PharmacologyOnLine
Archives • 2021 • vol.3 • 2032-2039

"Antibiotic stewardship in ICU during covid-19"

Mohamed J. Saadh1, Abeer M. Kharshid2*, Heba K. Aladailah2, Shahad Abunawas2, Wael Abu Dayyih2
[1]Middle East University, Amman, Jordan
[2]Faculty of pharmacy, Mutah University, Al Karak 61710, Jordan

*abeerkharshid2015@gmail.com

Abstract

Antibiotic resistance rates and illnesses caused by antibiotic-resistant organisms are on the rise. Antimicrobial overuse and misuse, as well as the need to optimize antimicrobial usage, are key contributors to resistance development. Although bacterial coinfection rates were modest in coronavirus illness, antibiotic consumption rates were relatively high. 2019 Antibiotic stewardship programs (ASPs) attempt to improve patient outcomes, reduce hospital costs, and avoid antibiotic resistance by optimizing antimicrobial prescribing patterns. Clinicians may be directed to administer antibiotics based on the presentation of patients with severe coronavirus illness in 2019. Because primary evidence implies that bacterial infection is uncommon in COVID 19, antibiotic selection through COVID 19 may promote antibiotic resistance. As a result, it's critical to keep antimicrobial stewardship initiatives going. The widespread use of antibiotics in the ICU has significant ecological consequences, promoting the spread of multidrug-resistant bacteria (MDRB) in this setting. As a result, the main goals of AMS programs in the ICU are to improve infection control and reduce AMR during the pandemic. Antibiotic resistance rates and illnesses caused by antibiotic-resistant organisms are on the rise. Antimicrobial overuse and misuse, as well as the need to optimize antimicrobial usage, are key contributors to resistance development. The number of people who used antibiotics was extremely significant.

Keywords: antibiotic, Antibiotic stewardship, pandemic, Antimicrobial Resistance, Covid-19.

Introduction

Microbes, primarily bacteria, have developed advanced antibiotic resistance over time. The World Health Assembly (1) endorsed the Global Action Plan on Antimicrobial Resistance (AMR) in May 2015, and the Political Declaration of the High-Level Meeting of the General Assembly on AMR (2) endorsed by the General Assembly in September 2017 both recognize AMR as a global threat to public health. These gestures acknowledged antimicrobial abuse and misuse as a major factor to the development of resistance, as well as the need to optimize antimicrobial use. (3)

Antibiotic resistance rates and illnesses caused by antibiotic-resistant organisms are on the rise, according to the Centers for Disease Control and Prevention (CDC) 2019 report, with over two million antibiotic-resistant infections and over 35 thousand fatalities occurring each year in the United States. (4) Antibiotic-resistant bacteria have infected around 670,000 people in the European Union, resulting in around 33,000 deaths every year. (5,6)

Antimicrobial abuse and misuse are recognized as key contributors to resistance development, as well as the need to optimize antimicrobial usage in these legislative endeavours. The Global Action Plan on AMR following the use of forceful communication, education, and training as a blueprint for governments adopting countrywide strategies on AMR, successfully drew attention and expertise to AMR. To reinforce and diminish infections caused by AMR, universal studies and research are used. With the help of appropriate sanitation, hygiene, and contamination-prevention measures being enforced. Antimicrobial drug use in humans and animals should be optimized, as well as developing a financial goal for long-term funding that incorporates the needs of all countries, as well as increasing funding for novel treatments, diagnostic tools, immunizations, and other interventions. (3)

These metrics are designed to help countries implement and achieve Worldwide Strategy Objective 4 – "Optimization of proper antimicrobial use" – by ensuring that they are following the relevant criteria for antibiotic stewardship programs and initiatives. All should be adopted in all low- and middle-income countries' healthcare systems. (3).

