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Investigation of secondary Bacterial lung Infections associated with Corona virus Covid19, and the extent of their Resistance to some types of Antibiotics in the city of Kirkuk

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Abstract

This study is conducted on patients infected with COVID19 Those who are hospitalized in intensive care units in Kirkuk General Hospital and Al-Shifa 14 Epidemiological Hospital in the city of Kirkuk, for the period from December 1, 2020 to March 1, 2021, for age groups (20-90 years) and of both sexes. As 170 sputum samples are collected, in order to investigate secondary bacterial infections associated with the emerging corona virus, 119 samples are growth-positive (70%) and 51 are growth-negative (30%). During the laboratory diagnosis, 135 bacterial isolates are obtained from the positive samples, of which 102 single isolates are pure (75.55%), 17 are mixed isolates (12.5%). The number of isolates of Gram-positive bacteria 64 (47.4%) isolates, which included 42 of ***Staphylococcus.aureus*** with a percentage of 31.1%, 22 isolates ***of Streptococcus*** and the included two sexes, 12 isolates of ***S.pneumoniae*** at a percentage of 8.8%, 10 of ***S.pyogenes*** and a percentage of 7.4%, as for the The number of Gram-negative bacterial isolates is 71 (52.5%), which included 40 from ***Klebsiella***, which are 37 (27.4%) from ***Klebsiella.pneumoniae***, 3 (2.2%) from ***Klebsiella.oxytoca***, 16 (11.8%) from ***Pseudomonas.aeroginosa***. , and 15 (11.1%) of ***Hemophilus.influenzae.*** The extent of resistance of some commonly used antibiotics against isolated bacterial species is evaluated, where the isolates varied in response to the antibiotics used in the current study. And they are more sensitive to the antibiotic Imepenem by 100%, ***S. pyogenes*** are more resistant to antibiotics and by 100% to Amoxicillin\Clavulanic acid, Levofloxacin, Ceftriaxone, Tetracycline, Ampicillin, Oxacillin, Amikacin, Trimethromycinacin, Trimethromycin, and Etitracycline. Sensitivity to Nitrofurantion and Gentamycin 100%. The results of the current study show that ***S.pneumoniae*** bacteria are resistant to many antibiotics of Ceftriaxon, Tetracyclin., Oxacillin, Nitrofurantion, Clindamycin by 100%, and the least resistance is 17% to Gentamycin. As for Gram-negative bacteria, the results show that they are resistant to most of the antibiotics used in the current study.

Key words: COVID-19, secondary and co-infections with COVID-19, antibiotic resistance.

Introduction

The past two decades had seen four severe viral outbreaks, including the 2002 severe acute respiratory syndrome (SARS) epidemic, the 2009 H1N1 influenza pandemic, the 2012 Middle East respiratory syndrome (MERS) outbreak, and most recently the Middle East respiratory syndrome outbreak. East Respiratory Syndrome (MERS). COVID-19 pandemic. The emergence of new deadly strains of coronavirus in humans is becoming more frequent and of global concern; The emerging coronavirus, COVID-19, caused the first major outbreak to appear in China in 2019, and the weight of this disease is much greater than that of SARS and Middle East respiratory syndrome. (Guarner, 2020; Kannan et al., 2020). The variation in clinical symptoms of COVID-19 is highly variable; Infection ranges from asymptomatic to acute viral pneumonia with respiratory failure, often fatal (Li et al., 2020). According to what was received from the World Health Organization, the number of deaths from the emerging corona virus was 4.5 million (until 1/9/2021), and the number of infections was 218 million in the world.

The main consequence of disease progression in patients at later stages of infection is secondary bacterial infection At least one in seven COVID-19 patients was also found to have a secondary bacterial infection with 50% of deaths during the SARS-CoV-2 epidemic caused by bacterial infection. Untreated secondary, in most cases, in the lung (Zhou et al., 2020).

Secondary bacterial infection develops in patients during or after the primary infection with an infectious disease, often a virus (Morris et al., 2017; Wang et al., 2018) and is associated with higher rates of infection and mortality as shown in Figure (1) (Mallia et al., 2012). Almost all seriously ill patients are treated with antibiotics to try to prevent secondary bacterial infections. (kash and Taubenberg-er, 2015; MacIntryrev et al., 2018) Co-infection is caused by multiple pathogens of viral, bacterial or fungal origin and occurs at the same time. (Jamison et al., 2010***). Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae, and Klebsiella pneumoniae*** are the most common bacteria isolated during secondary infection (Handel et al., 2009).

