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Post-COVID-19 Bacterial Pneumonia: Diagnosis and Treatment

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Abstract

COVID-19 patients, particularly those with severe symptoms, are more susceptible to developing secondary bacterial infections due to weakened immune systems. Antibiotics are often used to treat these infections, but the overuse of antibiotics has led to the emergence of antibiotic-resistant bacterial strains. *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Legionella pneumophila* are some of the bacteria commonly associated with COVID-19. Post-COVID-19 bacterial pneumonia is a potential complication that may arise after a person has recovered from COVID-19. Post-COVID-19 antibiotic resistance is a growing concern in healthcare as a significant increase in resistance was found in the bacterial isolates to Amoxycillin, Cephalosporins, Carbapenems, Azithromycin, Clarithromycin, and Ciprofloxacin.

Keywords

Bacterial pneumonia; Amoxycillin; Bacterial strains; Bronchodilators

Introduction

Antibiotic resistance has been a long-standing concern in healthcare, with the emergence of new bacterial strains that are resistant to traditional antibiotics. However, the COVID-19 pandemic has brought to light a new turmoil of antibiotic resistance. The widespread use of antibiotics in COVID-19 patients, particularly prophylaxis use of antibiotics due to the fear of co-infection in those with severe symptoms, has contributed to the development of new, antibiotic-resistant bacterial strains. The use of antibiotics in COVID-19 patients has been extensive, as clinicians have been treating secondary bacterial infections and using antibiotics as a preventative measure. However, this practice has led to the emergence of antibiotic-resistant bacterial strains in post-COVID-19 patients. As these patients have weakened immune systems, they are more susceptible to infections, and antibiotic-resistant bacterial strains can cause severe and potentially fatal infections [1].

Several studies have shown that patients with severe COVID-19 symptoms are more likely to develop secondary bacterial infections, which are typically treated with antibiotics. However, the overuse of antibiotics in COVID-19 patients has contributed to the emergence of new, antibiotic-resistant bacterial strains [2-5].

Post-COVID-19 Bacterial Pneumonia:

One of the complications of COVID-19 is the development of bacterial pneumonia. When a person's immune system is weakened by COVID-19, they may be more vulnerable to developing a secondary bacterial infection in their lungs. *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Haemophilus influenzae*, *Klebsiella pneumoniae, Acinetobacter baumannii*, *Escherichia coli*, *Pseudomonas aeruginosa,* and *Legionella pneumophila* are some of the bacteria commonly associated with COVID-19 [1,6-13]. The most common isolate from such cases was *Streptococcus pneumoniae*, while *Staphylococcus aureus* can cause a variety of infections, including skin infections, pneumonia, and sepsis. *Klebsiella pneumonia* and *Staphylococcus aureus* are the bacteria isolated in COVID-19 patients who are hospitalized or who require ventilator support [13-16].

People with COVID-19 may also be more prone to bacterial pneumonia because they may be bedridden, have difficulty coughing up mucus, and have a weakened immune system. Although COVID-19 and bacterial pneumonia are different illnesses caused by different pathogens, they can both affect the respiratory system and cause similar symptoms such as cough, fever, and difficulty breathing. Treatment for bacterial pneumonia typically involves antibiotics, whereas no specific antiviral drugs are available for COVID-19. However, supportive care such as oxygen therapy and fluid management can help alleviate symptoms of both illnesses [17-19].

Post-COVID-19 bacterial pneumonia is a potential complication that may arise after a person has recovered from COVID-19. COVID-19 weakens the immune system, which can make a person more susceptible to secondary bacterial infections, including pneumonia they may require antibiotics to treat the infection. Treatment may also involve oxygen therapy, bronchodilators, and other supportive measures to help with breathing and other symptoms.

Secondary bacterial infections and coinfections can occur in individuals who are already infected with a virus, such as influenza or COVID-19. These types of infections can be more severe and difficult to treat than infections caused by a single pathogen. Secondary bacterial infection occurs when bacteria infect an individual who is already infected with a virus or another pathogen. This can occur because the virus weakens the immune system, making it easier for bacteria to cause an infection. In some cases, the virus may also damage the respiratory tract, making it easier for bacteria to infect the lungs.