Antibiotic stewardships programs (ASPs):

Antibiotic stewardship programs (ASPs) definitions and their purposes

Stewardship is described as "the cautious and accountable control of something entrusted to one's care" (7). It became initially utilized in healthcare systems as a suggestion for optimizing antimicrobial usage, and the term "antimicrobial stewardship" was established to describe it (AMS) (8). Since then, stewardship has been used to manipulate healthcare systems as a whole, taking responsibility for the population's health and well-being and steering care structures on a national and international scale. (9)

Antibiotic stewardship is the process of tracking and improving how clinicians prescribe antibiotics and how patients use them. Higher antibiotic prescribing is critical for effectively treating illnesses, minimizing antibiotic overuse, and preventing antibiotic resistance. Antibiotic stewardship programs (ASPs) attempt to improve patient outcomes, reduce hospital costs, and avoid antibiotic resistance by optimizing antimicrobial prescribing patterns. (11) Antibiotic stewardship (ABS) is an important method for reducing antibiotic-resistant microorganisms and multidrug resistance. (12)

Among the most important stewardship tools are the application of national standards, the compilation of a specific list of antimicrobials, systematic stewardship visits, and related staff trainings. Therapy optimization can be achieved through proper antibiotic indication evaluation, antibiotic dose verification, and the selection of acceptable therapy duration. (12)

Antibiotic stewardship (ABS) in Intensive Care Units (ICU)

Importance of Antibiotic stewardship in ICU

Antibiotics are internationally utilized in intensive care units (ICUs). Although adequate empirical coverage and prompt administration are critical for curing community/hospital developed sepsis, antibiotics are not usually prompted and may be provided in the majority of patients' cases in without established infection.

Because of the ensuing selection pressure and the inadequate management of infections with antibiotic resistant bacteria, the ICU is a significant source of infections in hospitals. As major contributors to antimicrobial stewardship programs, critical care physicians should be at the forefront of establishing, optimizing, and promoting excellent guidelines alternatives for severe infections and sepsis, including limiting antibiotic usage (ASP). Additional detailed diagnostic techniques to detect bacterial sepsis are needed for antibiotic optimization in the ICU, as well as improved patient selection prone to multidrug-resistant-bacterial infection. Implementation of detailed dosing/administration recommendations to accomplish optimum antibiotic pharmacokinetics-pharmacodynamics (PK-PD) goals, in addition to individualized selection of one drug or numerous empirical therapies. Simultaneous source control, Simultaneous source control, as well as a reconsideration of early therapy, should be used to reduce simultaneous harm to normal flora systems by gradually withdrawing antibiotics and minimizing antibiotic courses. The current goal is to build actionable stewardship in the ICU for better patient outcomes and antimicrobial selection pressure, which could help reduce MDRB transmission in this situation (6).

Antibiotic stewardship (ABS) during covid-19

The spread of the coronavirus infection (COVID-19) / its influence on bacterial resistance:

Coronavirus illness (COVID-19), caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has had a significant influence on global health care delivery in both primary and secondary care since its initial report in December 2019 (14).

According to WHO, there have been over 200,000,000 confirmed cases of COVID-19 worldwide, with over five million deaths. More than 7,000,000,000 immunizations have been administered to date. (15)

Maintaining routine acute infection care is critical, and COVID-19 issues should be expected. For the vast majority of patients, COVID-19 will have an uncomplicated course, no hospitalization will be necessary, and recurrent infection will be uncommon (16).

The COVID-19 infection is occurring in the middle of the present international health problem of antibiotic resistance, which is having a significant impact on international healthcare systems. According to preliminary findings, bacterial/fungal co-infection with COVID-19 is uncommon, and selective antibiotic use during the COVID-19 infection may enhance antibiotic resistance. As a result, continuing antimicrobial stewardship initiatives around the world is vital. (17)

The current SARS-CoV-2 outbreak occurs at a time when drug resistance is already a major public health concern around the world. Antimicrobial-resistant pathogen infections are anticipated to kill 700,000 people per year around the world, complicating COVID-19 patient care and likely increasing mortality (18), as well as generating financial burden for individuals. Microbial infections that are resistant to antibiotics are evident during and after COVID-19. This could be a source of economic hardship, with estimates of over a hundred trillion dollars in the United States by the year 2000 (18), and they are projected to have a greater impact in the near future (17).

Around 5% of COVID-19 cases require admission to an intensive care unit, and those with multiple diseases require ventilator support (19). ICU hospitalizations increase the risk of secondary infections from various pathogens (bacterial, fungal, and viral) (20,21).