Many bacteria have acquired broad resistance to a range of antibiotics, and any increase in antibiotic use during the COVID-19 pandemic will have a detrimental effect on antibiotic resistance rates for bacterial pathogens (Reardon, 2020). Multi-drug resistance (MDR) has become a global health challenge because in many cases there are no (chemical) antibiotics to treat such infections, including secondary infections. Several major human pathogens show antibiotic resistance including methicillin-resistant ***Staphylococcus aureus*** (MRSA), multidrug-resistant streptococci, ***Klebsiella*** and carbapenem-resistant ***Pseudomonas aeruginosa*** (CRE), (kumar and Chordia,2017).

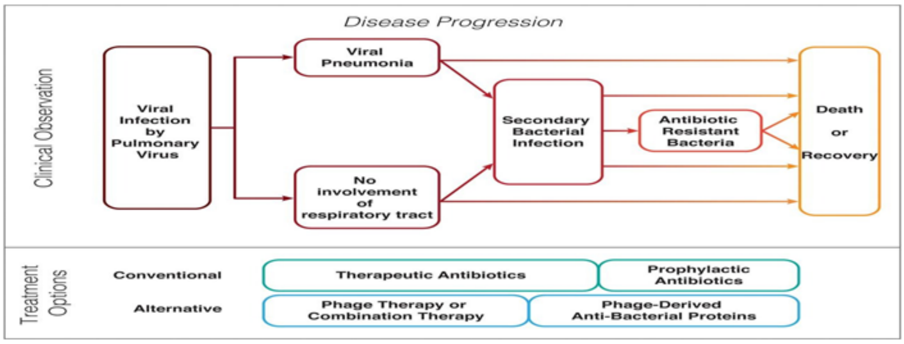

Figure (1) shows the potential clinical development of patients with pneumonia virus infection and the choice of treatment for bacterial secondary infection (Loh and Leptihn, 2020).

Given and to identify the bacterial species that cause secondary respiratory infections and their resistance to antibiotics, this research was conducted.

Material & Methods

170 sputum samples are collected from patients confirmed to have been infected with the emerging coronavirus, COVID-19, for both sexes (males - females) and for ages from 20-90 years and those in intensive care units (ICU) in epidemiological isolation hospitals, including Al-Shifa 14 Epidemiological Hospital and Kirkuk General Hospital, with the help of doctors Resident specialists with wearing a full protective kit during the period 1/12/2020 until 1/3/2021, the samples are transferred directly to the microbiology laboratory at the College of Education for Pure Sciences at Kirkuk University, sputum samples are planted on MacConkey agar medium and chocolate agar for growth Gram-negative

bacterial species, grown on blood agar medium, and cultured on Manitol salt agar medium and Nutrient agar for growth of Gram-positive bacterial species, and incubated at oc37 temperature for 18-24 hours, to investigate secondary bacterial species Associated with the emerging corona virus COVID-19, the bacteria were diagnosed through phenotypic and microscopic examination and through biochemical tests that included (oxidase, catalase, indole, citrate use The diagnosis is confirmed using the API diagnostic kit and in addition to the Vitek-2 compact system, a sensitivity test is conducted for all types of bacteria under study and to determine their resistance against 17 antibiotics by Disks method. Diffusion Method and based on (Kirby and Bauer 1966), which included (, Imipenem, Meropenem, (Amoxicillin + clavulanic acid), Gentamycin, Levofloxacin, Ceftriaxone Tetracycline, Ampicillin, Cloramphenical, Cipromethylacionacin, Nitrix, Oxyfurmethylacin, Oxamethasone Clindamycin Erythromycin) bearing in mind that the tablets used were manufactured by the Turkish company BIOANALYS, and the results are recorded by measuring the diameter of the inhibition zone around each tablet.