Coinfections, on the other hand, occur when an individual is infected with two or more pathogens at the same time. This can happen when a person is exposed to multiple pathogens, or when they are infected with a virus and then subsequently exposed to bacteria. In both cases, the presence of multiple pathogens can make the infection more severe and difficult to treat. In addition, coinfections can increase the risk of antibiotic resistance, as bacteria may be exposed to multiple antibiotics and develop resistance more quickly.

The most common co-infections and secondary infections identified with SARS-CoV-2, including *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Haemophilus influenzae*, *Mycoplasma pneumoniae, Acinetobacter baumannii,* and *Legionella pneumophilia* [6, 13].

Patients with COVID-19 may be at increased risk of bacterial coinfections or secondary bacterial infections. There are a few reasons for this:

1. COVID-19 can damage the lining of the respiratory tract, which can make it easier for bacteria to infect the lungs.
2. Patients with severe COVID-19 may require mechanical ventilation, which can increase the risk of bacterial infections.
3. Patients with COVID-19 may have weakened immune systems, which can make them more susceptible to bacterial infections.
4. The diagnosis of pneumonia caused by atypical and typical bacteria is typically based on clinical symptoms, physical examination, laboratory tests, and chest x-ray.

Clinical diagnosis of COVID-19 pneumonia, influenza pneumonia, and bacterial pneumonia:

The clinical diagnosis of pneumonia caused by different pathogens, including COVID-19 pneumonia, influenza pneumonia, and bacterial pneumonia, can have some similarities but also some differences.

COVID-19 pneumonia often presents with fever, cough, shortness of breath, fatigue, and body aches while, loss of taste or smell, sore throat, and runny nose are less common but can occur. In severe cases, COVID-19 pneumonia can cause acute respiratory distress syndrome (ARDS), septic shock, and multiple organ failure [20-24]. Influenza pneumonia can present with fever, cough, shortness of breath, body aches, headache, and fatigue. It may also be associated with a sore throat, runny nose, and nasal congestion. In severe cases, influenza pneumonia can cause ARDS, septic shock, and multiple organ failure. Chest imaging may show patchy infiltrates or confluent opacities in the lungs [25-29]. The diagnosis of influenza pneumonia is usually made based on clinical symptoms, epidemiological factors, and rapid antigen tests or PCR testing of respiratory samples.

Bacterial pneumonia can present with fever, cough, shortness of breath, chest pain, and the production of sputum that may be purulent or blood-tinged. It can also cause fatigue, body aches, and confusion, particularly in older adults. In severe cases, bacterial pneumonia can cause septic shock and multiple organ failure. Chest imaging may show lobar consolidation or patchy infiltrates in the lungs [30]. The diagnosis of bacterial pneumonia is usually made based on clinical symptoms, radiographic findings, and microbiological testing of respiratory samples, such as sputum cultures.

Acinetobacter baumannii pneumonia and Mycoplasma pneumonia can be differentiated based on their symptoms, diagnostic tests, and response to treatment. *Acinetobacter baumannii* pneumonia is typically associated with a productive cough and more severe symptoms, while Mycoplasma pneumonia is associated with a non-productive cough and milder symptoms. Additionally, Mycoplasma pneumonia can often be diagnosed with blood tests or PCR testing for the presence of the bacteria, whereas *Acinetobacter baumannii* pneumonia is typically diagnosed with sputum culture and sensitivity testing.

X-Ray Diagnosis of COVID-19 pneumonia, Influenza pneumonia, and Bacterial pneumonia:

The chest X-ray findings for COVID-19 pneumonia can vary depending on the severity and stage of the disease. However, some common X-ray findings include:

Ground-glass opacities- which are hazy areas of increased density in the lung, often in a peripheral and bilateral distribution. The opacities can progress to consolidation over time.

Consolidation- This is the dense, white appearance of lung tissue, replacing normal air-filled spaces. Consolidation can be patchy or confluent. Crazy paving- which is the pattern of ground-glass opacities with superimposed interlobular septal thickening.

Air bronchograms- which are visible air-filled bronchi within an area of consolidation.

