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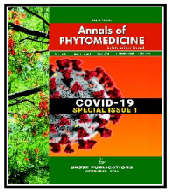

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Prevalence of coinfections with ESKAPE pathogens in COVID-19 patients: A review

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Abstract

The emergence and worldwide spread of the COVID-19 pandemic, which is being caused by a type of coronavirus named as SARS-CoV-2, has unprecedentedly challenged the healthcare system across the globe. To add to the catastrophe brought about by this viral infectious disease, coinfections by other microbial agents including bacteria and fungi further deteriorate the health of COVID-19 patients by developing multiple dreaded diseases, resulting in extended morbidity and high rate of mortality all over the world. There are a number of multidrug resistant bacterial species which cause these coinfections both in community environments and hospital set ups including in the ICUs. Among the multidrug resistant bacterial species that are responsible for tens of thousands of deaths per annum around the globe, the infectious diseases society of America (IDSA) has shortlisted and the world health organization (WHO) has recognized the importance of the most dangerous 'bad bugs' dubbed as 'ESKAPE' pathogens and the members are *Enterococcus faecium* (E), *Staphylococcus aureus* (S), *Klebsiella pneumoniae* (K), *Acinetobacter baumannii* (A), *Pseudomonas aeruginosa* (P) and *Enterobacter species* and *Escherichia coli* (E). Each one of the above mentioned bacterium has many MDR strains and complex antimicrobial resistance mechanisms. In this review, I try to find out the reported prevalence of these pathogens in COVID-19 patients admitted to various healthcare facilities across the world.

1. Introduction

It was just the beginning of an unprecedented pandemic catastrophe when a number of people were presented with a kind of atypical pneumonia in and around Wuhan city of Hubei Province in China in December 2019 (Ansari *et al*., 2021). As the spread went uncontrolled, the scientists began the detailed investigations and confirmed the cases as severe acute respiratory syndrome (SARS), caused by a kind of coronavirus, which later termed as SARS-CoV-2 by the coronavirus study group (CSG) of the International Committee on Taxonomy of Viruses (ICTV) (Zhu *et al*., 2020). As of May 23, 2021, there are 166,346,635 confirmed COVID-19 cases including 3,449,117 deaths worldwide (https://COVID-19. who.int/updated on 22/05/2021). The causative virus is an enveloped, Coronaviridae family member with a single stranded RNA (Sola *et al.*, 2015) and the disease caused by it was later officially named as COVID-19 on 11 February 2020 (Ansari *et al*., 2021; Rothe *et al.*, 2021) and on March 11 in the same year, the WHO declared the COVID-19 as a pandemic (Ghebreyesus, 2020).

COVID-19 is a systemic infection which affect a wide variety of cells and tissues (Vazzana *et al.*, 2021). The disease becomes more fatal when it gets complicated with bacterial and/or fungal coinfections or super infections and secondary infections especially with multidrug resistant (MDR) or antimicrobial resistant (AMR) resistant pathogenic strains, which of them were detected in 50% of COVID-19 deaths (Rossato *et al*., 2020; Cole *et al*., 2021; Rawson *et al*., 2021; Lai *et al*., 2021; Patel *et al*., 2021; Knight *et al*., 2021).

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Various AMR and MDR strains of different bacterial pathogens are responsible for around 700,000 annual deaths across the globe and is predicted to reach 10 million mortalities per year by 2050 (Fattorini *et al*., 2020; Rossato *et al*., 2020; Chen *et al*., 2020; Mazdeyasna *et al*., 2020; Rawson *et al*., 2020; Mirzaei *et al*., 2020; Rusic *et al*., 2021; Ansari *et al*., 2021; Rawson *et al*., 2021; Lai *et al*., 2021; Patel *et al*., 2021; Mayoral *et al*., 2021; Pelfrene *et al*., 2021; Majumder *et al*., 2021; Prasetyoputri 2021). Out of these 'bad bugs', in 2007, the Infectious Diseases Society of America (IDSA) had selected the five most dangerous AMR bacterial species which show cunning "escape" from antimicrobial agents through a variety of complicated resistance mechanisms, thereby causing higher mortality and more healthcare expenses, and are dubbed as "ESKAPE" pathogens (Musthafa *et al*., 2020; Majumder *et al*., 2021). They are *Enterococcus faecium* (E), *Staphylococcus aureus* (S), *Klebsiella pneumoniae* (K), *Acinetobacter baumannii* (A), *Pseudomonas aeruginosa* (P) and *Enterobacter* species and *Escherichia coli* (E) and the world health organization (WHO) has listed them in the Priority Pathogens List ('PPL'-published in 2017) of 12 bacterial pathogens against which potential antimicrobial agents are urgently required (Ramsamy *et al*., 2018; Mulani *et al*., 2019; Ansari *et al*., 2021). The major purpose of IDSA's antimicrobial stewardship (AMS) program, started in 2007 was to control this 'ESKAPE' menace (Majumder *et al*., 2021). The coinfections with the antimicrobial resistant ESKAPE members often result in life-threatening complications along with the COVID-19. This article reviews the catastrophe reported by the coinfections with each one of the members of the ESKAPE pathogens.

