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Assessment of The Prevalence Of Secondary Bacterial Infection Isolated From Covid-19 Virus Patients in Kirkuk City

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A B S T R A C T

The syndrome of Severe Acute Respiratory corona virus 2 (SARS-CoV-2),which was the main reason for corona infection during 2019 (called Covid-19).

The study aimed to assess thebacterial co-infection prevalence among (50) diagnosed COVID-19 hospitalizedpatients, with complete accurate physical examination, The main specimen needed was the sputum that taken from admitted patients in the care wards and respiratory concentrated unite (RCU) during The period from December 2021 to February 2022. The bacteria which was isolated were further diagnosed using Vitek 2 analyzer system in the Private Hospital / Hawler.city / Iraq .

Result: the old age group and those with underlying clinical disease such as hypertension (48%), diabetes (20%), chronic disease (26%), and cancer (6%) are mainly leading to become more complicated critical illnesses. The main strong relation of increased CRP (98%), D-Dimer (84%), lymphopenia (72%), ferritin (88%) level and the poor clinical results with the degree severity of the disease.

Conclusion: secondary bacterial infection is more common in COVID-19 patients and resulted to highly significant morbidity and mortality

Introduction

During December/ 2019, many patients of severe pneumonia of unknown origin presented in Wuhan,China [1], further more , they were diagnosed as (COVID-19) disease, coronavirus 2019 , whose the main causaivtive agent is SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) [2,3] the genus β from the the family Coronaviridae. The national organization World Health Organization (WHO) reported that this disease as a pandemic during March 11, 2020 [4]. The most commenest patients with this disease exisited in two main pictures, either are asymptomatic or may be presented in very simple mild disease. inspite of that , in a calculating the disease percentage , the respiratory disease needed an immediated admission to the hospital , and such infections can progress toserious illness with several complications like hypoxemic respiratory failure which supported by ventilatory venteliater [5].

themechanisms of Superinfection consiste of virus-inducedand immune system damage , decrease in mucociliary clearancer, and espiratory system damage. The virus can effecting lymphocytes, espically B cells, T cells, and NK cells, and by this mechanism , it leading to detoriartaion of immune system through out the disease progress . The essenital reason for superinfection isdue to lowering in host's immune functionand in lymphocytes count . further more, because there is still very little back ground information on this mechanism of interaction, which determining the kinetics of bacterial superinfection during the disease progress is difficult at the present time [6].

many articles has pointed at the incidence of bacterial superinfections in COVID-19 patientsreveling a huge disparate proportions (with variances of more than 50%) because of epidemiological and clinical facters of each location, in addition to criteria utilized, and diagnostic methods . inspite of this wide range of superinfection severity, many research has mentioned a number of serious risk factors, including kidney failure requiring hemodialysis, , admission to the intensive care unit, mechanical ventilation, being over 60 years old, pharmacological immunosuppression (steroids or biological therapy), and prolonged hospitalization [7]. Given variance in superinfection frequency, and the variability of the bacterial agents involved , this background never be be generalized to other populations.

Bacterial co-pathogens are commenly found in in viral respiratory tract disease such as influenza, and they are a a main causative agent of mortality and morbidity , needing very effective prompt identification and antibacterial therapy [8]. Although greatly challanges , bacterial co-infection has been reveled to be as high as 20-30% in patients complaining from severe influenza [9], and is correlated to an increased risk of mortality , higher severity of disease, and increased use of healthcare resources [10].The features of bacterial infection in patients infected with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) , prevalence, and incidence, have been recognised as a significant knowledge gap [11]. the scintific Understanding the proportion of COVID-19 patients with acute respiratory bacterial co-infection is critical for treating purposes and ensuring specific antibiotic administration, as well as reducing the harmful risk out come of antibiotic misuse [12]. Furthermore, this insight may be lead to future refinement of empirical antibiotic therapy guidelines for COVID-19 patients.

Aim of study

It was aimed to assess the prevalence of bacterial co-infection in (COVID-19 hospitalized diagnosed patients, with an examination of demographic, laboratory, and clinical parameters.

Methods

- **Ethical Issue**

A specific agreement was otained from kirkuk health directorates before starting the study (in the AL-Shifa 14 hospital).

- **Study period and design**

A descriptive cross-sectional study was prepared in kirkuk city / AL-Shifa 14 hospital ,with a total of 150 patients hositalized , out of them 128 admitted to the general ward, and the remaining22 patients were admitted to (RCU)the Respiratory care unit (RCU), during the period of December 2021 to February 2022.

- **Study subjects**

A total number of 50 adults diagnosed as COVID-19 patients admitted to the hospital between the period started from December 2021 and February 2022, who met the underlinig eligibility criteria: patients age more than 18 years old, with a positive molecular RT-PCR SARS-CoV-2 test (Amplification Kit Ref 09N77-090 according to the Berlin protocol) from the nasopharyngeal swab, assosiated with an evaluation by one clinical physicians of the

public health specialist, and infectious diseases group with the presence of at least one of the following risk factor that needed admission and hospitalization which are :

Patients age more than 60 years

positive tests for Diabetes mellitus.

positive tests for Cardiovascular disease (chronic heart failure,coronary artery disease)

presence of Lung disease (emphysema, asthma, and chronic obstructive pulmonary disease)

atients using Immunosuppression (prednisone > 20 mg/day for more than 14 days).

Hypoxemia with PAFI (partial arterial oxygen pressure PaO2) <90%, abnormal chest computed tomography (CT).