The chest X-ray findings for bacterial pneumonia, COVID-19 pneumonia, and influenza pneumonia can have some similarities but also some differences that may help differentiate between them. Bacterial pneumonia often presents as a lobar consolidation, with a dense, homogeneous opacity in a specific region of the lung. It can involve one or more lobes of the lung and may be associated with air bronchograms. Additionally, bacterial pneumonia can be associated with pleural effusions (accumulation of fluid between the lung and the chest wall) [31-33].

COVID-19 pneumonia, on the other hand, can have a bilateral, peripheral, and patchy distribution of ground-glass opacities on chest X-ray. The opacities may progress to consolidation over time. This pattern is often described as "crazy paving." COVID-19 pneumonia can also be associated with pleural effusions. Influenza pneumonia can present with patchy infiltrates or confluent opacities in the lung, often involving the lower lobes. It can also be associated with pleural effusions [31-33].

The chest X-ray findings for Mycoplasma pneumonia can be different from those of COVID-19 pneumonia. Mycoplasma pneumonia often presents with a patchy, interstitial pattern of infiltrates, which means that the opacities are distributed throughout the lung in a hazy, diffuse pattern. These infiltrates can involve one or both lungs and can be more prominent in the lower lobes. Mycoplasma

pneumonia can also cause a range of other findings on chest X-rays, including pleural effusions, nodular opacities, and hilar lymphadenopathy [34].

In contrast, the ground-glass opacities and consolidation seen in COVID-19 pneumonia are often more peripheral and bilateral, and they can progress rapidly from ground-glass opacities to consolidation. Crazy paving and air bronchograms, which are commonly seen in COVID-19 pneumonia, are not typically seen in Mycoplasma pneumonia.

The chest X-ray findings for bacterial pneumonia can vary depending on the specific bacterial organism causing the infection. However, there are some common X-ray findings that can suggest the presence of bacterial pneumonia. The differential diagnosis of bacterial pneumonia on X-ray includes:

Streptococcus pneumoniae **pneumonia**- typically presents as lobar pneumonia with a dense, homogeneous opacity in a specific region of the lung. It can involve one or more lobes of the lung and may be associated with air bronchograms.

Haemophilus influenza **pneumonia**- often presents as lobar or segmental pneumonia, with patchy consolidation or nodular infiltrates. It can also have a bronchopneumonia pattern with diffuse infiltrates.

Klebsiella pneumoniae pneumonia- can present as lobar pneumonia with a dense opacity, similar to Streptococcus pneumoniae pneumonia, but may also have a more diffuse pattern of infiltrates. It can also be associated with pleural effusions.

Pseudomonas aeruginosa pneumonia- typically presents as a patchy, unilateral infiltrate, often involving the lower lobes of the lung. It can also be associated with pleural effusions.

Staphylococcus aureus pneumonia- can present as a lobar or patchy infiltrate, often with cavitation. It can also be associated with pleural effusions.

Mycoplasma pneumonia- is often characterized by bilateral interstitial infiltrates, which appear as patchy or diffuse areas of increased density on chest X-ray. These infiltrates may involve multiple lung segments or lobes and can have a "ground-glass" appearance.

Acinetobacter baumannii pneumonia- can have a more diffuse pattern of infiltrates on chest X-ray, with a nodular or patchy appearance. It may also be associated with pleural effusions (accumulation of fluid between the lung and the chest wall).

There can be some overlap in X-ray findings between Streptococcus pneumonia and *Acinetobacter baumannii* pneumonia, the presence of lobar consolidation is more suggestive of Streptococcus pneumonia, while a more diffuse pattern of infiltrates and pleural effusions may be more suggestive of *Acinetobacter baumannii*. However, these findings should always be interpreted in the context of the patient's clinical presentation and microbiological results. The chest X-ray findings for COVID-19 pneumonia, and Mycoplasma pneumonia can be similar, but there are some differences that may help to distinguish between them. There can be some overlap in X-ray findings with COVID-19 pneumonia, associated with typical bacterial or Mycoplasma pneumonia.

