

MULTIPLE DRUG RESISTANT PATHOGENS IN ACTION AFTER COVID PANDEMIC

Navneet Kumar Ram Dayal Singh^{1,*} and Minal Chetan Thakkar²

Received: April 03, 2023; Revised: October 12, 2023; Accepted: November 09, 2023

Abstract

The COVID-19 pandemic impacted the unique means for prompting the scientific community to consider developing healthcare infrastructures and logistics that will deal with any future pandemics, may be in a manner comparable to dealing with biological war or an outside attack due to Manmade weapons. Biomedical experts have refocused their efforts on creating innovative vaccines and medicines to halt the deadly spread of these infections using new biological approaches. Only a small number of innovative nations have a healthy security policy on national level in the event of a biological attack that has been bio-weaponized by a human. After the Covid pandemic, It is assumed that the whole world may have a fight against Multiple resistant bacterial pathogens or microorganisms connected to water and food. MDR bacteria (like MRSA and VRSA) in addition to newly mutated microorganism may also infect human beings, birds, and animals.

Keywords: COVID-19; MRSA; VRSA

Review Article

The COVID-19 pandemic impacted the unique means for prompting the scientific community to consider developing healthcare infrastructures and logistics that will deal with any future pandemics, maybe in a manner comparable to dealing with biological war or an outside attack due to Manmade weapons. Biomedical experts have refocused their efforts on creating innovative vaccines and medicines to halt the deadly spread of these infections using new biological approaches. Only a small number of innovative nations have a healthy security policy on national level in the event of a biological attack that has been bio-weaponized by a human. Only highly industrialised nations have

unique and latest resources and laws in these circumstances to handle sudden deadly outbreaks of potentially very lethal and contagious viral or bacterial changes that develop naturally without the aid of man-made bioweapons (Salazar *et al.*, 2022).

Influenza pandemic of 1918 was serious one, there were decades of relatively low-virulent influenza circulation afterwards. Between 1957 to 1958 *Influenza virus* strain H₂N₂ pandemic, however, spreaded in 20 different countries in less than four months of small duration which resulted in nearly 60k additional deaths in the developed country like United States. Between September 1957 to March 1958 the respiratory excess death

¹ Department of Paramedical Sciences, Sumandeep Vidyapeeth Deemed University, Piparia, Vadodara, India. E-mail: navneetspan@gmail.com

² Shree P.M. Patel college of Paramedical Science & Technology, Anand, Anand People's Medicare Society (APMS), Sardar Patel University, India. E-mail: cmmilli@yahoo.co.in

* Corresponding author

DOI: <https://doi.org/10.55766/sujst-2023-06-e0930>

Suranaree J. Sci. Technol. 30(6):070069(1-5)

rate from the influenza pandemic was 1.9 per 10,000 population. One essential cutting-edge subject within the pandemic caused by *influenza virus* making plans was spread of bacterial pneumonia as a comorbidity. Bacterial contamination along with *influenza virus* have brought about maximum deaths at some point of the 1918 to 1919 pandemic (Alling *et al.*, 1981; Gupta *et al.*, 2008; Morens *et al.*, 2008; Cobos *et al.*, 2016).

In the current scenario whole world is facing the fight against pandemic of Covid-19 and epidemicity of different viruses like *Adenoviruses*, *Enteroviruses* and *Rhinoviruses* etc. Influenza outbreak, which is commonly taking place in less temperature zone, Such epidemic, endemic or outbreaks are always lethal to human society globally. *Hepatitis B and C*, Hepatitis alone, *Hepatitis B and D* as co-infection and *HIV/AIDS* also are an alarming situation for human kind. However we had been contained with the aid of using powerful clinical remedies and focused pharmacological agents for early cure.