2. Bacterial coinfections in COVID-19 in general

The unprecedented health crisis worldwide, due to the ongoing COVID-19 has multiplied with the concerns brought by the AMR bacterial coinfections (Rawson *et al*., 2021). An ever increased

prevalence of AMR infections have been reported with the COVID-19, ranging from common nosocomial infections to bacteremia, hospital-acquired pneumonia and ventilator-associated pneumonia (Garcia-Vidal *et al*., 2020; Rawson *et al*., 2021).

Different investigations found out COVID-19 bacterial coinfections at various levels, and the causative agents included MDR strains of high priority categories like vancomycin resistant *Enterococci* (VRE) including *Enterococcus faecium*, vancomycin-intermediate/resistant *Staphylococcus aureus* (VISA/VRSA), methicillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum *beta*-lactamase (ESBL) producing *Klebsiella pneumoniae* (ESBLKp), carbapenem-resistant *Acinetobacter baumannii* (CRAB), ESBL producing *Pseudomonas aeruginosa*, carbapenem-resistant *Enterobacteriaceae* (CREB), ESBL producing *Escherichia coli*, carbapenem-resistant NDM-producing Enterobacterales, clarithromycin-resistant *Helicobacter pylori* (CRHP), *Enterobacter cloacae*, fluoroquinolone resistant *Campylobacter* spp., *Salmonella* spp., cephalosporin and fluoroquinolone-resistant *Neisseria gonorrhoeae*, penicillin-resistant *Streptococcus pneumoniae* (PRSP), ampicillin-resistant *Haemophilus influenza*, fluoroquinolone-resistant *Shigella* spp., *Chlamydophila pneumoniae, Mycoplasma pneumoniae, Legionella pneumophila, Stenotrophomo nasmaltophilia, Mycobacterium tuberculosis, Serratia* spp. including *Serratia marcescens, Proteus* spp., *Mycoplasma* species, *etc*., were the bacterial pathogens most often observed (Sharifipour *et al*., 2020; Contou *et al*., 2020; Lai *et al*., 2020; Yang *et al*., 2020; Chen *et al*., 2020; Ansari *et al*., 2021; Rawson *et al*., 2021; Lai *et al*., 2021).Studies on bacterial coinfections in COVID-19 patients reported by (Sharifipour *et al*., 2020; Rawson *et al*., 2021; Lai *et al*., 2021) have also brought about the presence of other pathogenic bacteria which are resistant to resistant to third-generation cephalosporins and amoxicillin/clavulanate.

3. Coinfections by ESKAPE pathogens in COVID-19 patients

3.1 *Enterococcus faecium*

Enterococci are Gram positive, aerobic or facultative anaerobic, opportunistic pathogens frequently involved in healthcare associated infections (HAIs) or nosocomial infections and can cause severe infectious diseases especially among immunocompromised patients (Santajit and Nitaya Indrawattana, 2016; Said *et al*., 2020). Various studies have shown that this species is common in COVID-19 patients. A retrospective study conducted by Rothe *et al*., (2021) in 140 COVID-19 patients at the German University hospital admitted between February and April 2020 showed blood infection with vancomycin-resistant *Enterococcus faecium* including two Van B phenotypic strain confirmed by molecular technique. In another study, Feldman and Anderson (2021) described about the isolation of *Enterococcus faecium* along with other bacterial pathogens from the blood and BAL samples. An observational cohort analysis at the University Hospital Clinic of Barcelona for COVID-19 patients during the period of 28 February to 22 April 2020 showed the presence of *Enterococcus faecium* in 14.2% of the COVID-19 patients at the time of admission and in 18.7% of patients as hospital acquired super-infective complications after being admitted (Garcia-Vidal *et al*., 2020).