Resalt & Discusion

A total of 170 sputum samples are collected from patients confirmed to be infected with the emerging Coronavirus SARS-Cov-19 and those hospitalized in intensive care units in hospitals (Shifa 14 for epidemiological isolation, and Kirkuk General Hospital) in the city of Kirkuk. It Is found that 119 samples are positive for 70% growth and 51 samples are negative. The growth is 30%, 135 bacterial isolates are obtained. The isolates are distributed into 64 isolates (47.40%) belonging to Gram-positive bacteria, and 71 isolates (52.59%) belonging to Gram-negative bacteria, the number of pure single isolates is 102 (75.55%), as for For the mixed samples there are 17 samples (12.5%) and the mixed isolates included 3 (17.6%) isolates of the follower ***Staph.aureus+S.pneumoniae,*** 5 (29.4%) ***K.pneumoniae+Psedo.aeruginosa,*** 2 (11.9***%)*** ***Staph.aureus+S .pyogenes*** 3 (17.6%) ***H.influenzae+K.pneumoniae***, 1 (5.9%)***Psedo.aeruginosa+ Staph.aureus***, 3 (17.6%) ***S.pneumoniae+S.pyogenes***, as shown in Figure (2).

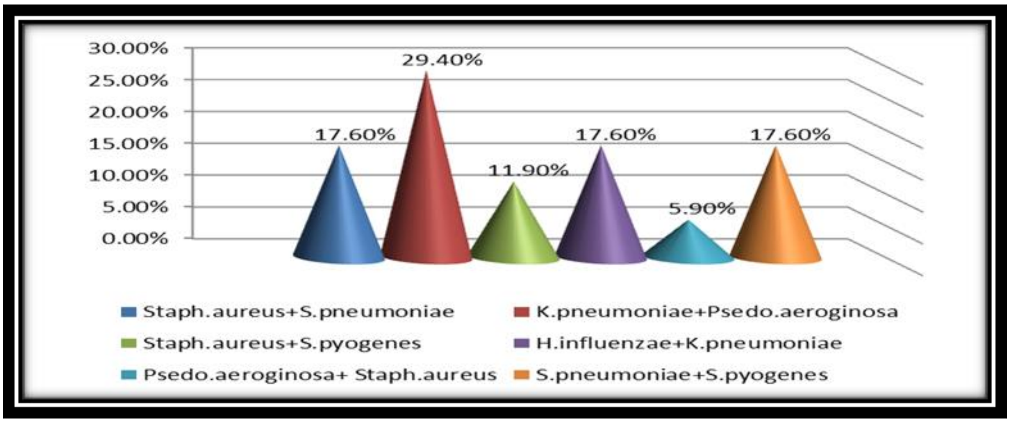

Figure 2 shows the percentage of mixed bacterial pathogens

The results show isolates of positive bacteria shown in Figure (3), that (42) isolates belonging to Staph.aureus, with a percentage of 31.11%, are the most frequent bacteria among the isolates of Karam-positive bacteria, where this result is consistent with what is found (Elabadi et al. .,2021), and it appeared that the secondary bacterial infection rate among those infected with COVID-19 is caused by ***Staph.aureus***, which causes various respiratory infections, including pneumonia, bronchitis and (12) isolates of ***S. Pneumonia,*** with a rate of 7.4%, which are among the bacterial causes that It is associated with secondary infection, that this bacteria naturally inhabits the respiratory passages, but it can enter the lungs by inhalation, and these results are consistent with (Brueggemann et al., 2021), where it is shown that it is one of the most common causes of pneumonia and (10) Isolation ***of S. pyogens*** with a percentage of 7.4% is one of the bacterial causes associated with secondary infection, and these results are consistent with what is reached (Musher et al., 2021). It indicated that ***S.pyogen*** bacteria possess many virulence factors that help it spread by breaking down connective tissues. Where Pfeiffer discovered during the outbreak of influenza in 1918 the bacterium ***Streptococcus pyogenes*** as a prominent bacterial organism in influenza, and these results also agreed with what is reached (Shakoor et al., 2019), where the study he concluded showed that the possession of these bacteria in the capsule is of great importance in the pathogenesis of bacteria.