We have faced the worst pandemic caused by Corona virus from 2019 to the running years, when it will be exterminated is yet not clearly understood by the scientist, Vaccination done globally to fight against the pandemic is highly successful. In India 198 crore vaccination doses have been administered, 91.6 crore populations are fully vaccinated which constituted 66.4 % Population of our country. The utilization of antibiotics on an ordinary and unnecessary basis in hospitals stay a main consideration in the blow-out of antibiotics resistant microbial pathogens. Patients release unused or generally low portions of non-processed antibiotics through urination and faecal sample, which could spread in the climate through sewage removal and advance the development of antibiotic resistant microorganisms which can cause emergency in future for spread of antibiotic resistant bacteria everywhere. After Covid pandemic, It is assumed that the whole world may have a fight against Multiple resistant bacterial pathogens or microorganism connected to water and food. MDR bacteria (like MRSA and VRSA) in addition to newly mutated microorganism may also infect human beings, birds and animals. The infections they will motive could be tougher to deal with than the ones due to non-resistant microorganism. Inevitably, antimicrobial resistance will purpose highly-priced medical logistic, sudden creations of infrastructure, and hospitalization cost together with excessive mortality. Currently due to coronavirus pandemic and earlier the *Ebolavirus*, *Hantavirus* and *Zikavirus* have already confirmed how rapid infectious disease can spread in humans beings and emphasise the vital prerequisite for a protocol for

fast vaccine development on immediate outbreaks for generating region wise vaccination for rapid fight against those viral biological weapons to prevent pandemics (Pitlik *et al.*, 2020).

Infectious agents like Viruses and bacterial pathogens unfold at a faster rate therefore, containment through fitness in population measures can't continually deliver pandemics beneath control. Instead, international vaccine packages because of advances in the scientific approach might be used to govern the unfold of the pathogens, resulting in development of herd immunity and decrease mortality rates in human beings. The amazing instance, a landmark within aspect the records of medication has been the producing of an appropriate vaccine, which have become evolved in a great deal within twelve months a very short interval compares to the traditional time duration for development of vaccine. In the case of infectious diseases, medical biotechnologist is required to make novel and operative vaccines, which may be used to increase immune response and for this reason a strong herd immunity inside the different racial group is pivotal. However, this isn't always possible, as in *HIV/AIDS* patients, which is only controlled through medical prophylaxis and powerful anti-retroviral medication under an experienced physician, and now no longer through vaccination.

Antibiotic resistance and the scarcity of recently developed antibiotics, is one of the major issues facing the world today. This threatens to reduce the efficiency of bacterial treatment for MDR patients generally. Antibiotic misuse, even when not necessary and reasonable, aids in the development of drug resistance, which is further exacerbated by unnecessary and excessive use. This is especially true for the situation in many developing nations, where uncontrolled distribution channels and the lack of a prescription for serious drug abuse is common. Antibiotic misuses as across food-animal production has also contributed to an increase in the prevalence of bacteria that are resistant to many antibiotics. In future for wealth creation, it will again be challenging to Food animal production industry (Seal *et al.*, 2018; Ameshe *et al.*, 2022; Chowdhury *et al.*, 2022).

Regardless of the newer development in vaccinology, immunization have now been progressed towards bacterial microorganisms comprising of *Salmonella typhi*, *Chlamydia trachomatis*, *Staphylococcus aureus*, *Haemophilus influenzae*, *Helicobacter pylori* and *Mycobacterium tuberculosis* vaccination. An occurrence of a latest success is most recent strategy for fostering an immunization towards the utility of RNA age, which transformed into used to lift an immunization concerning the plague causing bacteria *Yersinia*