Another retrospective analysis on 32 COVID-19 ICU patients admitted to the Monaldi Hospital, Naples, Italy in March and April 2020 revealed the prevalence of 13% of invasive MDR Enterococci with presence of 9% of *Enterococcus faecium* (Karruli *et al*., 2020). These isolates were even resistant to higher concentration of aminoglycosides and the study found out that one of one strains of *Enterococcus faecium* was resistant to even ampicillin. Rawson *et al*. (2020) observes that, critically ill patients receiving treatment using invasive catheters are at a high risk of secondary infections with MDR bacterial strains including that of *Enterococcus* spp. Ukuhor *et al*. (2021) also reported COVID-19 coinfections with AMR strains of *Enterococcus* spp.

3.2 *Staphylococcus aureus*

Staphylococcus aureus is Gram positive, coccus shaped and is the most common member of skin microflora with about 30% of skin or noses of healthy people are colonized with this bacterium (Navidinia *et al*., 2016; Taylor and Unakal, 2020). *Staphylococcus aureus has* been known for its involvement in severe clinical coinfections in COVID-19 patients and the coinfection by hospital acquired strains are like methicillin-resistant *Staphylococcus aureus* (MRSA) are of a great threat (Punjabi *et al*., 2020).

A cohort of COVID-19 ICU patients at a referral hospital in Qom, Iran was studied for their coinfections and found that 10% of them were infected with MDR *Staphylococcus aureus* including MRSA (Sharifipour*et al*., 2020). Another retrospective investigation in France found out that 28% of severely ill COVID-19 patients had bacterial coinfection including with that by methicillin-sensitive *Staphylococcus aureus* (Contou *et al*., 2020). A study conducted by Kathrin Rothe *et al*. (2021), with the respiratory samples of on 140 COVID-19 inpatients at a German University hospital during February-May 2020 detected the presence of *Staphylococcus aureus* at 13% including MRSA. At a Spanish hospital, in a prospective study, 26% of 92 COVID-19 patients were shown early infections (at the time or within 48 h of admission to the ICU) and 46.7% with later infections with *Staphylococcus aureus* (Barrasa *et al*., 2020). The study by Contou *et al*. (2020) also found out that the 28% of ICU COVID-19 patients at a French hospital were having early infections and *Staphylococcus aureus* was one of the prominent members. Wolfe (2020) and colleagues reported that 55.8% of total bacterial co-pathogens isolated from COVID-19 patients were *Staphylococcus aureus*. Garcia-Vidal *et al.*, (2020) in their report on coinfection and superinfection by bacterial pathogens in 989 COVID-19 inpatients at a hospital in Barcelona, Spain said that, 3% of the patients were having *Staphylococcus aureus* pneumonia with 44% of coagulase-negative *Staphylococci* as the most predominant in bloodstream infectious agent. Another retrospective study at Desio Hospital, Lombardy, Italy conducted on COVID-19 patients showed coinfections by *Staphylococcus aureus* at a level of 5% (Intra *et al*., 2020). Other investigations like that of Mayoral *et al*. (2021) also underline the findings, reporting the presence of *Staphylococcus aureus* up to 15% in among isolate in COVID-19 ICU patients.

A report by Duployez *et al*. (2020) mentioned about the presence of panton-valentine leucocidin (PVL) secreting *Staphylococcus aureus* which caused a dangerous necrotizing pneumonia in a COVID-19 patients. The microbiological investigations on COVID-19 patients hospitalized in New York identified the presence of *Staphylococcus aureus* in 44% of the patients (Sharifipour *et al*., 2020) and this finding was verified by Fattorini *et al*. (2020). An observational cohort analysis at the University Hospital Clinic of

Barcelona, which was mentioned elsewhere in this article could also find out the presence of methicillin resistant *Staphylococcus aureus* which contributed 4% of total bacterial isolates from COVID-19 ICU patients (Garcia-Vidal *et al*., 2020). Many clinical investigations across the world, like that of Rusic *et al.* (2021) have also pictured *Staphylococcus aureus* as the most prevalent cause for secondary bacterial infection in COVID-19 patients.

