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Effect of COVID-19 on Bacterial Resistance

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ABSTRACT

Background: The development of bacteria resistant to the antimicrobial (AM) in hospitals and other health care settings is a main concern of public health. Great AM consumption chiefly in hospitals frequently defined as the most vital factor leading to bacterial resistance. The aim of this study is to investigate the most common bacteria that encountered in medical institutions and bacterial resistance to AM before and after COVID-19.
Patient and method: The current study was conducted in eleven medical institutions in Baghdad through a period of six months from January to June 2020. Seven AM disc types were used which are amoxicillin-clavulanate, azithromycin, ceftriaxone, gentamicin, levofloxacin, meropenem and vancomycin. In this study, 1324 samples were isolated and examined for detection of bacterial resistance to AM before and after pandemic of COVID-19. Culture samples were tested directly by Vitek 2 that give dependable proof of identity and susceptibility outcomes after 18-24 h.
Results: Cultures revealed that the main isolated bacteria were Escherichia coli (E. coli), Klebsiella pneumonia (Kl. pneumonia) and Pseudomonas aeruginosa (Ps. aeruginosa) at a percentage of 54%, 23% and 23%, respectively. Meropenem was the main sensitive AM before COVID-19 whereas gentamicin was the main resistant AM. After pandemic of COVID-19, the resistance to all AM was increased.
Conclusion: The main isolated bacteria were E. coli and the more effective AM was meropenem. After spreading of COVID-19, the bacterial resistance to all tested AM was increased due to more frequent use of these medications in the treatment of secondary bacterial infections.

Keywords: COVID-19, bacterial resistance, antimicrobial, antibiotics sensitivity.

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INTRODUCTION

COVID-19 is the most dangerous virus that causes injury to the lung and various organs of the body. Such virus may cause life-threatening secondary bacterial infections. Unfortunately, the mixed infections may increase the bacterial resistance. Careful consideration in hospitals and in the community must be done due to a serious worldwide problem which is bacterial resistance to AM that increasing significantly and has consequences for morbidity, mortality [(1)].

Abuse is the main cause of emergence of resistance to AM agents [(2)]. In the community there is great indication of substandard use of AM. This involves the use for incorrect conditions, use of insufficient treatment periods and sub-curative doses. All of these are probable reasons to the development and broadening of bacterial resistance [(3)].

Bacterial infections that had been willingly cured by AM are lasting longer due to resistance emergence and this will lead to intense morbidity and mortality [(4)]. Furthermore, bacterial resistance leads to extra cost of healthcare that resulted from the medication itself, healthcare career, longer hospitalization, etc. Besides, it leads to more loss of currently available effective AM [(5)].

Reduction of resistant bacteria in hospitals can be done by lessen drugs rate use for which there is a resistance, lessen transmission between patients and from hospital staff to patients by successful infection control, rising patients turnover rate, lessen patients entrance that have resistant bacteria into hospitals, and adding new AM for which there is no resistance [(6)].

Reduction of resistant bacteria in hospitals and total reduction of these infections rate can be achieved if above measures made correctly. Furthermore, and most essentially, the effects of resistance execution should be apparent over a comparatively tiny period of time. Hence, great benefit can be gained for both health field and the patients [(7)].

One of important methods that used to detect bacterial resistance is the culture and sensitivity test (CST) which may be regarded as cornerstone in this aspect. The CST is an analytical lab technique used to recognize the type of bacteria and to conclude which AM can efficaciously combat an infection[(8)]. However, the nonexistence of bacteria does not necessarily denote there is no infection, as it could be a virus that will not propagate in a definite culture medium [(9)].

The main specimens used in CST are blood and urine samples. The culture of blood samples is done with straightforward blood draw made after the skin is applied with an alcohol pad, then mark messily with a suitable antibacterial solution [(10)]. However, a false-positive results may be obtained if blood is contaminated [(11)]. A culture of urine is a way to cultivate and detect bacteria that may be in the urine. The sensitivity test aids medical staff to choice the desirable AM to treat an infection[(12)]. The current study aim at investigation of the most common bacteria that encountered in Iraqi medical institutions and the most resistant AM before and after COVID-19.

