Review Article

Antimicrobial Resistance Pattern of Infections in Patients with Type II Diabetes Mellitus

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ABSTRACT

Diabetes mellitus is a major emerging threat to public health, since the infection rate is high in the diabetics than the non-diabetics. There are many studies analyzing the antibiotic resistance in the infection in diabetic patient. Infectious diseases constitute a real global health problem due to the evolving power of microorganisms. Diabetics are more susceptible to infections due to increased glucose levels and suppressed immune response as well as the neuropathy and decreased blood flow to extremities that lead to slow-healing wounds. The common infections seen are respiratory tract infections commonly pneumonia, urinary tract infection, gastrointestinal tract infection, skin infections etc. Current studies showed that *K.pneumoniae, E. coli, Staphylococcus spp., Staphylococcus epidermidis*, *S. aureus, S.pneumoniae* are more associated with diabetic infections. Urinary tract infections and respiratory tract infections are mostly seen in diabetic patients followed by gastro intestinal infections and skin infections. From many studies the mostly isolated organisms were found to be *E. coli* and *Klebsiella pneumonia*. The isolated bacterias has shown resistance to third generation cephalosporins and even to carbapenems. The emergence of AMR to third generation cephalosporins is worrisome because of increased infections and frequent use of antibiotics.

Keywords: Antimicrobial resistance, Type II diabetes mellitus, Infection, resistance pattern.

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INTRODUCTION

Antimicrobial resistance in a wide range of bacterial pathogens is a serious public-health threat and has been implicated in various infections. Infectious diseases constitute a real global health problem due to the evolving power of microorganisms, from social and technological attitudes associated with negligence, and the uncontrolled use of antibiotics. Infection is a relatively frequent reason for hospitalization or a physician office visit in people with diabetes. People with diabetes may be more susceptible to infectious disease than those without diabetes. Diabetics are more susceptible to infections due to increased glucose levels and suppressed immune response as well as the neuropathy and decreased blood flow to extremities that lead to slow-healing wounds. There are several microorganisms that often cause infections in diabetic patients. *Staphylococcus aureus*, Streptococcus pyogenes, *Staphylococcus epidermidis*, E. coli, Pseudomonas aeruginosa, Klebsiella pneumonia, Acinetobacter spp, Proteus spp and Enterococcus spp are some of the most common pathogens that cause infections [1].The large burden of T2DM, paired with its potential role as a risk and prognostic factor for infectious diseases, along with the global issue of antibiotic resistance, call to thoroughly study whether people with T2DM are at higher risk of infections with resistant bacteria. This knowledge may guide empirical treatment, with a subsequent positive impact on T2DM patients who would recover faster from infections, while also reducing the burden of antibiotic-resistant bacteria by prescribing more accurate treatments[2].

DISCUSSION

Bing Liu et al conducted a comprehensive exploration on antimicrobial resistance and risk factors for IHM (in-hospital mortality) in KP (Klebsiella pneumonia) patients with and without diabetes was carried out. The study showed that Antimicrobial resistance of KP to several commonly used drugs in pneumonia was lower in diabetics than in non-diabetics. Diabetics showed a lower prevalence of CRKP (carbapenem-resistant Klebsiella pneumoniae) in KP among patients admitted to ICU. pneumonia in diabetics were shown to be of higher severity in their study and previous studies. Out of their expectation, they found that diabetics were of lower resistance to antimicrobials than nondiabetics. A previous study has shown that diabetes was an independent risk factor for hypervirulent (hypermucoviscous) KP (HvKP or HMKP) infection [3]. While another study showed that KP possessed a higher resistance to some commonly used drugs in liver abscess [4]. A previous study, which considered discharge to hospice as death, reported an IHM of 39% both in CRKP pneumonia and CRKP-BSI(Blood stream infection) [5]. In this study, IHM in CRKP pneumonia was similar with the previous study but mortality in CRKP-BSI

was much higher. It was reported that glucose could stimulate the uptake of aminoglycoside antimicrobials by promoting the TCA cycle and thus restore the susceptibility of bacteria, including KP[6].