During a pandemic, one concern is that all resources are directed toward treating COVID-19-infected persons, leaving other vital health-care infections untreated or discounted. Antimicrobial stewardship (AMS) initiatives, on the other hand, are still vital and are expected to grow in importance (22). Confirmed inappropriate antibiotic use exacerbated AMR internationally during the COVID-19 epidemic. (17)

This study intends to raise awareness of AMR and highlight the importance of maintaining preparations to manage international antibiotic resistance, which poses a threat to every country during a pandemic, as well as upholding and continuing the AMS principles.

Antibiotic stewardship (ABS) in ICU during covid-19

SARS-CoV-2 infection is likely one of the most serious health-care issues in the last century. The coronavirus illness 2019 (COVID-19) has caused a large increase in demand for acute care beds in various countries. We'll explore at one of the unintended repercussions of the COVID-19 surge patients in the critical care unit in this piece (ICU). (23)

In these circumstances, maintaining fundamental patient management standards proved difficult. During the outbreak, the goals of antimicrobial stewardship programs (ASP) remain unchanged. To begin, avoiding antibiotic exposure in COVID-19 patients admitted to the ICU is crucial to preventing antimicrobial resistance in ventilated patients with long ICU stays. Second, toxicity is a serious worry because many antivirals and antibiotics have severe adverse effects and interactions. Finally, considering the significant mortality rate, It's vital to improve the patient's COVID-19 score (24)

There was no evidence that bacterial super infection was a major issue in ICU patients—there was solid evidence that the inflammatory response was the main driver of illness severity—and empirical antibiotic therapy was common (25). Super infection occurred in only 14 % of patients during the total ICU stay in the past, according to international guidelines (26), based on extrapolation from other viral diseases such as influenza, while for coronavirus infections in the past, super infection occurred in only 14 % of patients during the total ICU stay (27).

When bacterial pneumonia develops, it usually happens later in the course of the illness, and it's called late-onset ventilator-associated pneumonia (28).

According to a recent meta-analysis, only 3.5 % of all COVID19 patients have co-infection, and 14 % have infections later, in critically sick patients, an estimated 8% develop infections (including co-infection and secondary infection). (29)

Patients were hospitalized in the ICU for far longer than normal, increasing the risk of nosocomial infections. The inflammatory response in COVID-19 mimicked the clinical architecture of bacterial illness, making the diagnostic technique for bacterial infection difficult. Another consideration was the possibility of spreading the infection through intrusive testing techniques. At the same time, because to the challenges of donning and doing each time, it was more difficult to assess a patient as usual. Because of the aerosol created during the process, it was difficult to disconnect ventilator circuits and sample the airways, resulting in fewer microbiological samples being obtained. (23)

This study intends to illustrate the need for continued effort to combat the worldwide AMR epidemic during the COVID-19 pandemic, as well as the need of upholding and continuing the principle of AMS programs in ICU. First, it examines the key issues of improving infection control and reducing AMR during the pandemic.

Discussion

Key challenges to control infections and further lessen antimicrobial resistance

Persistent common infections

During the COVID-19, general infections such as influenza virus infections, bacterial infection, other tropic infection like malaria still exist (30). These infections must be treated otherwise through the COVID-19 era (30). Guidelines for proper care infection management and resistance issues must be implemented. Wrong usage of antimicrobial to treat viral and unselective infections for instance the use of broad-spectrum antibiotics may lead to resistance.

Worldwide governments closed down their cities to control the pandemic, most of healthcare funds and staff were directed to control COVID-19 spreading (31). Moreover, there is new evidence showed that healthcare staff at AMS has been asked to prioritize response and management of COVID-19, reducing it AMS activities (17).

Experimental antimicrobials usage for COVID-19 patients:

Careful evaluation of COVID-19 symptoms is crucial to identify the possible source of infection. Nevertheless, the symptoms COVID-19 infection are nonspecific from them bacterial-caused pneumonia or influenza. Some of the primary guidelines

recommendations published consider empiricism broad-spectrum antimicrobials COVID-19 patients suffering from similar symptoms are admitted to ICUs (32). However, it is important to note that the use of broad-spectrum antibiotics can lead to C. difficile infection and a rise in antimicrobial resistance.

Antibiotics is not recommended as preventive or cure measures for mild COVID-19, according to WHO guidelines, and antibiotic therapy must be used only if a confirmed bacterial infection and/ or moderate COVID-19 cases (33). Early empirical antimicrobials can be given to patients with severe COVID-19 for the treatment of all possible infections depending on clinical practice guidelines, infected individual characteristics (33).