MATERIALS AND METHODS

Study Population

This study was done in eleven medical institutions in Baghdad. The data was collected with assistance of pharmacists and laboratory staffs. Seven AM disc types were used which are amoxicillin-clavulanate, azithromycin, ceftriaxone, gentamicin, levofloxacin, meropenem and vancomycin. Different samples were taken e.g., blood, urine, sputum, ear swap and cerebrospinal fluid. The study continues for six months from 1/January to 1/June/2020 with a total number of samples of 1324 (both males and females). Of these, 745 samples were before and 579 were after COVID-19 spreading. Approval was obtained from the institutional ethical committee prior of the study.

RESULT

The current study was conducted in eleven of Baghdad health institutions. A total of 1324 different samples were studied. Results revealed that three main types of bacteria were isolated, that is, *E. coli*, *Kl. pneumoniae* and *Ps. aeruginosa* at a percentage of 54%, 23% and 23%, respectively (figure 1).

Table (1) shows that the *E. coli* resistance to amoxicillin-clavulanate, azithromycin, ceftriaxone, gentamicin, levofloxacin, meropenem and vancomycin before spreading of COVID-19 was 63, 25, 63, 66, 39, 11 and 39%, respectively whereas the *Kl. pneumonia* resistance to the above AM was 66, 45, 71, 27.5, 28.5, 9.75 and 28.5%, respectively in contrast to 100, 100, 75, 66, 47.3, 35.8 and 100%, respectively as a bacterial resistance of *Ps. aeruginosa* against the above mentioned AM. These facts are better clarified in figure (2).

On the other hand, most of bacterial resistance against the tested AM was increased after COVID-19 as showed in table (1). It was found that the *E. coli* resistance to amoxicillin-clavulanate, azithromycin, ceftriaxone, gentamicin, levofloxacin, meropenem and vancomycin was 85, 28, 77, 75, 44, 22 and 39%, respectively while that of *Kl.* pneumonia against the above AM was 100, 45, 82, 54, 29, 14 and 50%, respectively in contrast to a *Ps. aeruginosa* resistance of 100, 100, 100, 100, 48.9, 50 and 100%, respectively (figure 3).

Figure (4) is better clarifying the increment of bacterial resistance after COVID-19. It is obvious from figure (4) that bacterial resistance to all AM was increased. It is worth mentioning that the resistance of *Ps. aeruginosa* to amoxicillin-clavulanate, azithromycin and vancomycin was not changed not due to the efficiency of these three AM, instead, these AM show full resistance (100%) before and after COVID-19.

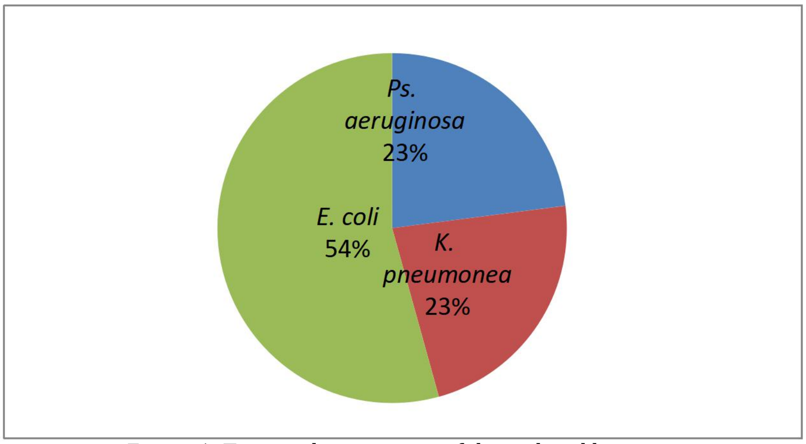

Figure 1: Type and percentage of the isolated bacteria.

Table (1): The Bacterial Resistance Against The Tested AM Before and After COVID-19.