B A Bulolo et.al conducted a study on Antibiotic sensitivity pattern of bacteria from diabetic foot infections and they found that Klebsiella pneumonia are the most common bacteria found as the etiologic agent in the DFIs (Diabetic foot infections), followed by *E. coli*. The study showed similarity with some other studies in which gram-negative microorganisms were the most common bacteria found in DFIs (*Klebsiella spp, P.aeruginosa spp, and E. coli* spp) [7]. The present study confirms that multi-drug-resistant organisms (MDROs) infection are extremely common in hospitalized patients with DFIs, similar to the results of Hartmann-Heurtier et al[8]. and Kandemir et al[9].A total of 51.3% of MDROs were Gram-positive bacteria, among which the top 3 were *Staphylococcus aureus*, *Staphylococcus epidermidis* and Enterococcus spp. The gram-negative bacteria accounted for 48.7%, mainly including Enterobacter spp, Pseudomonas aeruginosa, and Proteus mirabilis bacteria. They found that the most sensitive antibiotics in treating DFIs were Amikacin, Imipenem, Meropenem, Erythromycin, and Cefoperazone/sulbactam. Meanwhile, the most resistant antibiotics were Ciprofloxacin, Cotrimoxazole, Ampicillin, Ceftriaxone and Cefotaxime and Levofloxacin[1].

Arsene Tejiogni Signing et.al conducted a study on Antibiotic Resistance Profile of Uropathogenic Bacteria in Diabetic Patients at the Bafoussam Regional Hospital. In this study, the resistance of germs to beta-lactamines was very high. Kibret and Abera also found in their study high rates of resistance to antibiotics such as AMX (amoxicillin) and cephalothin [10].Likewise, Ejaz et al. obtained high resistance for CFM (cefixime) and TOB (tobramycin) antibiotics[11]. These resistance rates were 90.6% and 72% respectively. They also noticed that bacteria were also much more resistant to antibiotics of the aminoglycoside and tetracycline class, which is in line with the work carried out by Kibret and Abera[10]. These differences in the sensitivity of germs to antibiotics, which vary widely from one study to another, could be explained by the differences in bacterial ecologies and the conditions of antibiotic use, which remain very variable. The very high resistance rates against beta-lactamines and quinolones found in this work could be explained by the known practice of self-medication, the illicit sale and use of drugs, and the proliferation of clandestine health care units managed by unqualified health personnel who routinely prescribe antibiotics in doses and durations that are noncompliant. This could also explain the fact that the bacterial species Escherichia coli, Klebsiella pneumoniae, and *Staphylococcus aureus* are most multidrug-resistant. This study also revealed that there is an association between antibiotic resistance and diabetic status. Research and interventions must be focused on the elderly diabetic population in order to fight against the occurrence of drug-resistant uropathogenes[12].

Waseem Abu-Ashour et.al conducted a study on Diabetes and the occurrence of infection in primary care[13]. When comparing their results with other studies, it was found that increased rates of infections in patients with diabetes compared to patients without[14]. For example, Shah and Hux examined the association between diabetes and different types of infections using administrative databases from Ontario, Canada. They quantified the risk of infections in patients with diabetes using an administrative dataset over relatively short study duration (1 year), and also found an increased risk of infectious disease in patients with diabetes, with an even higher risk ratio of infectious disease related hospitalization. Another cohort study conducted in Japan examined risk factors for infection and concluded that diabetes was one of the important risk factors. Using hospital records and community data the authors reported more than double the risk of infection in patients with diabetes compared to those without[15]. The findings of this study may not be generalizable to primary care patients as the study population had autoimmune diseases. In addition, important confounders that may have affected the outcome, such as corticosteroid therapy, were not taken into consideration. A case-control study that was consistent with their findings found more than double the risk of infection in patients with diabetes compared to patients without diabetes[16]. Shortcomings of this study that should be noted are the small study population and a reliance on self-reported data. In contrast, Lipsky et al. studied risk factors for acquiring pneumococcal infections in a general medical clinic and found that diabetes was not a risk factor for developing pneumococcal infections[17].

Michaela J. Day et.al conducted a study on Significant increase in azithromycin resistance and susceptibility to ceftriaxone and cefixime in Neisseria gonorrhoeae isolates[18]. The increase in cefixime susceptibility might be due to the use of recommended ceftriaxone/azithromycin dual therapy since 2012 or ceftriaxone monotherapy (500–1000 mg), which has become increasingly common in the most recent years in the EU/EEA (European Union/European Economic Area) countries[19]. The same shift towards cefixime susceptibility was observed in the United States (US) between 2014 and 2018 with the proportion of isolates with decreased susceptibility to cefixime[20]. Azithromycin MICs (minimum inhibitory concentration) are, in contrast to those observed for ceftriaxone and cefixime, shifting towards MICs above the azithromycin ECOFF and this has been recently reported in many countries internationally. An Australian gonococcal surveillance programme has observed a decrease in the percentage of isolates with azithromycin MICs > 1 mg/L after the peak of 9.3% was reached in 2017 to 4.6% in 2019[21]. In the Euro-GASP 2009–2016 data, ciprofloxacin resistance was significantly associated with urogenital sites[22], in 2019 both ciprofloxacin and azithromycin resistance were significantly associated with pharyngeal infections. Pharyngeal infections are considered to have a major role in the development of resistance to several