pestis, which a gram negative bacteria associated with genus *Yersinia* (*Y. pseudotuberculosis* and *Y. enterocolitica*). These vaccines might be used against various bacterial microorganisms, comprising of novel microbes because of the advancement of non-pathogenic bacterial taxa. Latest improvement in nanoparticle-principally based absolutely immunizations give a glittery new chance to fast improvement of antibacterial vaccines for human as well as living animals. For instance, different polymers and lipid-based nano transporters boost the immunogenicity of oral vaccinations by activating fundamentally safe and mucosal responses. For saving the impact of a pandemic interceded with the guide of utilizing a one of a kind bacterium stress it's far imperative to widen new antibiotics equipped for integrate the spread of microorganisms into the general human population and to modify utilizing by and by used anti-toxins. Fewer unique use of antibiotic is achieving in modern medical settings. One rationale in that is the extreme improvement charges to find out and pass new anti-infection agents like antibiotics on to commercial centre with susceptibility with inside the cap competence of drug partnerships to recover the ones concerns. Progress towards the improvement of most recent antimicrobials has thus been slow, with easiest controlled reach to be had for boundless use to think about bacterial diseases. This is a referenced mission with some of public and individual joint efforts running toward finding new elucidations to this issue. Encouragingly, using antimicrobial boom promoters must be currently forbidden in many nations all through food animal production centres (Czaplewski *et al.*, 2016; Lewies *et al.*, 2019; Attia *et al.*, 2021).

The number of bacterial strains recovered from sputum and blood were mostly Gram-negative bacteria, including *A. baumannii* and *K. pneumoniae*, and COVID-19 patients admitted to ICUs had greater rates of bacterial coinfection than non-ICU patients. Except for colistin, which can be employed in treatment plans, *A. baumannii* were resistant to all tested antibiotics. Gram-negative bacteria isolated from COVID-19 patients had a high level of resistance, particularly in patients receiving intensive care. It is crucial to continuously monitor the patterns of bacterial coinfection and resistance as well as to enhance infection control procedures in order to both locally and globally to counter the pandemic. (Bazaid *et al.*, 2022).

Experts from the working groups of the World Health Organization (W.H.O) and the Food and Agriculture Organization (F.A.O.) of the United Nations define probiotics as, "live strains of strictly selected microorganisms which, when administered in adequate amounts, confer a health benefit on the

host". This definition was also reserved by the International scientific association for probiotics and prebiotics (I.S.A.P.P). Probiotics have been the subject of more research than any other human illness therapies during the earlier 20 years. The impact of probiotics on illnesses vacillating from necrotizing enterocolitis and colic in new-borns to constipation, irritable bowel syndrome and hepatic encephalopathy in adults was examined by many research papers done as meta-analyses. The clinical conditions like acute infectious diarrhoea, acute respiratory tract infections (R.T.Is), necrotizing enterocolitis, antibiotic-associated diarrhoea and colitis provide the greatest evidence in support of probiotics. In a recent study conducted in India human colostrum comprises a significant amount of lactic acid bacteria (LAB) with significant probiotic potential. Human colostrum is the initial, thick milk produced right after delivery. Its structure and actions are very different from those of natural milk. Proteins, vitamins, immunoglobulins, carbs, amino acids, and a variety of other nutrients are present in high concentrations (Moossavi *et al.*, 2018).

The effectiveness of oncolytic viruses, a novel class of multi-modal immunotherapies for cancer, depends heavily on the antitumor immunity that the oncolytic viruses elicit. As its clinical usefulness as a monotherapy is still restricted, researchers have been experimenting with other anti-cancer drug combinations and have found that certain combinations have increased therapeutic efficacy. These cellular and molecular modifications offer interesting targets for logical cancer treatment design since cancer cells have evolved to modify important signalling pathways for increased cell proliferation, cancer growth, and metastasis. These comprise of monoclonal antibodies, the use of invulnerable designated spot inhibitors, receptive T-Cells move, most malignant growths immunizations comprehensive of dendritic cells arrangements, and the use of modulators of the resistant machine comprehensive of dissolvable variables, comprising of cytokines. Thus, in light of the fact that the immunotherapeutic techniques develop it should be capable to apply those procedures to build up the safe machine to battle microbial contaminations. The blended utilization of the above innovation in battling bacterial diseases keeps on being in its earliest stages, and might most extreme at some point presumably find programs inside the near predetermination. They ought to likely be utilized for the counteraction of a destructive pathogenic miniature creature and thus, control the presence of fate pandemics due to MDR bacterial pathogens. By relocating faecal microbiomes across monogastric producing animals (e.g. chickens) and microbiological source mining like yeast and