3.3 *Klebsiella pneumoniae*

Klebsiella pneumoniae is Gram negative, rod shaped, non-motile, bacteria that belongs to *Entero bacteriaceae* family (Ashurst and Dawson, 2021). Together with *Escherichia coli*, they pose a great health threat as they are prevalent globally in community areas and hospital environments (Pendleton *et al*., 2013). Investigation on COVID-19 patients in various healthcare facilities across the world have shown theat this bacterium has been playing a crucial role in extended morbidity and higher rate of mortalities. 11 samples out of 23 respiratory samples from the COVID-19 patients at the German University hospital, a study mentioned elsewhere in this review, could show the presence of *Klebsiella* spp. with one sample having *Klebsiella pneumoniae* (Rothe *et al.*, 2021). Rawson *et al.* (2021) describes about a study at a Barcelona Hospital ICU for COVID-19 patients where pathogens including *Klebsiella* spp. were responsible for some clinical complications like bacteraemia, hospital-acquired pneumonia, ventilator-associated pneumonia, *etc*. Another study reported by Intra *et al.*(2020) at the COVID-19 ICU of Desio Hospital, Lombardy, Italy also confirmed the presence of 3% *Klebsiella pneumoniae*. In Wuhan, China, Li *et al*. (2020) reported that, 30.8% of the total isolates caused acquired secondary infections among COVID-19 patients were due to *Klebsiellapneu moniae*. Chen *et al.* (2020) conducted a retrospective study based at a COVID-19 care facility in Wuhan, on 99 cases in 2019 and reported that *Klebsiella pneumoniae* was one of the prominent members that caused bacterial coinfections. The A retrospective study among the ICU patients at the German University hospital during February - May 2020 by Kathrin Rothe *et al*., (2021), with the respiratory samples of on 140 COVID-19 inpatients revealed the presence of *Klebsiella* spp. in 7.9% of isolates.

The presence of *Klebsiella pneumoniae* in SARS-CoV-2 patients with bacterial coinfections were also confirmed by Cevik *et al*. (2020) and Root-Bernstein *et al.* (2021). Chen *et al.* (2020) repot that 5.1% of clinical isolates from 99 COVID-19 patients in Wuhan, China showed the presence of *Klebsiella pneumoniae*. At the same time, another study among COVID-19 patients in New York reported the infection with *Klebsiella* spp. having 10% prevalence with *Klebsiella pneumoniae* strains showing reduced sensitivity to major antibiotics like ciprofloxacin, cephalosporins and meropenem by 10% (Nori *et al*., 2021). The instigation by Li *et al.* (2020) on secondary bacterial infections in 102 COVID-19 patients shown presence of 159 strains with carbapenem-resistant *Klebsiella pneumoniae*. The study by Ukuhor *et al*. (2021) also lists AMR *Klebsiella pneumoniae* as one of the major isolates from the COVID-19 inpatients. The prevalence of *Klebsiella pneumoniae* was further confirmed by Garcia-Vidal *et al*. (2020) as they were present in 14.2% of the isolates from COVID-19 patients at the time of their admission, in 25% of isolates as hospital acquired pneumonia agents and in another 25% of isolates from urinary tract infection agents. The study conducted by Karruli *et al*. (2020) in COVID-19 ICU patients at Monaldi Hospital, Naples, Italy during March and May 2020 declared carbapenem-resistant *Klebsiella pneumoniae* were the most common MDR bacterial pathogen isolated.

3.4 *Acinetobacter baumannii*

Acinetobacter baumannii is Gram negative, short, rod-shaped but round (coccobacillus) bacterium (Howard *et al*., 2012). Being an opportunistic pathogen, it affects human and became a very commonly encountered species in patients in intensive care units (ICUs), and are responsible for a number of health complications including urinary tract infections, meningitis, bacteremia, central venous catheter-related infections, ventilator associated pneumonia, wound infections, *etc*. (Michalopoulos and Falagas 2010; Howard *et al*., 2012). *Acinetobacter baumannii* was the largest single common species of bacteria with a prevalence of 35.8% when analyzed by Li *et al*. (2020) in Wuhan, China and surprisingly, 91.2% of them were carbapenem resistant. Carbapenem resistant *Acinetobacter baumannii* infections among COVID-19 patients were also reported by Perez *et al*. (2020) in the beginning of the pandemic itself in a New Jersey hospital. Rawson *et al*. (2020) and Chen *et al*. (2020) describe the incidents of secondary infections in COVID-19 patients with MDR *Acinetobacter baumannii* in different parts of the world including Wuhan, China. Mayoral *et al*. (2021) evaluated the coinfection by *Acinetobacter baumannii* in COVID-19 patients in a tertiary hospital in the community of Castilla and León, Spain. They reported that *Acinetobacter baumannii* caused the most of the MDR bacteremia and they concluded that, in ICU patients with COVID-19, the outbreak of this particular bacterium was the determining factor in the high rate of infection, morbidity and mortality. The coinfections by *Acinetobacter baumanii* in COVID-19 ICUs were also explained by Duployez *et al*. (2020). An investigation conducted by Sharifipour *et al*. (2020) at a COVID-19 referral hospital in Iran found out that, 90% of the ICU patients were infected with *Acinetobacter baumanii* and from those patients, 17 strains of *Acinetobacter baumanii* were isolated of which all were resistant to all of the evaluated antibiotics. Fattorini *et al*. (2020) also listed *Acinetobacter baumanii* as one of the three most prevalent bacterial pathogens (with 91.7% carbapenem-resistance among them) causing coinfections in COVID-19 patients, and also notes that they form mixed infections often with *Klebsiella pneumoniae*. They also reported that, from the ICU-death group who were having bacterial coinfections, carbapenem resistant *Acinetobacter baumannii* was isolated. Karruli *et al*. (2020) also made a serious finding that, most of the MDR pathogens among the 23 isolates from COVID-19 patients in the ICU of Monaldi Hospital, Naples, Italy, most of them were *Acinetobacter baumannii* and carbapenem-resistant *Klebsiella pneumoniae*. The study by Patel *et al*. (2021) also underlines the above mentioned findings.