antimicrobials, such as beta-lactam antimicrobials. There are some limitations of Euro-GASP, These limitations include, for example, that a limited number of gonorrhoea patients and N. gonorrhoeae isolates from many diverse countries are examined, many gonorrhoea cases in the EU/EEA are diagnosed with molecular diagnostics and no N. gonorrhoeae isolates are available from many of these cases, the majority of examined N. gonorrhoeae isolates are obtained from urogenital sites and the number of isolates from rectal and pharyngeal sites are more limited, and in many countries the completeness of reported epidemiological data (particularly of sexual orientation) is suboptimal.

Chung-Huei Huang et.al conducted a study on Antimicrobial resistance and outcomes of community-onset bacterial bloodstream infections in patients with type 2 diabetes[23]. This study demonstrated the major bacterial pathogens, their prevalence and antimicrobial resistance among type 2 diabetic patients with CO-BSIs (community-onset bloodstream infections) in Taiwan. A similar observation was reported in patients with methicillin resistance with a higher 90-day post-discharge mortality rate , which was mainly attributed to nosocomial infections[24]. In contrast, a study analyzing 215 CO-BSIs caused by S. aureus in the general population revealed similar mortality rates for MRSA (methicillin-resistant S. aureus) and MSSA (methicillin-susceptible S. aureus) infections[25]. A previous study on the general population in Spain reported that CO-BSIs caused by E. coli resulted in a higher 14-day mortality rate among individuals with ESBL (extended-spectrum β-lactamases)-producing strains and that empirical antimicrobial treatment was less appropriate in this group[26]. A worldwide observational study reported a high 14-day mortality rate associated with ESBL-producing K. pneumoniae in 455 episodes of K. pneumoniae bacteraemia[27]. Use of a carbapenem was associated with a significantly lower 14-day mortality rate than the use of other antibiotics. Several meta-analyses have identified an association between a higher mortality rate and antimicrobial resistance in various kinds of infections, including *S. aureus, enterococci, K. pneumoniae, P. aeruginosa* and *A. baumannii* in the general population[28]. In the current study, older age was identified as a predictor of antimicrobial-resistant CO-BSIs in patients with type 2 diabetes. Furthermore, a lower level of serum albumin was found to be an independent predictor of 30-day mortality for patients with monomicrobial CO-BSIs. This finding is consistent with their previous study on mortality in K. pneumoniae CO-BSIs among diabetic patients[29].

CONCLUSION

Diabetes mellitus (DM) is considered one of the largest emerging threats to health in the 21st century. It is estimated that there will be 380 million persons with DM in 2025. Besides the classical complications of the disease, DM has been associated with reduced response of T cells, neutrophil function, and disorders of humoral immunity also Diabetes mellitus is associated with various types of infections notably urinary tract, respiratory tract skin, mucous membrane, soft tissue, and surgical and/or hospital-associated infections. However diabetic patients are more prone to have infection than non-diabetic patients by a wide range of bacteria. Therefore, AMR (Antimicrobial resistance) is an important issue in patients with diabetes both because of being prone to infection and because of the frequent exposure to antibiotics to treat infections. As per current studies K. pneumoniae, E. coli, Staphylococcus spp., *Staphylococcus epidermidis*, S. aureus, S. pneumoniae are more associated with diabetic infections. Urinary tract infections and respiratory tract infections are mostly seen in diabetic patients followed by gastro intestinal infections and skin infections. From many studies the mostly isolated organisms were found to be E. coli and Klebsiella pneumonia. The isolated bacterias has shown resistance to third generation cephalosporins and even to carbapenems. The emergence of AMR to third generation cephalosporins is worrisome because of increased infections and frequent use of antibiotics. From several studies it was found that E. coli, Klebsiella pneumonia, Staphylococcus spp and Acinetobacter baumannii were shown resistance to most of the antibiotics also it is clear that gram negative organisms are more resistant than gram positive organisms.

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