

# Multi Drug Resistant *Escherichia coli* Superinfection in Patient with COVID-19

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## Abstract

**Background:** Coronavirus Disease 2019 (COVID-19) has infected millions people worldwide and is continuing to spread rapidly. Patients with COVID-19 may be superinfected with other microorganisms. The prevalence of bacterial superinfection among coronavirus patients is not well understood. **Aim:** The aim of presenting this case is to highlight the problem of Multi-Drug Resistant (MDR) bacterial infection in COVID-19 patients. **Case Presentation:** Here we reported a 46 years old patient with the previous history of *Escherichia coli* urinary tract infection. A few weeks later, the patient was recovered from COVID-19 infection and was treated with antiviral therapy until PCR results become negative. Meanwhile, the patients developed urinary tract infection with MDR *Escherichia coli* even resistant to imipenem and required a critical treatment. **Conclusion:** Our finding suggests that greater attention should be paid to coronavirus infection complications and prophylaxis use of antibiotics. In addition, more studies are required to better understand the risk factors which are responsible for the superinfection and emergence of drug-resistant strains during COVID-19 infection.

## Keywords

Bacterial Resistance, Superinfection, COVID-19

## 1. Introduction

COVID-19 is continuing to spread worldwide in addition to antimicrobial resistance which is also an ongoing threat. A little is known about COVID-19 asso-

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ciated superinfections. The high number of patients suffering from COVID-19 admitted to the hospital intensive care units is more vulnerable to acquiring secondary infections [1]. It was reported that 5% - 10% of COVID-19 patients suffered from life-threatening complications such as pneumonia, sepsis and organ failure [2]. These complications lead to death in around 50% of the cases [3] [4]. The use of corticosteroids, immunotherapy like anti interleukin 6 monoclonal antibodies and the overuse of antibiotics in the treatment of COVID-19 patients may play an important role in developing secondary infection and emerging of antibacterial resistance [4]. The most common type of infection among intensive care unit patients was pneumonia, bloodstream and urinary tract infection. The most common bacteria which are responsible for such infection Extended Spectrum Beta Lactamase (ESBL)-producing *Escherichia coli*, *Klebsiella Pneumoniae*, and carbapenem-resistant *Klebsiella pneumoniae*, ESBL-producing *Klebsiella Pneumoniae*, ESBL-producing *Pseudomonas aeruginosa* [5] [6]. The case under discussion is a patient who recovered from a respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The patients suffered from urinary tract infection and the results of urine culture-confirmed superinfection with MDR *Escherichia coli*. As a result of difficulties in the treatment of superinfection and selecting the effective appropriate antibiotic, we presented this case and provided suggestions and recommendations to avoid further superinfection in COVID-19 patients in the future.

## 2. Case Report

A 46 years old woman suffered from urinary tract infection symptoms. The urinalysis results showed gross hematuria, ardor urinae and positive nitrite test. The urine culture results showed *Escherichia coli* positive. Kidney function was normal with normal creatinine levels. The patients' antibiotic resistant profile showed sensitivity to penicillins and most other antibiotics (cefdinir, cefixime, amoxicillin & clavulanic acid, cefotaxime, cefaclor, ceftriaxone, ceftazidime, cefpodoxime, tri-sulfa, gentamycine, amikacin, nitrofurantoin, ciprofloxacin, norfloxacin, ofloxacin, levofloxacin, cefuroxime, cefepime). The patient treated with cotrimoxazole (trimethoprim/sulfamethoxazole) with 800 mg of trimethoprim and 160 mg of sulfamethoxazole every 12 hours for 14 days and nitrofurantoin with 100 mg every 12 hours for 3 days. A few weeks later the patient developed an acute respiratory condition and suspicion of COVID-19, we analyzed a nasopharyngeal swab by real time PCR (RT-PCR) and confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The patient was admitted to the reference hospital for symptoms suggestive of pneumonia secondary to the COVID-19. During the hospital admission the patients showed a mild neutrophilia (80%) and marked lymphopenia (4.1%). C-reactive protein was increased to 98 mg/l. The patients' oxygen saturation was 78% and put on ventilator. The patients were treated with azithromycin 500 mg daily. After 10 days the patients' oxygen saturation was increased to 91% but the patients suffered from

respiratory tract infection complications during this period. It was decided to treat the patients with (ceftriaxone 1000 mg + sulbactam 500 mg) twice daily per 10 days to avoid any other complication secondary to the COVID-19 sever infection. But the patients suffered next time from the same urinary tract infection symptoms, gross hematuria, ardor urinae and positive nitrite tests. The urine culture results showed MDR *Escherichia coli* and the antibiotic resistance profile exhibited resistance to (cefdinir, cefixime, amoxicillin & clavulanic acid, cefotaxime, cefaclor, ceftriaxone, ceftazidime, cefpodoxime, tri sulfa, nitrofurantion, ciprofloxacin, norfloxacin, ofloxacin, levofloxacin, cefuroxime, cefepime), intermediate resistance to levofloxacin and sensitive to gentamycin and amikacin. The patient had a hearing problem so it was not possible to be treated with gentamycin or amikacin. The *Escherichia coli* showed also resistance to imepenem. Therefore, it was not possible to give the patient imipenem. The patient treated with levofloxacin which is intermediately effective against isolated MDR *Escherichia coli* with 750 mg daily for one week but the results of urine culture is still positive for MDR *Escherichia coli*. The patients showed improvement of the respiratory condition and COVID-19 but still suffering from COVID-19 urinary tract infection complications with MDR *Escherichia coli* confirmed by urine culture results. Finally, it was decided to give the patients colisitn 5 mg/kg every 12 hours. An informed consent was obtained from the patient to report this case.