Bacteria Type / AM	Before COVID-19						After COVID-19					
	E. coli		*Kl. pneumonia*		*Ps. aeruginosa*		*E. coli*		*Kl. pneumonia*		*Ps. aeruginosa*	
	Samples No.	Resistance %	Samples No.	Resistance %	Samples No.	Resistance %	Samples No.	Resistance %	Samples No.	Resistance %	Samples No.	Resistance %
Amoxicillin-clavulanate	33	63	6	66	7	100	39	85	4	100	3	100
Azithromycin	40	25	11	45	4	100	57	28	84	45	2	100
Ceftriaxone	116	63	42	71	8	75	13	77	22	82	6	100
Gentamicin	137	66	40	27.5	9	66	8	75	11	54	7	100
Levofloxacin	20	30	14	28.5	19	47.3	65	44	10	29	11	48.9
Meropenem	131	11	41	9.75	39	35.8	9	22	7	14	4	50
Vancomycin	18	39	7	28.5	3	100	23	39	2	50	9	100

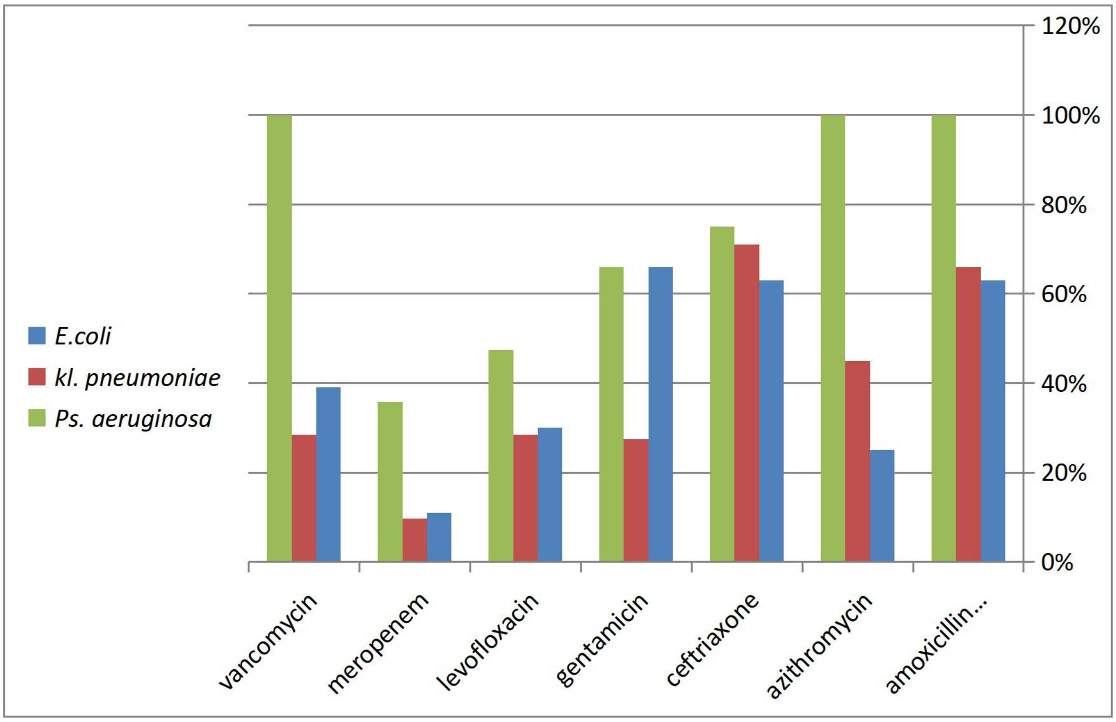

Figure 2: Percentage of bacterial resistance to AM before COVID-19.