Bacteria to find innovative antibacterial chemicals with efficient properties, probiotics are established. The second international symposium on antibiotic alternatives aimed to identify promising research results and advanced systems that can provide antibiotic substitutes for use in animal health and production, to assess technical issues in their approval and commercialization, and to provide a practical approach for developmental strategy findings. The goal of the conference was to develop microbiome-derived products and introducing new technologies, such as mining, using CRISPR-Cas nucleases for the preparation of sequence specific antibiotics preparations. Various other studies have concentrated on the ongoing development of antimicrobial peptides including the recently identified bacteriocins as antibiotic alternatives, using bacteriophages in tandem with the creation of innovative, cutting-edge techniques like the microbial ecology-guided identification of anti-biofilm substances and lytic proteins with particular cell-wall binding domains, which are often found in marine settings (Jinek *et al.*, 2012; Pellagatti *et al.*, 2015; León-Buitimea *et al.*, 2022). Current research and reporting on bacterial and fungal infections in COVID-19 patients are insufficient. Only a few clinical studies with hundreds of published clinical data have described secondary infections, the most of them without specific pathogen information. The secondary infection complication of bacterial or fungal infection was not taken into account in the prognosis analysis in the majority of published publications, even in studies for which secondary infection data were available. The antibiotics use rate 94-100% were substantially higher than the reported incidence of secondary infection (10%-15%). Prevention of subsequent fungal or bacterial infection. In fact, 50.0% of COVID-19 patients who died had secondary infections. an alarming situations for the world to face in coming era. 15.5% of hospitalized COVID-19 patients have bacterial infections overall. However, the majority of studies that are currently available describe co-infections with bacteria and viruses that were identified at the time of COVID-19 diagnosis. The bulk of them were brought on by bacterial pathogens like *Streptococcus pneumoniae* and *Haemophilus influenzae* and respiratory viruses that were spread by people in the community. Bacterial pathogens as secondary infections, on the other hand, are those that develop during a hospitalization or illness is very common nowadays. (Langford *et al.*, 2020; Lansbury *et al.*, 2020; Zhou, *et al.*, 2020)

Early on, the broad application of artemisinin-based combination therapies signalled a new era in the efficient management of drug-resistant *Plasmodium falciparum* malaria. However, the

proliferation of parasites that are less susceptible to artemisinin (ART) derivatives and ACT auxiliary medicines has already been recorded in various Southeast Asian nations, which has raised the risk of treatment failure. It is urgent for scientific organisations to evaluate developments in the creation of antimicrobial compounds and their substitutes that could stop the emergence and spread of antimicrobial resistance among bacterial and protozoan pathogens given the ongoing concerns about antimicrobial resistance around the world. The World Health Organization has already recognised the most harmful drug-resistant germs for which new treatments are urgently required. By identifying these priority pathogens, W.H.O hopes to direct funding toward the creation of the most important antibiotics. The list, according to researchers, serves as a helpful reminder of the risk posed by bacteria that are developing antibiotic resistance. According to estimates, 700,000 individuals die every year from antibiotic resistance globally, and if no action is taken to combat it or create new medicines, that figure may increase to 10 million by the year 2050. A global eradication campaign is necessary to fight MDR infections and sustain the superior hospital practises recommended by the WHO (Blasco *et al.*, 2017; Wu, *et al.*, 2021; Bikard *et al.*, 2017; Hoelzer *et al.*, 2018; Willyard *et al.*, 2017).