Infections associated with long hospital stay:

While there is no indication that COVID-19 patients are usually prone to be infested with multidrug resistant bacteria (MDRD) in addition to fungal infection, there is a more risk of healthcare-associated infections in COVID-19 cases who are hospitalized for an extended period of time (34).

In a Seattle research (35), a substantial number of cases were hospitalized due to severe symptoms (75%). Hospital/acquired pneumonia, which is usually associated with MDRD bacterial type (17).

Recommendations for clinical practice modifications in the context of COVID-19

Consider the AMS Principles that already exist:

To avoid over- and incorrect prescribing of antimicrobials during the pandemic, it is critical to follow local, national, and international guidelines. To make antimicrobial prescribing and COVID-19 management guidelines more accessible, the Commonwealth Pharmacists Association (London, UK) created the Commonwealth Partnerships for Antimicrobial Stewardship (CwPAMS) app, which is a smartphone app that includes national antimicrobial prescribing guidelines from Ghana, Tanzania, Uganda, and Zambia, as well as international guidelines from the World Health Organization. (36)

Despite the lack of evidence for the effectiveness of AMS interventions in low- and middle-income countries, AMS, together with infection prevention and control (IPC), continues to be the cornerstone of AMR prevention (37,38).

The Commonwealth Pharmacists Association recently released a CwPAMS toolkit, which outlines tactics and initiatives that can be implemented as part of an AMS workplan by a healthcare facility. This could be useful as a guide for countries with low resources to start AMS programs (39).

Control Access to Antimicrobials That Work

Antibiotics and other vital treatments should not run out of stock in hospitals, and recommendations on which medicines to stockpile should be supplied. The World Health Organization (WHO) has released the COVID-19 Essential Supplies Forecasting Tool, which gives information on essential medications, such as antimicrobials and consumables, that are needed to treat severely or critically sick patients (40).

Individual countries will need to perform active surveillance and implement early warning methods to get notifications anytime a medicine shortage is expected, particularly for antibiotics, by evaluating a drug utilisation review. This is especially true for antibiotics, which are routinely used to treat community-acquired bacterial infections and lower respiratory tract infections, as shortages are projected to increase urgent care visits and even hospital admissions. (17).

It has also been proposed that AgNPs have intracellular antiviral effects by interacting with viral nucleic acids [19]. Zinc-containing AgNPs have antiviral activity against influenza viruses H5N1, H9N2, SARS-Cov2 and PPRV (40-45). Also,

it can be conjugated the silver nanoparticles with antibiotics to increase activity (46).

Conclusion

The COVID-19 pandemic is a major and emerging public health hazard, putting excessive strain on all healthcare providers. The on-going worldwide AMR problem, on the other hand, must not be disregarded. Persistent common infections, experimental antimicrobials usage for COVID-19 patients, and infections associated with protracted hospital stays are among the key obstacles to controlling infections and reducing antimicrobial resistance. Given these obstacles, we believe that immediate action is essential to keep AMS practices going during the pandemic. Specifically, we recognise the importance of focusing on established AMS principles across the hospital sector, particularly in the intensive care unit (ICU) during the COVID-19 pandemic. Other suggestions include ensuring that effective antimicrobials are available, and Finally, during the current pandemic and in the post-pandemic era, AMS advocacy must continue at all levels.