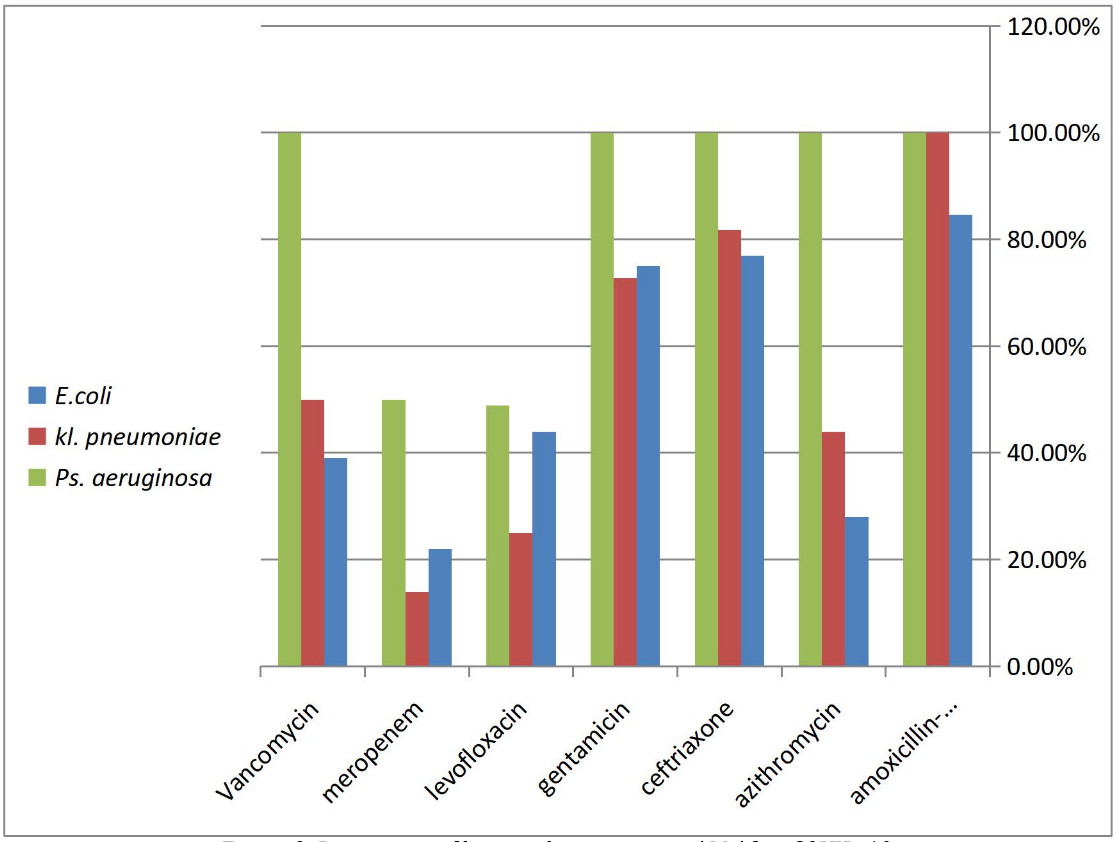

Figure 3: Percentage of bacterial resistance to AM After COVID-19.

