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Implementation of antimicrobial stewardship in patient with sepsis in critical care unit

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ABSTRACT

Antimicrobial resistance continues to increase among bacteria which cause disease in both community and hospital setting. Antimicrobial stewardship (AMS) is a global initiative it includes the 4 Ds approach (appropriate selection of the drug, dosage, duration of administration and de-escalation of antimicrobial therapy). We aim to have a microbiological profile and to assess the uses of antibiotics in critically ill patients in a critical care unit. This was cross-sectional study of 200 Intensive Care Unit patients in Medical City Teaching Hospital from June to August of 2017. The patients divided into two groups, 100 for each, the 1st without, the 2nd with biologic profile comparing both data. We included 200 (148 males and 52 females). The two most common microorganisms isolated by sample cultures are Klebsiella pneumonia and Pseudomonas aeruginosa (54%). Patient fate includes improvement and discharges well in 38% and death in 46%. In the 1st group, 28% the antibiotics selection completely matched with culture and sensitivity results while 20% of these cases did not match, while in the second group the completely matching was 61% and the non-matching reduced to 14%. Klebsiella pneumonia is the most common microorganism, followed by Pseudomonas aeruginosa. The right selections of empirical antibiotics play an important role in clinical outcome.

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INTRODUCTION

Antimicrobial drugs are effective in the treatment of infections because of their selective toxicity. In most instances, the selective toxicity is relative rather than absolute, requiring that the concentration of the drug be carefully controlled to attack the microorganism, while still being tolerated by the host (Kisgen, 2015). Although antibiotics are undoubtedly one of the most beneficial discoveries of science, their use does carry risks. They can adversely affect patients by eliciting allergic reactions, causing direct toxicity, or altering the normal bacterial flora, leading to super infections with other organisms. Antibiotic use is the primary driving force in the development of antibiotic resistance, which can affect not only the treated patients but other patients by transmission of resistant organisms. It is important to keep in mind all of these potential adverse consequences when using antibiotics. Many studies have documented the relationship between antibiotic use and resistance, both at a patient level and a society level (Gallagher and MacDougall, 2018). Bacteria are considered resistant to an antibiotic if the maximal level of that antibiotic that can be tolerated by the host does not halt their growth. The worldwide emergence of antimicrobial resistance is a major public health problem and significantly impacts patient treatment and outcomes (Congress, 1995). It has been estimated that two-third of all patients receive at least one antibiotic during hospitalization, and the cost involved is therefore correspondingly high and up to 40% of a total hospital's drug expenditure may be devoted to the purchase of antibiotics (Singh et al., 2016). The analysis of European Prevalence of Nosocomial Infection in Intensive Care Units (EPIC I study) published in 1995 showed that amongst 10,038 patients hospitalized in 1,417 intensive care units (ICU) in Europe: 44.8% of patients suffered from respiratory tract infections and 62% of them antimicrobial agents were administered (Clark et al., 2016).