### 3. Discussion

According to the CDC, Urinary Tract Infections (UTI) are the most common infections require a medical care, with an estimated 67,700 UTIs in acute care hospital in 2015. UTIs account for 9.5% of infections reported by health care hospitals [7]. Around 60% of the women have at least one symptomatic urinary tract infection during their life time [8]. Gram negative bacteria are most causative agent for the UTIs. Around (75% - 95%) of the UTIs are caused by *Escherichia coli*, *Klebsiella pneumonia*, *Staphylococcus saprophyticus*, *Enterococcus faecalis*, group *B streptococci* and *Proteus mirabilis* with lower percentage. Antibiotic resistant *Escherichia coli* and *Pseudomonas aeruginosa* are the most common pathogens in complicated UTIs [8]. The multi drug resistant (MDR) organisms have become more spread in community and hospital acquired infections [9]. The genetic pressure and overuse of antibiotics like cephalosporins and quinolones in human as well as animals have an important role in this ongoing problem [10]. ESBL producing organisms have spread due to genetic elements transfer especially for *Escherichia coli* [11] [12]. Many of these strains have additional resistance against other classes of antibiotics. The overuse of antibiotic in therapy and prophylaxis use of antibiotics considered as a risk factor for MDR UTIs. It was observed that the increases risk in UTI ESBL *Escherichia coli* was associated with the long term use of antibiotics [13] [14]. However, for resistant *Escherichia coli* infection with ESBL *Escherichia coli*, carbapenems are still recommended in the treatment of MDR UIT. There is no reported study compared between

carbapenems in treatment of MDR UTIs. One study showed that meropenem has better bacteriological and clinical response than imipenemcilastatin with fewer side effects [15]. And ertapenem have more compliance for outpatient [16]. Bacterial co-infection is frequently determined in the viral respiratory tract infection like influenza virus infection and co-infections are associated with increase in the mortality and morbidity [17]. It was also observed by a histopathological study on archived tissues between 1918 and 1919 that streptococcus pneumonia was the leading cause of death of patients with influenza [18]. It was also observed that patients with influenza virus co-infected with bacterial infection had a worse outcome and required mechanical ventilation and longer Intensive Care Unit (ICU) stays than patients without co-infection [19]. Recently, antimicrobial resistance is an ongoing threat and COVID-19 pandemic further contributes to complicate this growing problem. Here we described a case of respiratory tract infection complication and urinary tract infection with MDR *Escherichia coli* superinfected patients diagnosed with COVID-19. The isolated MDR *Escherichia coli* exert resistance even to the fourth generation cephalosporin and carbapenem. Many therapeutics are suggested as alternatives to carbapenems in MDR carbapenem resistant *Escherichia coli* treatment such as colistin, aminoglycosides, tigecycline, fosfomycin, ceftazidime/avibactam and ceftolozan/tazobactam [20]. Furthermore, it was also found in a study conducted in a maryland academic hospital that multidrug resistant gram negative acquisition increased about 3% within COVID-19 patients [21]. Clinical outcomes in patients with COVID-19 and bacterial co-infections are not well understood and failing of treatment of associated bacterial infection are always reported with worse clinical outcomes and increase mortality [22]. It was reported in a case of patients with COVID-19 and *Mycoplasma pneumonia* co-infection that the failure to treat other causes of infections increased morbidity and mortality [23]. Furthermore, secondary infections were reported in 13.5% - 44% among ICU COVID-19 patients [24] [25]. The most common infection reported is bacterial and fungal pneumonia, the patients also susceptible to the urinary tract infection. It is well known that bacterial superinfection especially pneumonias can complicate the COVID-19 situation [4]. The studies about bacterial superinfection in COVID-19 patients are scarce and the data about management such infections are incomplete. It was reported that bacterial superinfection was observed in 8% of hospitalized and 16% of critically ill patients [26]. In a study developed in Wuhan 6% from the nonsurvival patients from sever COVID-19 developed hospital acquired pneumonia, 3% bacteraemia and 3% urinary tract infection [27]. There is increase in the prevalence of superinfection in COVID-19 patients like urinary tract, blood stream infection and the effect of this complicated infection on the antimicrobial treatment pattern is unclear [4]. It was also observed in a cohort study analysis on blood culture that the most common cause of bacteremia in COVID-19 patients are *Escherichia coli* (16.7%), *Staphylococcus aureus* (13.3%) and *Klebsiella pneumonia* (10%) [28]. Moreover, patients with tuberculosis (TB) which is an infectious disease usually

attack lungs and MDR TB patients who become ill with COVID-19 may have increased risk of mortality because they have increased number of cavities and lobar volume decrease compared with patients with drug sensitive TB [29]. It was reported that most of COVID-19 pathology occurs through immune mediated mechanism. Therefore, lymphopenia, reduced peripheral blood T-cells and increase the pro-inflammatory cytokines are the most common immunological complications during the acute phase of infection which may be related to the frequent MDR superinfection during COVID-19 patients [30]. Anti microbial stewardship will have fundamental role in limiting the overuse and unnecessary use of antimicrobial and stop emerging of antimicrobial resistance and superinfection in COVID-19 patients [4].

#### 4. Conclusion

COVID-19 is a dangerous microorganism and more attention should be paid to coronavirus short and long-term complications. Differential diagnosis between viral and bacterial infection by specific identification is fundamental to better manage the treatment. The right diagnosis leads to the right prescribing of antibiotics during coronavirus bacterial coinfection or superinfection to avoid emerging of MDR and XDR strains which are responsible for lethal untreatable infections. Prospective studies are needed for further understanding of superinfection in COVID-19 patients and verifying the hidden role of SARS-CoV-2 in acquiring such infection in order to reform the antimicrobial prescribing patterns.

#### Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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