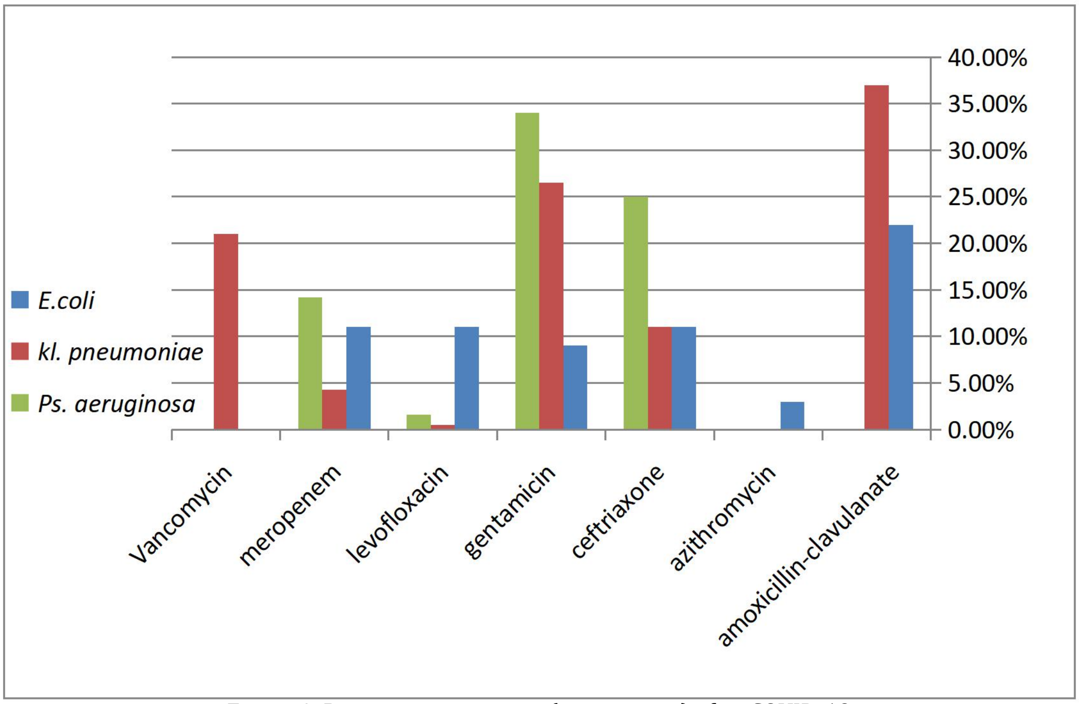

Figure 4: Resistance increment (as a percent) after COVID-19.

DISCUSSION

According to World Health Organization, improper use of AM is a major cause of increment in antibacterial resistance globally [13]. The CST is an indicative laboratory technique used to detect the bacterial kind and to conclude which AM can effectively combat an infection [8].
In this study, cultures showed that *E. coli* was the main isolated strain at a percentage of 54%, followed by 23% of both *Kl. pneumonia* and *Ps. aeruginosa*. These results were approximately similar to that obtained by other researcher [14].
The suggested groupings of AM agents with FDA clinical indications are sometimes not followed by some clinicians. This means wasting of money, time and effort with rising of morbidity and mortality rates. For example, FDA chart suggested grouping advises to use ceftazidime, gentamicin, tobramycin and piperacillin for *Ps. aeruginosa* while in practice amoxicillin-clavulanate is routinely used [14]. This is one of the answers about the question that why the bacterial resistance is growing.
In the current study, cultures showed that the more efficient AM against *E. coli* and *Kl. pneumonia* were azithromycin, levofloxacin, meropenem and vancomycin. In fact, these results are nearly parallel to that obtained by other researchers [15,16]. In addition, meropenem and levofloxacin were also effective against *Ps. aeruginosa*. One can say that meropenem and levofloxacin were the most effective in comparing with other AM and this may be due to the high cost and limited use of these two AM which in turn, decreases their bacterial resistance. Actually, these findings are similar to what is found in the neighboring countries [19].
On other hand, the ineffective (resistant) AM were amoxicillin-clavulanate, ceftriaxone and gentamicin. The study revealed that there is increasing in the bacterial resistance to the 3rd generation cephalosporin, e.g., ceftriaxone due to unreasonable use of this AM [17,18]. Although it is ineffective against *Ps. aurogenosa* with full resistance (table 1), azithromycin is still efficient against *E. coli* and *Kl. pneumonia* when compared with other AM that have low efficacy, higher cost and less available in some medical institutions. In addition, azithromycin is relatively cheap, easily available drug with reasonable adverse effect [20].
Also the current study demonstrated the ineffectiveness of ceftriaxone and azithromycin for treating the blood bacterial infections [17, 20]. These results can be explained by the blind use of AM in the treatment of infection which affects negatively on bacterial resistance [21].
Finally, it is worth mentioning that the bacterial resistance to all AM was increased after spreading of COVID-19 due to the over usage of AM to treat respiratory, gastrointestinal infections and septicemia that concomitantly happened with infection of COVID-19. The another cause of increasing bacterial resistance was the misuse of AM which gives rise to new resistant bacteria and new strains that are insensitive to traditional AM.

CONCLUSION

To decrease bacterial resistance, old AM are good choice due to high sensitivity of most strains of bacteria especially *Kl. pneumonia* and *E. coli*, low cost and availability. Levofloxacin and meropenem should be saved for high resistant bacteria in order to decrease the emergence of resistance against these new AM. The CST should be regarded as an essential step before the administration of AM. The combination of more than one AM can potentiate their action, thereby minimize bacterial resistance.