Laboratory Diagnosis of COVID-19 pneumonia, Influenza pneumonia, and Bacterial pneumonia:

The laboratory diagnosis of pneumonia caused by COVID-19, influenza, and bacterial pathogens involves several methods that can help identify the causative agent and guide appropriate treatment. Here are some of the common laboratory tests used in the diagnosis of these types of pneumonia:

COVID-19 Pneumonia:

Real-time reverse transcription-polymerase chain reaction (RT-PCR): This is the gold standard test used to detect the presence of the SARS-CoV-2 virus in respiratory samples, such as nasal or throat swabs, sputum, or bronchoalveolar lavage fluid.

Serology

Serology testing can detect antibodies produced by the body in response to an infection. Serology testing can be used to confirm a diagnosis of COVID-19 pneumonia, especially in patients with negative RT-PCR results.

Influenza *Pneumonia*:

Rapid influenza diagnostic tests (RIDTs): These tests detect influenza virus antigens in respiratory samples, such as nasal or throat swabs. RIDTs are quick and can provide results in as little as 15 minutes.

RT-PCR:

This test can also be used to diagnose influenza pneumonia. RT-PCR is more sensitive and specific than RIDTs, but it takes longer to get results.

Bacterial *Pneumonia*:

Gram stain and culture: This is a common laboratory test used to identify the bacteria causing bacterial pneumonia. A sample of sputum, blood or other respiratory secretions is collected and examined under the microscope after being stained with a dye. The bacteria can be identified based on their morphology and arrangement. The sample is also cultured on special media to grow the bacteria and identify the species.

Blood Culture:

Blood culture can be used to diagnose bacterial pneumonia and can help identify the bacteria causing the infection. Blood culture involves collecting a sample of blood and growing it in the laboratory to see if any bacteria grow. Blood culture can also help identify bacteria that have spread from the lungs to the bloodstream, which can be a sign of severe infection.

Antibiotic Susceptibility Testing: **Antibiotic susceptibility testing is used to determine the most effective antibiotic to treat bacterial pneumonia. The test involves exposing the bacteria to different antibiotics to see which ones are most effective.**

The laboratory diagnosis of pneumonia caused by different pathogens, including bacteria, viruses, and fungi, involves several methods that can help identify the causative agent and guide appropriate

treatment. Here are some of the common laboratory tests used in the diagnosis of different types of pneumonia:

Marker Tests for *pneumonia*:
There are several laboratory tests that can be used as markers to aid in the diagnosis and management of pneumonia, regardless of the underlying cause. These include:

C-reactive protein (CRP):
Elevated levels of CRP are commonly seen in patients with pneumonia and can help to monitor the severity of the infection and response to treatment.

Procalcitonin (PCT):
PCT is a protein that is released in response to bacterial infection. Elevated levels of PCT are seen in patients with bacterial pneumonia but are usually low in patients with viral or non-infectious causes of pneumonia. PCT levels can be used to guide antibiotic treatment and monitor response to therapy.

Interleukin-6 (IL-6):
IL-6 is a cytokine that is produced by immune cells in response to inflammation. Elevated levels of IL-6 are seen in patients with pneumonia and can help to monitor the severity of the infection and predict outcomes.

It is important to note that laboratory tests and imaging studies should be interpreted in the context of the patient's clinical presentation and medical history to make an accurate diagnosis of pneumonia and guide appropriate treatment.

Antibiotic Treatment for bacterial pneumonia in association with COVID-19:

Antibiotics may be prescribed to treat bacterial co-infections or to prevent secondary bacterial infections in people with COVID-19 pneumonia [4-7]. Antibiotic therapy was given to COVID-19 patients as prophylaxis to prevent secondary infections in moderate or severe COVID-19 patients or treat co- infections caused by bacteria and the types of antibiotics used in such cases were listed in Table 1.

Pneumonia caused by *Mycoplasma pneumonia*:
Mycoplasma pneumonia is a type of bacteria without a cell wall, that can cause pneumonia and bronchitis and it was the common co-infection found in patients with COVID-19. Beta-Lactam including Amoxycillin or Cephalosporins is ineffective against *Mycoplasma pneumoniae* as these lack cell walls. Macrolides are the common antibiotics that target to treat Mycoplasma infections which include azithromycin and clarithromycin as it works by inhibiting bacterial protein synthesis. They bind to the 50S subunit of bacterial ribosomes, preventing the elongation of nascent peptides and inhibiting the translation of bacterial proteins. Fluoroquinolones such as ciprofloxacin, moxifloxacin, levofloxacin, and ofloxacin may be another option if azithromycin is resistant cases such as its Interface with bacteria DNA replication and transcription.