References

1. Resolution WHA 68-7. Global action plan on antimicrobial resistance. In: Sixty-eighth World Health Assembly, Geneva, 26 May 2015. Annex 3. Geneva: World Health Organization; 2015.
2. A/RES/71/3. Political declaration of the high-level meeting of the General Assembly on antimicrobial resistance. New York: United Nations; 2016.
3. 3. World Health Organization. "Antimicrobial stewardship programmes in health-care facilities in low-and middle-income countries: a WHO practical toolkit." (2019).
4. CDC. Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2019.
5. Cassini, A., Högberg, L.D., Plachouras, D., et al., Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis. Lancet Infect Dis. 2019; 19: 56-66.
6. Önal, U., Halis, A., "Coronavirus Disease 2019 and Antibiotic Stewardship-Antibiotic Usage in Adult Patients: Is It Necessary? When Should It be Concerned?." Balkan medical journal. 2021; 150-155.
7. McGowan, J.E., Gerding, D.N., Does antibiotic restriction prevent resistance? New Horiz. 1996; 4: 370–376.
8. Travis, P., Egger, D., Davies, P., Towards better stewardship: concepts and critical issues. Geneva: World Health Organization; 2002.
9. Sanchez, G.V., Fleming-Dutra, K.E. Roberts, R.M., Hicks, L.A., "Core elements of outpatient antibiotic stewardship." Morbidity and Mortality Weekly Report: Recommendations and Reports. 2016; 1-12.
10. Branstetter, J.W., et al., "Challenges of Antibiotic Stewardship in the Pediatric and Neonatal Intensive Care Units." The Journal of Pediatric Pharmacology and Therapeutics. 2021; 26: 659-668.
11. 11. Wendt, S., et al. "Antibiotic Stewardship (ABS). Teil 2: Anwendung." Der Internist. 2020; 61: 475-486.
12. COVID-19 Significantly Impacts Health Services for Noncommunicable Diseases. Available online: https://www.who.int/news-room/detail/01-06-2020-covid-19-significantly-impacts-health-servicesfor-noncommunicable-diseases
13. Langford, B.J.; So, M.; Raybardhan, S.; Leung, V.; et al., Bacterial co-infection and secondary infection in patients with COVID-19: A living rapid review and meta-analysis. Clin. Microbiol. Infect. 2020; 26: 1622–1629.
14. Khor, W.P.; Olaoye, O.; D'Arcy, N.; Krockow, E.M.; Elshenawy, R.A.; Rutter, V.; Ashiru-Oredope, D. The Need for Ongoing Antimicrobial Stewardship during the COVID-

19 Pandemic and Actionable Recommendations. Antibiotics 2020; 9: 904.
15. Brogan, D.M., Mossialos, E. A critical analysis of the review on antimicrobial resistance report and the infectious disease financing facility. Global Health. 2016; 12: 6.
16. Alanio, A.; Dellière, S.; Fodil, S.; et al., Prevalence of putative invasive pulmonary aspergillosis in critically ill patients with COVID-19. Lancet. Respir. Med. 2020; 8: e48–e49.
17. Lescure, F.X.; Bouadma, L.; Nguyen, D.; et al., Clinical and virological data of the first cases of COVID-19 in Europe: A case series. Lancet Infect. Dis. 2020; 20: 697–706.
18. Kim, D.; Quinn, J.; Pinsky, B.; et al., Rates of co-infection between SARS-CoV-2 and other respiratory pathogens. JAMA 2020; 323: 2085–2086.
19. Kim, D.; Quinn, J.; Pinsky, B.; Shah, N.H.; Brown, I. Rates of co-infection between SARS-CoV-2 and other respiratory pathogens. JAMA 2020; 323: 2085–2086.
20. Getahun, H.; Smith, I.; Trivedi, K.; Paulin, S.; Balkhy, H.H. Tackling antimicrobial resistance in the COVID-19 pandemic. Bull. WHO 2020; 98: 442.
21. Arabi, Y.M., Murthy, S., Webb, S., COVID-19: a novel coronavirus and a novel challenge for critical care. Intensive Care Med. 2020; 46: 833–836.
22. De Waele, J.J., Derde, L., Bassetti, M., "Antimicrobial stewardship in ICUs during the COVID-19 pandemic: back to the 90s?." Intensive care medicine. 2021; 47: 104-106.
23. Rawson, T.M., Moore, L.S.P., Zhu, N., et al., Bacterial and fungal co-infection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. Clin Infect Dis. 2020; 71: 2459–2468.
24. Alhazzani, W., Møller, M.H., Arabi, Y.M., et al., Surviving sepsis campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). Intensive Care Med. 2020; 46: 854–887.
25. Lansbury, L., Lim, B., Baskaran, V., Lim, W.S., Co-infections in people with COVID-19: a systematic review and meta-analysis. J Infect. 2020; 81: 266-275.
26. Dudoignon, E., Caméléna, F., Deniau, B., Bacterial Pneumonia in COVID-19 critically ill patients: a case series. Clin Infect Dis. 2020; 72: 905–906.
27. Langford, B.J., So, M., Raybardhan, S., et al., Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and metaanalysis. Clin Microbiol Infect. 2020; 26: 1622-1629.
28. https://www.who.int/bulletin/volumes/98/7/20-268573.pdf
29. World Health Organization. Clinical Care for Severe Acute Respiratory Infection Toolkit; World Health Organization: Geneva, Switzerland, 2020. https://apps.who.int/iris/handle/10665/331736
30. Xiao, A.T.; Tong, Y.X.; Zhang, S. False-negative of RT-PCR and prolonged nucleic acid conversion in COVID-19: Rather than recurrence. J. Med. Virol. 2020; 92: 1755–1756.
31. World Health Organization. Clinical Management of COVID-19 Interim Guid.—May 2020; World Health Organization: Geneva, Switzerland, 2020. https://apps.who.int/iris/handle/10665/332196
32. Hassan, M.; Tuckman, H.; Patrick, R.; et al., Hospital length of stay and probability of acquiring infection. Int. J. Pharm. Healthc. Mark. 2010; 4: 324–338.
33. Bhatraju, P.K.; Ghassemieh, B.J.; Nichols, M.; et al., Covid-19 in Critically Ill Patients in the Seattle Region—Case Series. New Engl. J. Med. 2020; 382: 2012–2022.
34. Olaoye, O.; Tuck, C.; Khor, W.P.; et al., Ashiru-Oredope, D. Improving access to antimicrobial prescribing guidelines in 4 African countries: Development and pilot implementation of an App and cross-sectional assessment of attitudes and behaviour survey of healthcare workers and patients. Antibiotics 2020; 9: 555.
35. Cox, J.A.; Vlieghe, E.; Mendelson, M.; et al., Antibiotic stewardship in low-and middle-income countries: The same but different? Clin. Microbiol. Infect. 2017; 23: 812–818.
36. Huebner, C.; Flessa, S.; Huebner, N.O. The economic impact of antimicrobial stewardship programmes in hospitals: A