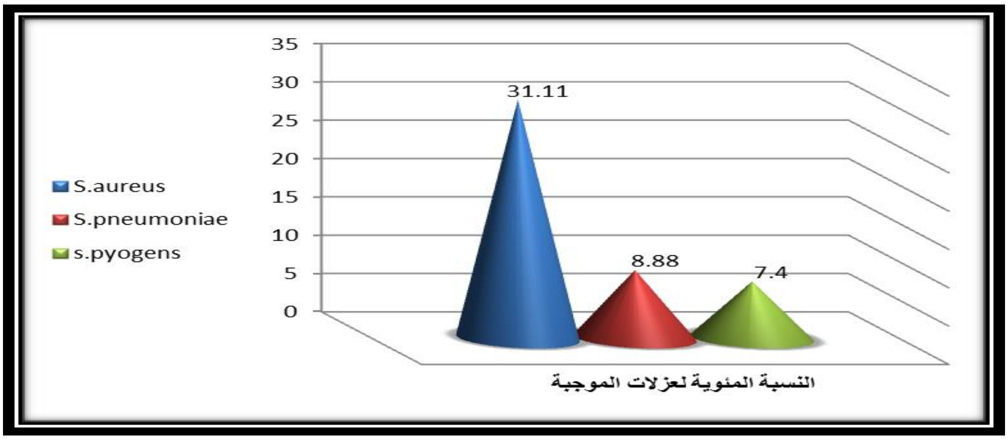

Figure (3) Percentage of positive bacterial species

As for the number of isolates of Gram-negative bacteria, shown in Figure (4), that (37) isolates ***of K**.**pneumoniae*** are 27.40%, and the highest percentage of Gram-negative bacterial causes associated with secondary infection and resistance to antibiotics are consistent with what is reached (Ahmed et al.,2021) and at a rate of (40.5%), where this bacteria is one of the transient natural flora present on the body, as it is considered an opportunistic infection in patients and hospitals. When the results showed that ***Pseudo. aeruginosa*** is infected with 11.85% (16 isolates), these results are consistent with what was found (Lansbury et al., 2020), ***P. aeruginosa*** was closely associated with bacterial co-infection that occurs in patients during the critical stage of the disease. COVID-19, ***Pseudomonas aeruginosa*** is an opportunistic biofilm-forming pathogen that causes chronic infections in immunocompromised patients and results in a high mortality rate. The results of the current study also show that the bacteria ***Haemophilus.influenzae,*** with an infection rate of 11.11% (15 isolates), the results of the current study agreed with what is reached (Ali et al., 2016; Zou., 2020), where it was showed in his study that colonization of H. .Respiratory influenzae is the leading cause of respiratory infections and tissue damage. The results also show that (3 isolates) of the ***K***. ***oxytoca*** with a percentage of 2.22% are among the least number of isolates, because it is from the normal flora in the mouth and nose in addition to the intestines, but it is considered opportunistic when it moves to other places and can cause pneumonia.