3.5 *Pseudomonas aeruginosa*

These facultative anaerobic bacteria are Gram negative bacilli which form a part of the normal gut flora (Iglewski,1996). They have already developed a number of MDR strains which would be resistant to at least three of five major antibiotics, *viz.*, carbapenems, antipseudomonal penicillins, cephalosporins, aminoglycosides and fluoroquinolones, thereby causing prolonged morbidity and higher rate of mortality(Santajit and NitayaIndrawattan, 2016). Fu *et al*. (2020) analyzed that *Pseudomonas aeruginosa*was one of the causative agents responsible for MDR coinfection in five seriously

ill COVID-19 patients. The retrospective study performed on 140 COVID-19 patients at a German University hospital showed the presence of *Pseudomonas aeruginosa* in 8.6% of the patients having bacterial coinfections (Rothe *et al.*, 2021).

An investigation by Barrasa *et al*. (2020) in a Spanish ICU for COVID-19 patients reported that, those patients who had a longer stay in the ICU got secondary infection by *Pseudomonas aeruginosa*. During a study on COVID-19 patients in a Barcelona, Spain hospital. Garcia-Vidal *et al*. (2020) observedthat, the hospital acquired coinfections had *Pseudomonas aeruginosa* as one of the important pathogens. Zhang *et al*. (2020) also noted the *Pseudomonas aeruginosa* as a major agent causing coinfection in COVID-19 patients in Wuhan, China. Patel *et al*. (2021) described the presence of MDR *Pseudomonas aeruginosa*. According to Rawson *et al*. (2020), the secondary infections with MDR strains of pathogens like *Pseudomonas aeruginosa* may get easily infected when they receive therapies using invasive catheters. Many observations (including the those from Perez *et al*., 2020; Knight *et al*., 2021) are there which indicate that the hospital acquired infections like that of *Pseudomonas aeruginosa* is like a byproduct of this pandemic COVID-19. Different other studies also list *Pseudomonas aeruginosa* as one of the prime agents of COVID-19 bacterial coinfections. They include the studies conducted by Rusic *et al*., (2021) in New York, which reported 16% of the bacterial coinfections were caused by *Pseudomonas aeruginosa* and the investigation by Fattorini *et al*. (2020) which describes *Pseudomonas aeruginosa* as the main member causing coinfections in COVID-19 patients.

The study by Garcia-Vidal *et al*. (2020) at the Hospital Clinic of Barcelona (Spain), showed a notable presence of *Pseudomonas aeruginosa* as a bacterial coinfective agent in COVID-19 patients. Two COVID-19 patients who had bacterial coinfection in their lower respiratory tract showed the presence of *Pseudomonas aeruginosa* in them. Out of 11 patients showed hospital acquired infections, 3 of them were having *Pseudomonas aeruginosa* as one of the agents. Also, out of twelve, one of the urinary tract infections in COVID-19 patients was also by *Pseudomonas aeruginosa*. Karruli *et al*. (2021) found out that all the three identified *Pseudomonas aeruginosa* isolates were carbapenem-resistant, which were isolated during a study on 32 patients at the COVID-19 ICU of the Monaldi Hospital, Naples, Italy. According to Knigh *et al.* (2021), patients who have been left with structural damages to the lungs after COVID-19 are at a high risk infection with MDR *Pseudomonas aeruginosa* due to possible continuous usage of antibiotics and hospitalizations.