References

- Alling, D.W., Blackwelder, W.C., and Stuart-Harris, C.H. (1981). A study of excess mortality during influenza epidemics in the United States, 1968-1976. *American Journal of Epidemiology*, 113(1):30-43. <https://doi.org/10.1093/oxfordjournals.aje.a113063>
- Ameshe, A., Engda, T., and Gizachew, M. (2022). Antimicrobial Resistance Patterns, Extended-Spectrum Beta-Lactamase Production, and Associated Risk Factors of *Klebsiella* Species among UTI-Suspected Patients at Bahir Dar City, Northwest Ethiopia. *International Journal of Microbiology*, 18:8216545. <https://doi.org/10.1155/2022/8216545>
- Attia, M.A., Essa, E.A., Elebyary, T.T., Faheem, A.M., and Elkordy, A.A. (2021). Brief on Recent Application of Liposomal Vaccines for Lower Respiratory Tract Viral Infections: From Influenza to COVID-19 Vaccines. *Pharmaceuticals*, 14(11):1173. <https://doi.org/10.3390/ph14111173>
- Bazaid, A.S., Barnawi, H., Qanash, H., Alsaif, G., Aldarhami, A., Gattan, H., Alharbi, B., Alrashidi, A., Al-Soud, W.A., Moussa, S., and Alfouzan, F. (2022). Bacterial Coinfection and Antibiotic Resistance Profiles among Hospitalised COVID-19 Patients. *Microorganisms*, 10(3):495. <https://doi.org/10.3390/microorganisms10030495>
- Bikard, D., and Barrangou, R. (2017). Using CRISPR-Cas systems as antimicrobials. *Current Opinion in Microbiology*, 37:155-160. <https://doi.org/10.1016/j.mib.2017.08.005>
- Blasco, B., Leroy, D., and Fidock, D.A. (2017). Antimalarial drug resistance: linking *Plasmodium falciparum* parasite

