10229), 1054-1062.

22. Zhu, X., Ge, Y., Wu, T., Zhao, K., Chen, Y., Wu, B., ... & Cui, L. (2020). Co-infection with respiratory pathogens among COVID-2019 cases. *Virus Research, 285*, 198005.