In 1970 *Acinetobacter* spp. strains were susceptible for ampicillin. Ten years later almost all the strains were susceptible for carbapenems, and in 1990 the large number of *Acinetobacter* spp. was susceptible for colistin and tigecycline only. In the United States the number of infections caused by *Acinetobacter* spp. increased from 9% in 1995 to 40% in 2004. (Grundmann et al., 2006) In one study Acinetobacter baumannii has been found to cause approximately 80% of reported Acinetobacter infections. (Arjuna and Nandi, 2017) The damaging effects of antimicrobial resistance (AMR) are already being observed. AMR infections currently claim at least 50,000 lives annually across Europe and the US. In other areas of the world reliable estimates of the true burden are scarce but it is estimated that the deaths amount to many hundreds of thousands. It is estimated that if there is a continued rise in resistance levels, by 2050 it would lead to 10 million deaths annually. (Glance et al., 2011) Additionally, AMR leads to longer hospital stays, higher rates of hospitalization and rise in the treatment cost. (Grundmann et al., 2006) Preliminary research which considers only a part of the impact of AMR estimates that by 2050 the economic burden would be 100 trillion USD. (Glance et al., 2011) The National Action Plan for Combating Antibiotic-resistant Bacteria provides a roadmap to guide the Nation in rising to this challenge; developed in response to Executive Order 13676: Combating Antibiotic-Resistant Bacteria—issued by President Barack Obama on September 18, 2014—the National Action Plan outlines steps for implementing the National Strategy for Combating Antibiotic-Resistant Bacteria and addressing the policy recommendations of the President's Council of Advisors on Science and Technology (PCAST). Although its primary purpose is to guide activities by the U.S. Government, the National Action Plan is also designed to guide action by public health, healthcare, and veterinary partners in a common effort to address urgent and serious drug-resistant threats that affect people in the U.S. and around the world. Implementation of the National Action Plan will also support World Health Assembly resolution 67.25 (Antimicrobial Resistance), which urges countries to take urgent action at the national, regional, and local levels to combat resistance (2015). The goals of the National Action Plan include: Slow the Emergence of Resistant Bacteria and Prevent the Spread of Resistant Infections, Strengthen National One-Health Surveillance Efforts to Combat Resistance, Advance Development and Use of Rapid and Innovative Diagnostic Tests for Identification and Characterization of Resistant Bacteria, Accelerate Basic and Applied Research and Development for New Antibiotics, Other Therapeutics, and Vaccines, Improve International Collaboration and Capacities for Antibiotic-resistance Prevention, Surveillance, Control, and Antibiotic Research and Development. (Mendelson, 2015, 2015) Antimicrobial stewardship (AMS) is a global initiative that refers to a collection of interventions geared toward optimizing the prescribing of antimicrobials. It includes the 4 Ds approach (appropriate selection, dosing, duration and de-escalation of antimicrobial therapy). The primary goal of AMS is to optimize clinical outcomes while minimizing unintended consequences of antimicrobial use (including toxicity, the selection of pathogenic organisms, and the emergence of resistance). A secondary goal of AMS is to reduce health care costs without adversely impacting quality of care. (Dellit et al., 2007) The Impact of Antimicrobial stewardship (AMS) are: Reductions in antimicrobial utilization (11%–38% DDD/1000 patient-days), Lower total antimicrobial costs (US$ 5–10/ patient-day), Shorter average duration of antibiotic therapy, and Less inappropriate use and fewer antibiotic adverse events. (Kaki et al., 2011)

Studies revealed that initial inadequate therapy (wrong selection or/and wrong dosage) is prescribed with a relatively high frequency, and that administration of initial inadequate therapy is associated with high mortality rates. Most critically ill patients with serious infection have the potential to benefit from empirical, broad-spectrum antimicrobial therapy. Multiple studies conducted over the past two decades have found that inadequate initial antimicrobial therapy is an independent risk factor for mortality. In each of these studies, mortality rates were higher for patients given initial inadequate therapy compared with patients given initial adequate therapy. Studies have documented that up to 50% of all in-hospital antimicrobial use is inappropriate.(Dunagan et al., 1989, Arbo and Snydman, 1994)

PATIENTS AND METHODS

A total number of 200 patients (148 males and 52 females) included in the study; divided into two groups; first group is 100 Intensive Care Unit patients in Medical City Teaching Hospital, using the already existing data from medical archive of Ghazi al-Hariri teaching Hospital from June to August of 2017. A written informed consent were taken from all patients or from their legal representative if the patients was unable to communicant or if the patients is unconscious, that describe the nature of the study, all this was in accordance with Helsinki declaration of human rights and accordance with our local IRB ethical approval system.

With use of biological profile of antimicrobial resistance pattern, a second group of newly admitted 100 patients from October till December 2017 studied. For this group empirical antibiotics were given; modified according to the results of the biological profile.

The data collected from both groups included the demographic information (name, age, gender and date of administration), diagnosis, empirical therapy, culture and sensitivity results, types of microorganisms, antimicrobial therapy used after culture and sensitivity results and finally the fate of patients. Chi square method used, also binary logistic used to calculate the odd ratio, and the 95% confidence interval of OR calculated using Baptista-Pike method, GraphPad Prism 7.0 software package used to make the statistical analysis, p value considered when appropriate to be significant if less than 0.05

RESULTS

The results show that the most common type of microorganism in Intensive Care Unit of Ghazi al-Hariri Hospital is *klebsiella pneumonae* which account (30%) of total microorganisms followed by *Pseudomonas aregenosa* (24%), *Actinobacter baumannii* (16%), *Staphylococcus aurous* (12%) , *Baerkholderia capcia* (4%) , coagulase (-) *Staphylococcus aureus* (4%), and *Proteus mirabilis* (4%), while only (4%) of the cases did not show any microorganism in their culture and sensitivity test, this biological profile account for group 1. For patients in group 1 about 38% of them discharged well, and 46% of the patients in group 2 discharged well, despite there was no statistically significant difference between group 1 and 2 in term of outcome, but in term of odd ratio group 2 had lower risk of worse outcome (OR<1.0), indicating a better outcome for group 2, as illustrated in table 1.