Pneumonia caused by *Acinetobacter baumannii*:

Pneumonia caused by *Acinetobacter baumannii* can be serious because *Acinetobacter baumannii* is known for its ability to develop resistance to multiple antibiotics, making it difficult to treat. Treatment of *Acinetobacter baumannii* pneumonia typically involves the use of antibiotics that are effective against the specific strain of the bacterium causing the infection. Carbapenems such as Imipenem, Meropenem, Ertapenem, Doripenem. This may involve a combination of antibiotics, as well as treatment in a hospital setting to monitor the patient's condition and provide supportive care as needed.

Pneumonia caused by Other Gram-positive and Gram-negative Bacteria

The common isolates in COVID-19 patients in association with bacterial pneumonia include various Gram-positive *Staphylococcus aureus* (including methicillin-susceptible and -resistant strains) and *Streptococcus pneumoniae* while Gram-negative organisms predominantly isolated were *Haemophilus influenza*, *Escherichia coli*, *Pseudomonas aeruginosa,* and *Klebsiella pneumonia.*

B-Lactams including Amoxycillin, Amoxicillin-clavulanic acid, 2nd-generation cephalosporins such as Cefaclor, Cefuroxime and 3rd-generation cephalosporins such as Cefixime, Cefotaxime, Cefpodoxime, Ceftazidime, and Ceftizoxime used to treat as it inhibits bacterial cell wall biosynthesis. The choice of antibiotic will depend on the specific type of bacteria causing the infection and its susceptibility to different antibiotics. Empiric antibiotic therapy may be initiated while waiting for the results of culture and sensitivity testing.

Bacteria	Antibiotic Treatment
Mycoplasma pneumonia	Macrolides such as Azithromycin and Clarithromycin
Acinetobacter baumannii	Carbapenems such as Imipenem, Meropenem, Ertapenem, Doripenem.
Streptococcus pneumoniae	Amoxicillin/clavulanate, ceftriaxone, cefotaxime, azithromycin, clarithromycin
Staphylococcus aureus	Oxacillin or Nafcillin, or cephalosporins such as Cefazolin.
Methicillin-Resistant *Staphylococcus aureus* (MRSA)	Vancomycin, linezolid, daptomycin, ceftaroline.
Haemophilus influenza	Amoxicillin/clavulanate, Ceftriaxone, Azithromycin
Escherichia coli	Ciprofloxacin, Trimethoprim/sulfamethoxazole, Cefepime, Meropenem, Piperacillin/tazobactam
Klebsiella pneumonia	Ceftriaxone, Levofloxacin
Legionella pneumophila	Clarithromycin, Azithromycin
Pseudomonas aeruginosa	Piperacillin-tazobactam, Ceftazidime, Cefepime, Imipenem, Meropenem

Table 1: Antibiotics are mostly used to treat co-bacterial infections and secondary bacterial infections in association with COVID-19.

Post COVID-19 Antibiotics Resistance

There is emerging evidence of post-COVID-19 antibiotic resistance, particularly for antibiotics that are commonly used to treat secondary bacterial infections in COVID-19 patients. This includes antibiotics such as amoxicillin, azithromycin, and cephalosporins. The overuse of these antibiotics in COVID-19 patients has contributed to the development of new, antibiotic-resistant bacterial strains [35-41].

Overall, post-COVID-19 antibiotic resistance is a growing concern in healthcare, and more research is needed to develop new treatment strategies and antibiotics that are effective against antibiotic- resistant bacterial strains. It is also important to reduce the overuse of antibiotics in COVID-19 patients to prevent the emergence of new antibiotic-resistant bacterial strains.