REFERENCES

1. Franco B., Martínez M., Rodríguez M., Wertheimer AIJI, The determinants of the antibiotic resistance process. 2009;2:1.
2. Organization WH. WHO global strategy for containment of antimicrobial resistance. Geneva: World Health Organization; 2001.
3. Watson RL, Dowell SF, Jayaraman M, Keyserling H, Kolczak M, Schwartz BJP. Antimicrobial use for pediatric upper respiratory infections: reported practice, actual practice, and parent beliefs. 1999;104(6):1251-7.

4. Dean A, Lee D. Bedside laboratory and microbiologic procedures. 2014.
5. Gonzales R, Steiner JF, Sande MAJJ. Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians. 1997;278(11):901-4.
6. Smith R, Coast JJB. The true cost of antimicrobial resistance. 2013;346:f1493.
7. Haber M, Levin BR, Kramarz PJBid. Antibiotic control of antibiotic resistance in hospitals: a simulation study. 2010;10(1):254.
8. Hockberger RS, Marx JA, Walls RM. Emergency Medicine: Concepts and Clinical Practice: Mosby; 2006.
9. Jung CL, Lee M, Chung WSJKJoCM. Clinical evaluation of the multiplex PCR assay for the detection of bacterial pathogens in respiratory specimens from patients with pneumonia. 2010;13(1):40-6.
10. Schwalbe R, Steele-Moore L, Goodwin AC. Antimicrobial susceptibility testing protocols: Crc Press; 2007.
11. Bisno AL, Gerber MA, Gwaltney Jr JM, Kaplan EL, Schwartz RHJCID. Practice guidelines for the diagnosis and management of group A streptococcal pharyngitis. 2002:113-25.
12. Hooton TM, Bradley SF, Cardenas DD, Colgan R, Geerlings SE, Rice JC, et al. Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. 2010;50(5):625-63.
13. World Health Organization, Available at Regional strategy on preventionand containment of antimicrobial resistance; 2010 http://www.searo.who.int/entity/antimicrobial resistance/BCT hlm-407.pdf.
14. Al-Marzoqi AHJMJoB. Etiology and antimicrobial sensitivity of common uropathogens in Hilla infants. 2008;5(3-4):579-86.
15. Shaikh S, Fatima J, Shakil S, Rizvi SMD, Kamal MAJSjobs. Antibiotic resistance and extended spectrum beta-lactamases: Types, epidemiology and treatment. 2015;22(1):90-101.
16. Góngora Rubio F, Oliveira VDC, Rangel RMC, Nogueira MCL, Almeida MTGJBJoID. Trends in bacterial resistance in a tertiary university hospital over one decade. 2013;17(4):480-2.
17. Meyer E, Schwab F, Schroeren-Boersch B, Gastmeier PJCc. Dramatic increase of third-generation cephalosporin-resistant E. coli in German intensive care units: secular trends in antibiotic drug use and bacterial resistance, 2001 to 2008 .2010;14)3:(R113.
18. Straus WL, Qazi SA, Kundi Z, Nomani NK, Schwartz B, Lancet PC-tSGJT. Antimicrobial resistance and clinical effectiveness of co-trimoxazole versus amoxycillin for pneumonia among children in Pakistan: randomised controlled trial. 1998;352)9124:(270-4.
19. Bechashk SM, Moradi G, Mohsenpour B, Ramazanzadeh R. Prevalence of Cefepime-Resistant Escherichia coli in Iran: A Meta-Analysis (2007-2016). Iranian journal of public health. 2019;48(4):603-11.
20. Chetchotisakd P, Chaowagul W, Mootsikapun P, Budhsarawong D, Thinkamrop BJTAjotm, hygiene. Maintenance therapy of melioidosis with ciprofloxacin plus azithromycin compared with cotrimoxazole plus doxycycline. 2001;64(1):24-7.
21. Gonzales R, Bartlett JG, Besser RE, Cooper RJ, Hickner JM, Hoffman JR, et al .Principles of appropriate antibiotic use for treatment of acute respiratory tract infections in adults: background, specific aims, and methods. 2001;37(6):690-7.