For the microorganisms *Klebsiella pneumonae* the most sensitive antibiotic was MEROPENM and IMIPENEM in equal percentage (57%) in 16 patients out of 28 that were prescribed to their conditions, followed by AMIKACIN (28%). For *Pseudomonas aeruginosa* the most sensitive antibiotic was IMIPENEM 79% (19 patients from 24), followed by CIPROFLOXACILLINE which was effective in 14 out of 24 patients (58%).

In regard of the selection of the empirical therapy, the result shows that in 28% of cases the empirical antibiotics were given before culture/selectivity results were completely matching the culture/sensitivity results, which means that appropriate antibiotics used before and after C&S results). Nearly 52% of cases are partially matched, which means that (not all the antibiotics used as empirical therapies were identical to that used after) while 20% of cases received inappropriate empirical antimicrobial therapy. Group had significantly higher rate of matching compared to groups, and lower rate of both partially matched and no match compared to group 1, as illustrate in table 2.

Table 1: The association between different groups and outcome

Groups	Outcome		OR (95%CI)	p-value
	Discharge well	Getting worse		
Group 1	38	62	0.720 (0.418 – 1.279)	0.252
Group 2	46	54		

OR: odd ratio, CI: confidence interval

Table 2: The association between matching of prescribe empirical therapy with groups

	Completely matched	Partially matched	No matching	p-value
Group 1	28	52	20	<0.001
Group 2	61	25	14	

DISCUSSION

Antimicrobial resistance is a global public health challenge, which has accelerated by the overuse of antibiotics worldwide. Increased antimicrobial resistance is the cause of severe infections, complications, longer hospital stays and increased mortality. The use of antimicrobial stewardship programs, the active participation of clinicians in audits, the utilization of valid rapid point-of-care tests, the promotion of delayed antibiotic prescribing strategies, the enhancement of communication skills with patients with the aid of information brochures and the performance of more pragmatic studies in primary care with outcomes that are of clinicians' interest, such as complications and clinical outcomes. (Llor and Bjerrum, 2014)

The first was to emphasize our biological profile in our unit, hence we found that the most common type of microorganism in our Intensive Care Unit of Ghazi al-Hariri Hospital are klebsiella, pseudomonas aregenosa, Actinobacter, staphylococcus aurous, coagulase (-) staphylococcus and proteus, also found that for the microorganisms klebsiella the most sensitive antibiotic were Meropenem and Imipenem in equal percentage, followed by Amikacin. While strains of pseudomonas aeruginosa, were sensitive to imipenum, followed by Ciprofloxacin. These results used as a baseline in building a protocol of prescribing the empirical antimicrobial therapy used for the second group.

About the fate of the patients we found that (38%) of patients were discharge well while when we modify our approach according to the results of biological profile the frequency of patients discharged well increased to (46%). This improvement in patient's conditions is not only due to modification of treatment because also the death in critical care environment is multi factorial and initial appropriate antimicrobial therapy is necessarily and an important in patient's survival. Generally the worsening is due to the difference in response of patients to treatment and the bacterial resistance to drug, because it cannot be guaranteed which patient resistant to which drug before the results of culture and sensitivity.

The results we gained from the comparison between antibiotics that used before culture and sensitivity test (initial antimicrobial therapy) and after it shows that 28% of the cases that given antibiotics are totally matching in first group, 52% were partially match and 20 % of cases their empirical antibiotics were not match their C&S results at all. While in second group the totally matching become 61%, and the partially matched were 25 % and the non-matching were 14%. This change occurs after applying the result from first group using the biological profile as a base line indicator in prescribing the antimicrobials in our unit. Despite this the modification of the empirical treatment the non-matching cases were high (14%) in group 2, this phenomenon may be due to patients' variation and bacterial resistance which cannot be accurately predicted without the result of culture and sensitivity.