3.6 *Enterobacter* species and *Escherichia coli*

Enterobacter spp. are Gram negative facultative anaerobic, motile enteric bacilli which are now generally called eneterobacterales that are significantly responsible for urinary and respiratory tract infections and bloodstream infections (McAdam *et al*., 2020; Davin-Regli *et al*., 2019). *Enterobacter* spp. cause fatal nosocomial infections and display a broad multidrug resistance including to extended-spectrum cephalosporins (ESC), making them one of the major health concerns (Paterson, 2006; Mezzatesta *et al*., 2012; Davin-Regli and Pagès, 2015). Including in hospitalized people and immunocompromised patients, these bacteria, which have a wide range of antibiotic resistance mechanisms, cause opportunistic infections (Santajit and Nitaya Indrawattana, 2016).

Mahmoudi (2020) reported that, a study conducted on secondary infections in COVID-19 patients has found out the presence of *Escherichia coli* in 7 (16.28%) of the samples and *Enterobacter* species in 5(11.63%) of the samples analyzed. Another study by Saber *et al*. (2021) in Bangladesh showed the presence of MDR *Enterobacter* spp. along with other coinfectors in a COVID-19 patient. The work of Garcia-Vidal *et al*. (2020) at a Spanish hospital, as described elsewhere in this article, also reported the presence of *Escherichia coli* as a major nosocomial infecting agent in COVID-19 patients. Lv *et al*. (2020), during their retrospective cohort analysis on 354 COVID-19 patients admitted to Wuhan University Renmin hospital found that, a critically ill patient was infected by *Escherichia coli* along with *Candida* sp. Zhang *et al*. (2020) also noted the coinfection of bacteria including *Escherichia coli* along with fungi in seriously ill COVID-19 patients in Wuhan, China. A research review study conducted Intra *et al*. (2020) at the COVID-19 ICU of Desio Hospital, Lombardy, Italy, on 61 patients revealed the coinfection by *Escherichia coli* and *Enterobacter* sp. by 3% each. The study conducted by Patel *et al*. (2021) at University of Maryland Medical Center, USA reported the presence of 44 *Escherichiacoli* isolates including 33 MDR and 11 cefepime-resistant strains. According to Chen *et al*. (2020), patients receiving treatment using invasive catheters were more vulnerable to secondary infections with different MDR pathogens including with *Escherichia coli.* Rothe *et al*. (2020) found out that in the respiratory samples from 23 COVID-19 patients, one had the presence of *Enterobacter* sp. and six had *Escherichia coli* in them.

Rusic *et al*. (2021) in their study at a New York COVID-19 hospital reported that, 4% of the cases contained *Escherichia coli*. They also noted an increase by 42% in carbapenem resistant *Entero bacteriaceae* during in this pandemic season. Li *et al*. (2020) reports about an investigation in which 159 strains of bacteria causing coinfections in COVID-19 patients were isolated with 75% of the patients showing the presence of ESBL-producing *Escherichia coli*. The observational cohort analysis conducted by Garcia-Vidal *et al*. (2020) on 74 COVID-19 patients at the University Hospital Clinic of Barcelona, Spain, found *Escherichia coli* coinfection at various levels. 14.2% of the patients had coinfections with *Escherichia coli* at the time of admission itself. In 12.5% of them, *Escherichia coli* was present as a member of bacteraemia and in 33.5% of them, *Escherichia coli* was there as a urinary tract infecting agent. Contou *et al*. (2020) and Ghosh *et al*. (2021) also describes about the coinfections by *Enterobacteriaceae*.

4. Conclusion

The pandemic COVID-19, which have already infected more than 166 million people claiming more than 3.4 million lives worldwide continues its spree with no effective drugs developed so far. Rather than the viral infection itself, in most of the cases, they are the bacterial coinfections and secondary infections make the disease more dreaded by making the extended morbidity and higher mortality. When these infections are with MDR bacterial agents, the situation worsens. As analyzed in this review, the ESKAPE bacterial pathogens have a crucial role in making this disease a fatal one by their highly virulent and drug resistant strains. As we find in this retrospective investigation, the higher prevalence of each one of the ESKAPE member is concerning and it strongly demands the need for the development of potential, novel antibacterial agents.

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Conflict of interest

The author declares that there are no conflicts of interest relevant to this article.

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