- biology to the clinic. *Nature Medicine*, 23(8):917-928. <https://doi.org/10.1038/nm.4381>
- Chowdhury, A.M.M.A. and Uddin, K.N. (2022). Analysis of the Occurrence of Antibiotic Resistant Bacteria in the Hospital's Effluent and its Receiving Environment. *Microbiol Insights*, 14;15:11786361221078211. <https://doi.org/10.1177/11786361221078211>
- Cobos, A.J., Nelson, C.G., Jehn, M., Viboud, C., and Chowell G. (2016). Mortality and transmissibility patterns of the 1957 influenza pandemic in Maricopa County, Arizona. *BMC Infectious Diseases*, 16(1):405. <https://doi.org/10.1186/s12879-016-1716-7>
- Czaplewski, L., Bax, R., Clokie, M., Dawson, M., Fairhead, H., Fischetti, V.A., Foster, S., Gilmore, B.F., Hancock, R.E., Harper, D., Henderson, I.R., Hilpert, K., Jones, B.V., Kadioglu, A., Knowles, D., Ólafsdóttir, S., Payne, D., Projan, S., Shaunak, S., Silverman, J., Thomas, C.M., Trust, T.J., Warn, P., and Rex, J.H. (2016). Alternatives to antibiotics-a pipeline portfolio review. *Lancet Infectious Disease*, 16(2):239-251. [https://doi.org/10.1016/S1473-3099\(15\)00466-1](https://doi.org/10.1016/S1473-3099(15)00466-1)
- Gupta, R.K., George, R., and Nguyen-Van-Tam, J.S. (2008). Bacterial pneumonia and pandemic influenza planning. *Emerging Infectious Diseases*, 14(8):1,187-1,192. <https://doi.org/10.3201/eid1407.070751>
- Hoelzer, K., Bielke, L., Blake, D.P., Cox, E., Cutting, S.M., Devriendt, B., Erlacher-Vindel, E., Goossens, E., Karaca, K., Lemiere, S., Metzner, M., Raicek, M., Collell-Suriñach, M., Wong, N.M., Gay, C., and Immerseel, F.V. (2018). Vaccines as alternatives to antibiotics for food producing animals. Part 1: challenges and needs. *Veterinary Research*, 49(1):64. <https://doi.org/10.1186/s13567-018-0560-8>
- Jinek, M., Chylinski, K., Fonfara, I., Hauer, M., Doudna, J.A., and Charpentier, E. (2012). A Programmable Dual-RNA-Guided DNA Endonuclease in Adaptive Bacterial Immunity. *Science*, 337(6096):816-21. <https://doi.org/10.1126/science.1225829>
- Langford, B.J., So, M., Raybardhan, S., Leung, V., Westwood, D., MacFadden, D.R., Soucy, J.R., and Daneman, N. (2020). Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. *Clinical Microbiology and Infectious*, 26(12):1,622-1,629. <https://doi.org/10.1016/j.cmi.2020.07.016>
- Lansbury, L., Lim, B., Baskaran, V., and Lim, W.S. (2020). Co-infections in people with COVID-19: a systematic review and meta-analysis. *Journal of Infection*, 81(2):266-275. <https://doi.org/10.1016/j.jinf.2020.05.046>
- León-Buitimea, A., Balderas-Cisneros, F.J., Garza-Cárdenas, C.R., Garza-Cervantes, J.A., and Morones-Ramírez, J.R. (2022). Synthetic Biology Tools for Engineering Microbial Cells to Fight Superbugs. *Frontiers in Bioengineering and Biotechnology*, 4(10):869206. <https://doi.org/10.3389/fbioe.2022.869206>
- Lewies, A., Du-Plessis, L.H., and Wentzel, J.F. (2019). Antimicrobial Peptides: the Achilles' Heel of Antibiotic Resistance?. *Probiotics and Antimicrobial Proteins*, 11(2):370-381. <https://doi.org/10.1007/s12602-018-9465-0>
- Moossavi, S., Miliku, K., Sepehri, S., Khafipour, E., and Azad, M.B. (2018). The Prebiotic and Probiotic Properties of Human Milk: Implications for Infant Immune Development and Pediatric Asthma. *Frontiers in Pediatrics*, 24(6):197. <https://doi.org/10.3389/fped.2018.00197>
- Morens, D.M., Taubenberger, J.K., and Fauci, A.S. (2008). Predominant Role of Bacterial Pneumonia as a Cause of Death in Pandemic Influenza: Implications for Pandemic Influenza Preparedness. *The Journal of infectious diseases*, 198(7):962-970. <https://doi.org/10.1086/591708>
- Pellagatti, A., Dolatshad, H., Valletta, S., and Boultwood, J. (2015). Application of CRISPR/Cas9 genome editing to the study and treatment of disease. *Archives of Toxicology*, 89(7):1,023-1,034. <https://doi.org/10.1007/s00204-015-1504-y>
- Pitlik, S.D. (2020). COVID-19 Compared to Other Pandemic Diseases. *Rambam Maimonides Medical Journal*, 11(3):e0027. <https://doi.org/10.5041/RMMJ.10418>
- Salazar, C.B., Spencer, P., Mohamad, K., Jabeen, A., Abdulmonem, W.A., and Fernández, N. (2022). Future pandemics might be caused by bacteria and not viruses: Recent advances in medical preventive practice. *International journal of health sciences*, 16(3):1-3. <https://doi.org/10.53350/pjmhs22161827>
- Seal, B.S., Drider, D., Oakley, B.B., Brüssow, H., Bikard, D., and Rich, J.O., Miller, S., Devillard, E., Kwan, J., Bertin, G., Reeves, S., Swift, S.M., Raicek, M., and Gay, C.G. (2018). Microbial-derived products as potential new antimicrobials. *Veterinary Research*, 49:66. <https://doi.org/10.1186/s13567-018-0563-5>
- Willyard, C. (2017). The drug-resistant bacteria that pose the greatest health threats. *Nature*, 543(7643):15. <https://doi.org/10.1038/nature.2017.21550>
- Wu, Y., Battalapalli, D., Hakeem, M.J., Selamneni, V., Zhang, P., Draz, M.S., and Ruan, Z. (2021). Engineered CRISPR-Cas systems for the detection and control of antibiotic-resistant infections. *Journal of Nanobiotechnology*, 19(1):401. <https://doi.org/10.1186/s12951-021-01132-8>
- Zhou, P., Liu, Z., Chen, Y., Xiao, Y., Huang, X., and Fan, X. (2020). Bacterial and fungal infections in COVID-19 patients: A matter of concern. *Infection Control & Hospital Epidemiology*, 41(9):1,124-1,125. <https://doi.org/10.1017/ice.2020.156>