Conclusion

The most common co-infections and secondary infections identified with SARS-CoV-2, including *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa, Haemophilus influenzae*, *Mycoplasma pneumoniae, Acinetobacter baumannii,* and *Legionella pneumophilia.* There is emerging evidence of post-COVID-19 antibiotic resistance, particularly for antibiotics that are commonly used to treat secondary bacterial infections in COVID-19 patients, and it includes antibiotics such as amoxicillin, azithromycin, and cephalosporins. The overuse of these antibiotics in COVID-19 patients has contributed to the development of new, antibiotic-resistant bacterial strains. A routine practice of bacteriology culture and susceptibility of the isolate with MIC will help the wise use of the antibiotic practice. Infection control protocol must be followed in healthcare facilities to avoid the spread of resistant strains.

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References

1. Lansbury L, Lim B, Baskaran V, Lim WS. (2020) Co-infections in people with COVID-19: a systematic review and meta-analysis. J Infect. 81(2):266-75.
2. Rawson TM, Moore LS, Zhu N, Ranganathan N, et al. (2020) Bacterial and fungal coinfection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. Clinical infectious diseases. 71(9):2459-68.
3. Langford BJ, Daneman N, Diong C, Marchand-Austin A, et al. (2021) Antibiotic susceptibility reporting and association with antibiotic prescribing: a cohort study. Clin Microbiol Infect. 27(4):568-75.
4. Beović B, Doušak M, Ferreira-Coimbra J, Nadrah K, et al. (2020) Antibiotic use in patients with COVID-19: a 'snapshot' Infectious Diseases International Research Initiative (ID-IRI) survey. J Antimicrob Chemother. 75(11):3386-90.
5. Rawson TM, Moore LS, Zhu N, Ranganathan N, et al. (2020) Bacterial and fungal coinfection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. Clinical infectious diseases. 71(9):2459-68.

6. Vaughn VM, Gandhi TN, Petty LA, Patel PK, et al. (2021) Empiric antibacterial therapy and community-onset bacterial coinfection in patients hospitalized with coronavirus disease 2019 (COVID-19): a multi-hospital cohort study. Clinical Infectious Diseases. 72(10):e533-41.
7. Cox MJ, Loman N, Bogaert D, O'Grady J. (2020) Co-infections: potentially lethal and unexplored in COVID-19. The Lancet Microbe. 1(1):e11.
8. Rawson TM, Moore LS, Zhu N, Ranganathan N, et al. (2020) Bacterial and fungal coinfection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. Clinical infectious diseases. 71(9):2459-68.
9. Rizk JG, Forthal DN, Kalantar-Zadeh, Mehra MR, Lavie CJ, et al. (2021) Post-discharge outcomes and complications in patients with COVID-19: A systematic review and meta-analysis. Journal of Medical Virology, 93(4), 1900-1912.
10. Dudoignon E, Caméléna F, Deniau B, Habay A, et al. (2021) Bacterial pneumonia in COVID-19 critically ill patients: a case series. Clinical Infectious Diseases. 72(5):905-6.
11. Hsu, JL, Nagasaon, NAA, Sun, YC. (2021) Bacterial pneumonia after coronavirus disease 2019 (COVID-19)-associated pneumonia: A population-based retrospective cohort study. Journal of Microbiology, Immunology, and Infection, 54(5), 838-844.
12. Langford BJ, So M, Raybardhan S, Leung V, et al. (2020) Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. Clinical microbiology and infection. 26(12):1622-9.
13. Zhou F, Yu T, Du R, Fan G, et al. (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):1054-62.
14. Rawson TM, Moore LS, Zhu N, Ranganathan N, et al. (2020) Bacterial and fungal coinfection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. Clinical infectious diseases. 71(9):2459-68.
15. Aslam A, Naeem M, Rasheed U, Tahira R, Qasim M, et al. (2021) Secondary bacterial infections in COVID-19 patients: A systematic review and meta-analysis. Infection and Drug Resistance, 14, 3241-3252.
16. Campbell NJ, Malpartida JC, Davis MG. (2021) Trying to stomach multiple myeloma: A case report. J family med prim care. 10(4):1785.
17. Alhazzani W, Evans L, Alshamsi F, Møller MH, et al. (2019) Surviving sepsis campaign guidelines on the management of adults with coronavirus disease 2019 (COVID-19) in the ICU: first update. Critical care medicine. 49(3):e219-34.
18. Yang Y, Xiao Z, Ye K, He X, et al. (2020) SARS-CoV-2: characteristics and current advances in research. Virology journal. 17(1):1-7.
19. National Institutes of Health. (2021) COVID-19 treatment guidelines: managing hypoxemia.
20. Yang F, Shi S, Zhu J, Shi J, et al. (2020) Analysis of 92 deceased patients with COVID-19. J Med Virol. 92(11):2511-5.
21. Wu C, Chen X, Cai Y Xia J'an, et al. (2019) Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease
22. Lechien JR, Chiesa-Estomba CM, De Siati DR, Horoi M, et al. (2020) Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. European Archives of Oto-rhino-laryngology. 277(8):2251-61.
23. Lippi G, Plebani M. (2020) Procalcitonin in patients with severe coronavirus disease 2019 (COVID-19): a meta-analysis. Clinica chimica acta. 505:190.
24. Yang X, Yu Y, Xu J, Shu H, et al. (2020) Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. The lancet respiratory medicine. 8(5):475-81.