CONCLUSION

The biological profile in the ICU reveals that Klebsiella pneumonia is the most common microorganism, followed by Pseudomonas aeruginosa. The right selections of antibiotics play an important role in clinical improvement of patients.

Conflict of interest

None

REFERENCES

2015. *National Action Plan for Combating Antibiotic-Resistant Bacteria* [Online]. Available: https://obamawhitehouse.archives.gov/sites/default/files/docs/national_action_plan_for_combating_antibotic-resistant_bacteria.pdf [Accessed 1 march 2018 2018].

ARBO, M. D. & SNYDMAN, D. R. 1994. Influence of blood culture results on antibiotic choice in the treatment of bacteremia. *Arch Intern Med,* 154**,** 2641-5.

ARJUNA, A. & NANDI, D. 2017. EMERGENCE AND ANTIBIOTIC SENSITIVITY PATTERN OF ACINETOBACTER BAUMANNII IN HOSPITAL FACILITY. *Asian Journal of Pharmaceutical and Clinical Research,* 10**,** 77-79.

CLARK, N. M., ZHANEL, G. G. & LYNCH, J. P., 3RD 2016. Emergence of antimicrobial resistance among Acinetobacter species: a global threat. *Curr Opin Crit Care,* 22**,** 491-9.

CONGRESS, U. S. 1995. Office of technology assessment. *Adolescent health,* 1.

DELLIT, T. H., OWENS, R. C., MCGOWAN, J. E., JR., GERDING, D. N., WEINSTEIN, R. A., BURKE, J. P., HUSKINS, W. C., PATERSON, D. L., FISHMAN, N. O., CARPENTER, C. F., BRENNAN, P. J., BILLETER, M. & HOOTON, T. M. 2007. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis,* 44**,** 159-77.

DUNAGAN, W. C., WOODWARD, R. S., MEDOFF, G., GRAY, J. L., 3RD, CASABAR, E., SMITH, M. D., LAWRENZ, C. A. & SPITZNAGEL, E. 1989. Antimicrobial misuse in patients with positive blood cultures. *Am J Med,* 87**,** 253-9.

GALLAGHER, J. C. & MACDOUGALL, C. 2018. General Approach to Infectious Diseases. *In:* GALLAGHER, J. C. & MACDOUGALL, C. (eds.) *Antibiotics simplified.* 4th ed.: Burlington, MA : Jones & Bartlett Learning.

GLANCE, L. G., STONE, P. W., MUKAMEL, D. B. & DICK, A. W. 2011. Increases in Mortality, Length of Stay, and Cost Associated With Hospital-Acquired Infections in Trauma Patients. *Archives of Surgery (Chicago, Ill. : 1960),* 146**,** 794-801.

GRUNDMANN, H., AIRES-DE-SOUSA, M., BOYCE, J. & TIEMERSMA, E. 2006. Emergence and resurgence of meticillin-resistant Staphylococcus aureus as a public-health threat. *The Lancet,* 368**,** 874-885.

KAKI, R., ELLIGSEN, M., WALKER, S., SIMOR, A., PALMAY, L. & DANEMAN, N. 2011. Impact of antimicrobial stewardship in critical care: a systematic review. *Journal of Antimicrobial Chemotherapy,* 66**,** 1223-1230.

KISGEN, J. 2015. Principles of Antimicrobial Therapy. *In:* FINKEL, R., WHALEN, K., FINKEL, R. & PANAVELLI, T. A. (eds.) *Pharmacology.* 4th ed. Philadelphia: Wolters Kluwer.

LLOR, C. & BJERRUM, L. 2014. Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem. *Therapeutic Advances in Drug Safety,* 5**,** 229-241.

MENDELSON, M. 2015. Role of antibiotic stewardship in extending the age of modern medicine. *SAMJ: South African Medical Journal,* 105**,** 414-419.

SINGH, A. P., GUPTA, D. U. & DAS, S. 2016. MONITOR THE USE OF ANTIBIOTICS IN INTENSIVE CARE UNITS WITH SPECIAL FOCUS ON RESTRICTED ANTIBIOTICS IN TERTIARY CARE HOSPITAL OF INDIA. *Asian Journal of Pharmaceutical and Clinical Research,* 9**,** 256-259.