systematic literature review. J. Hosp. Infect. 2019; 102: 369–376.
37. Commonwealth Pharmacists Association. Commonwealth Partnership for Antimicrobial Stewardship (CwPAMS) Toolikit. https://commonwealthpharmacy.org/launch-of-the-commonwealthpartnerships-for-antimicrobial-stewardship-cwpams-toolkit.
38. COVID-19 Essential Supplies Forecasting Tool. https://www.who.int/publications/m/item/covid-19-essential-supplies-forecasting-tool.
39. Kharshid, A.M., Saadh, M.J., Taani R.I., et al., "Antibiotic Misuse during COVID-19 Pandemic: Review Study". Pharmacologyonline. 2021; 3: 1038-1047.
40. Saadh, M.J., Synthesis, role in antibacterial, antiviral, and hazardous effects of silver nanoparticles. Pharmacologonline. 2021; 2: 1331-1336.
41. Saadh, M.J., Almaaytah AM, Alaraj M, et al. Punicalagin and zinc (II) ions inhibit the activity of SARS-CoV-2 3CL-protease in vitro. Eur Rev Med Pharmacol Sci 2021; 25: 3908-3913.
42. Saadh, M.J., Almaaytah, A.M., Alaraj, M., et al. Sauchinone with zinc sulphate significantly inhibits the Activity of SARS-CoV-2 3CLProtease. Pharmacologyonline. 2021. 2: 242- 248.
43. Saadh, M.J., Aggag, M.M., Alboghdadly, A., et al., Silver nanoparticles with epigallocatechin gallate and zinc sulphate significantly inhibits avian influenza A virus H9N2. Microb Pathog 2021; 158: 105071. 13.
44. Saadh, M.J., Aldalaen, S.M., Inhibitory effects of epigallocatechin gallate (EGCG) combined with zinc sulfate and silver nanoparticles on avian influenza A virus subtype H5N1. Eur Rev Med Pharmacol Sci 2021; 25: 2630-2636.
45. Saadh, M.J., Epigallocatechin gallate (EGCG) combined with zinc sulfate inhibits Peste des petits ruminants virus entry and replication. Saudi Journal of Biological Sciences. 2021, 28: 6674-6678.
46. Saadh, M.J., Effect of silver nanoparticles on the antibacterial activity of Levofloxacin against methicillin-resistant Staphylococcus aureus. Eur Rev Med Pharmacol Sci. 2021; 25: 5507-5510.