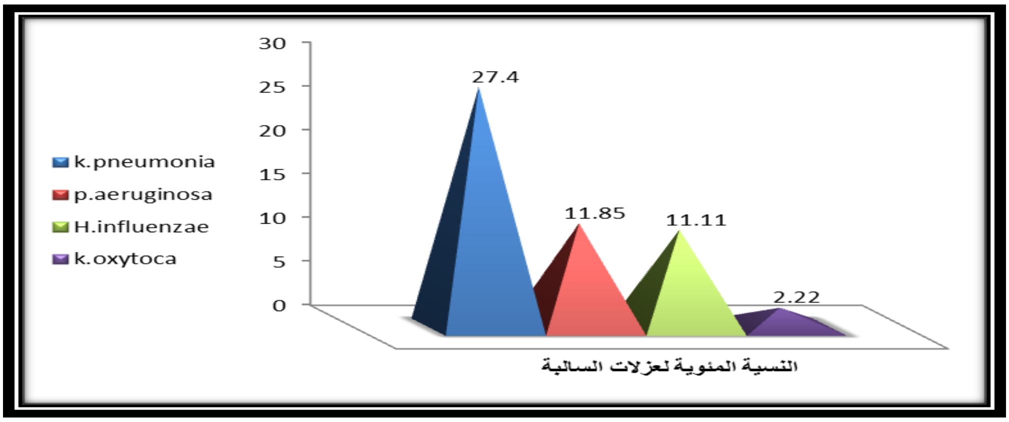

Figure (4) Percentage of negative isolates

The clone among the number of isolates 135 isolates, the most infected is dependent on the number of Gram-negative bacterial isolates of 71 (52.5%), while for Gram-positive bacteria, the number of isolates is 64 (47.4%), and it is showed that the percentage of respiratory infections caused by gram-negative bacteria is higher compared with the gram-positive bacteria, and the reason for this can be due to the natural presence of most of the gram-positive bacteria in the upper respiratory tract, which has a clear effect on infections of the lower respiratory tract associated with cases of weak immunity, where the reason is due to the bacteria possessing many resistance mechanisms and the ease of spreading determinants This resistance is through plasmids and through the processes of conjugation or transformation between them due to their presence in one environment (Goldman and Green, 2021). The resistance of positive and negative bacterial isolates to the cream dye to antibiotics is conducted against (17) antibiotics, and by the method of diffusion around the discs, based on (Kirby Bauer 1966), and the results of the study show a clear discrepancy in the resistance of the studied bacterial isolates as shown in Table (2).

The results show *that* ***Staph.aureus*** bacteria are resistant to multiple antibiotics, including Ampillicin, Oxacillin, Azethromycin, Trimethoprin, Erythromycin (100%). In humans, this can be due to the widespread use of antibiotics as well as the lack of health awareness of community members. In staphylococcus, resistance to azithromycin may occur due to ribosomal modifications resulting from the enzyme (Methylase enzyme 23s rRNA) by genes (ermA, ermB, ermC). The results of the current study also show that ***S.pneumoniae*** bacteria are resistant to antibiotics to Ceftriaxon, Tetracyclin, Oxacillin, Nitrofurantion, and Clindamycin with a percentage of 100%. Prescription and misuse of antibiotics. As for ***S.pyogenes,*** they are resistant to all antibiotics by 100% except for Imipenem, meropenem, Gentamyci, azithromycin, and nitrofurantion. These results agreed with what is reached (kebede et al., 2021), and bacterial resistance is due to the risk of infection with multidrugs - Resistance (MDR) in elderly and immunocompromised subjects. As for Gram-negative bacteria, K. pneumoniae were resistant to Amoxicillin/Clavulanic acid, Oxacillin, Erythromycin, Levofloxacin, Ampicillin, Azethromycin, Ceprofloxacin Trimethoprin, by 100%, followed by ceftriaxone, 91%, due to the excessive use of ctetracycline, tetracycline. Vitality and resistance of isolates to antibiotics are the cause of a public health problem. As for ***K.oxytoca*** bacteria, they were resistant to all antibiotics, and 100% except for Amoxicillin/Clavulanic acid, Gentamyci, ceftriaxone chloramphinical, tetracycline trimethoprin amikacin, and clindamycin are less resistant. These results are close to what was found (AL-Khikani et al., 2020). Increasing the resistance of the antimicrobials of the type of Kepsella bacteria by a number of internal and external factors and due to the production of beta-lactam enzymes and extended-spectrum beta-lactam and biofilm formation (Kuinkel et al., 2021). As for ***H.influenzae***, they are resistant to all antibiotics, and 100% except for imipenem, meropenem, amoxicillin/Clavulanic acid, gentamycin, levofloxacin, cloramphinical amikacin, nitrofurantion, and Azethromyci are less resistans(Dessie ., 2021), and indicated that bacterial resistance to these antibiotics may be due to various reasons, including poor drug quality, misuse or excessive prescriptions due to poor diagnostic preparation. The results showed that ***P. aeruginosa*** was resistant to all antibiotics by 100% except for Azethromyci, meropenem and gentamycin. Antibiotics because their genes have specific resistance, such as catB, which confers resistance to chloramphenicol, and APC promoter, which encodes lactamase, since inappropriate use or overuse of antibiotics is known to be an important driver of the emergence of antimicrobial resistance (Mahmoudi., 2020).

Table (2) shows the number of isolates and their resistance to the antibiotics used

acteria ics	ram positive bacteria			am negative bacteria			
		oniae		*oniae*		*osa*	*zae*
m		7				6	
hem	9	3				.0	.3
lin\Clavulanic	33	4	0	7		6	
ycin	023	2				.4	.0
acin	34	7	0	7		6	.3
one	35	2	0	34		6	5
line	9	2	0	34		6	5
n	2	3	0	7		6	5
henical	5	3	0	24		6	
xacin	.2	5	0	7		6	5
	2	2	0	7		6	5
mycin	2	3		7		.0	5
antion		2		26		6	.0
n	.3		0	2		6	.1
oprin	2	3	0	7		6	5
ycin		2	0	4		6	5
nycin	2	4	0	7		6	5

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