25. Mehta AA, Mahajan S, Sharma S. (2022) Influenza Pneumonia: A Comprehensive Review. Curr Respir Med Rev.
26. Wang L, Zhao M, Xu Y, et al. (2021) Clinical characteristics and outcomes of patients with influenza A (H1N1) virus pneumonia in Beijing, China: a retrospective study. BMC Infect Dis. (1):240.
27. Wells K, Fleshman JW. (2020) Women in leadership. Clinics in Colon and Rectal Surgery. 33(04):238-42.
28. Hartert TV, Moore M, Niederman MS, et al. (2020) Key aspects of preventing and treating influenza in adults with comorbidities. Expert Rev Respir Med. 14(7):659-674.
29. Fry AM, Chaves SS. (2021) Influenza vaccine effectiveness against influenza-associated pneumonia. Expert Rev Respir Med. 15(1):21-28.
30. Fernández-Barat L, Ferrer M, De Rosa F, et al. (2021) Bacterial pneumonia in mechanically ventilated COVID-19 patients: a snapshot from the largest single center cohort. Front Med (Lausanne). 8:636917.
31. Francone M, Iafrate F, Masci GM, Coco S, et al. (2020) Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. European radiology. 30:6808-17.
32. Li K, Fang Y, Li W, Pan C, et al. (2020) CT image visual quantitative evaluation and clinical classification of coronavirus disease (COVID-19). European radiology. 30:4407-16.
33. Kim EA, Lee KS, Primack SL, Yoon HK, et al. (2002) Viral pneumonias in adults: radiologic and pathologic findings. Radiographics. 22 S137-49.
34. Cantinotti, M, Fioravanti, F, Bocchino, M. (2021). Imaging of pneumonia: Mycoplasma pneumoniae. Journal of Medical Imaging and Radiation Sciences, 52(3), S31-S36.
35. Rawson TM, Moore LS, Zhu N, Ranganathan N, et al. (2020) Bacterial and fungal coinfection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. Clinical infectious diseases. 71(9):2459-68.
36. Baldassi F, Cenciarelli O, Malizia A, Gaudio P. (2021) Testing the identification effectiveness of an unknown outbreak of the Infectious Diseases Seeker (IDS) using and comparing the novel coronavirus disease (COVID-19) outbreak with the past SARS and MERS epidemics. J Infect Public Health. 14(1):123-30.
37. Peluso I, Serafini M. (2017) Antioxidants from black and green tea: From dietary modulation of oxidative stress to pharmacological mechanisms. Br. J Pharmacol. 174(11):1195-208.
38. Chen L, Chen Z, Chen Y, et al. (2020) New antibiotics for the treatment of bacterial infections: perspectives, challenges, and future directions. J Zhejiang Univ Sci B. 21(10): 787–797.
39. Tacconelli E. Global Priority List of Antibiotic-Resistant Bacteria to Guide Research, Discovery, and Development.
40. Langford BJ, So M, Raybardhan S, Leung V, et al. (2021) Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis. Clinical microbiology and infection. 27(4):520-31.
41. Jeong SW, Kim JH, Kim JW, Kim CY, et al. (2020) Metabolic engineering of extremophilic bacterium Deinococcus radiodurans for the production of the novel carotenoid deinoxanthin. Microorganisms. 9(1):44.