- ## Sampling collection and techniques

The bacterial superinfection was diagnose in patients admitted with COVID-19 was based on the simultaneous presence of the following three main diagnostic criteria which had to be presented during 48 hours or after admission later on :

- **The first Clinical criteria** was the presence of apurulent sputum, continous fever (> 38.3 C), and hemodynamic instability.
- **patients needed** vasopressor support, and there was a continous deterioration of pulmonary parameters and lung function test .
- **Paraclinical criteria:** including lowering of leukocytosis and elevated in C-reactive protein.
- **Radiological criteria:** bivous worsening of the chest radiological pattern (basal consolidation, cavitation, pleural effusion, and nodules) [13].

When the above 3 main diagnostic criteria were met, then sputum examination was done twice, the first one at the time of admission and the second sample was done after 72 hours of admission in order to detct the causative agent which is responsible for the superinfection. In the cultures(Blood, MacConkey, Chocolate agar), the isolation of a single or predominant bacterium was considered positive. the isolation was identified using the VITEK-2 system (bioMerieux 8.01).

Result

Of all patients, 40 (80%) were adults aging over 50 years and 26 (52%) were male and 24 (48%) were female; the main comorbidities were diabetes mellitus 10 (20%), heart failure 5 (10%), and hypertension 24 (48%),). further more , 15 (30%) of patients needed RCU, and 30 (60%) having a continuous positive airway pressure (CPAP), and 20 (40%) on O2 with a mortality of 21 (42%). In this study, it was receled that bacterial superinfection was 88% which is higher in patients aged more than 50 years in comparsion to patients less than 50 years of age (Table 1).

the over all prevalence rate

Table 1. Characteristics of Covid-19 patients

Characteristics		Levels			Number	%
demographic	age	Over 50 years	42 (84%)	Bacterial superinfection	22	88
		Less than 50 years	8 (16%)	Bacterial superinfection	3	12
			Male		26	52
			Female		24	48
Comorbidities			Hypertension		24	48
			Diabetes		10	20
			Chronic kidney disease		8	16
			Heart failure		5	10
			Cancer		3	6
Outcome			Hospital stay> 8 days		35	70
			Required respiratory care unit (RCU stay)		15	30
			Required continuous positive airway pressure(CPAP)		30	60
			Use of steroids		50	100
			Death		21	42

The prevalence of bacterial superinfection in patients hospitalized for COVID-19 was 25 (50%), identifying 6 different species of bacteria, with Klebsiella pneumoniae and Staphylococcus aureus being the most frequent(26%, 10%) respectively (Table 2).

Table 2. Distribution of bacterial superinfection among patients with Covid-19

Bacterial superinfection	Number	%
Klebsiella pneumoniae	13	26
Staphylococcus aureus	5	10
Escherichia coli	3	6
Acinetobacter baumannii	2	4
Enterobacter cloacae	1	2
Serratia marcescens	1	2

Figure 1. presents the main types of bacterial infection in different ager

Allthe studied patients 50 (100%)were received antibiotics for at least one week , and 45 (90%) as monotherapy, with Meropenem regared as the the most prescribed antibiotic 24 (48%), followed by Levofloxacin 10 (20%), Piperacillin/tazobactam 4 (8%), Ceftriaxone 3 (6%) (Table 3).

Table 3. Distrubution of antibiotics used for covid- 19 hospitalized patients with bacterial superinfection

Variable	Levels	Number	%
Duration of antibiotic treatment	1–7 days	29	58
	8–14 days	15	30
	15 or more days	6	12
Type of antibiotic treatment	Monotherapy	45	90
	Multi-therapy	5	10
Antibiotic used	Meropenem	24	48
	Meropenem+ Vancomycin	3	6
	Levofloxacin	10	20
	Piperacillin/tazobactam	4	8
	Piperacillin/tazobactam+ Levofloxacin	2	4
	Ceftriaxone	3	6
	Vancomycin	1	2
	Azithromycin	2	4
	Amoxicillin/Clavulanic acid	1	2

All the received CT scan images were dagnosed and analyzed by speciliazed reviewiers radiologist. The severity score was calculated based on the percentage of lung involvement each patient. 20 (40%) patients were with score 2 and 10 (20%) were with score 3 , while12 (24%) of the patients with score 4 and 8 (16%) were in score 5 as demonstrate in (Table 4) [14].

Table 4. Chest radiology (lung involvement) in patient with Covid-19

Score		Number	%
Score 1:	5%	0	0
Score 2:	6-25%	20	40
Score 3:	26-50%	10	20
Score 4:	51-75%	12	24
Score 5:	>75	8	16

the main Clinical presentation for 50 paitents was dyspnea , fever, fatigue, and anaroxia . In Table 5 there was a high WBC count were record in the all the cases and mainly seen in 40 (80%) of the patients, also the study reveled strong relation ship between lymphopenia (which mean low lymphocyte count less than 0.5%) with the severity of the disease were 36 (72%) of patients mentioned with lymphocytopenia, and only 11 (22%) of patients had normal lymphocyte count (1-1.5%).

Table 5. Hematological examination of infected patients with Covid-19

Count		Total	%
WBC	Low	0	0
	Normal	10	20
	High	40	80
Lymphocyte	Low 0.5-0.9	36	72
	Normal 0.9-5	11	22
	High > 5	3	6

There was a positive Strong relation seen between increased ferritin level , CRP, D-Dimer and the severity of Covid-19 infection, CRP level ≥ 10 mg/ml found in 7(14%) and CRP ≥ 30 seen in 42(84%). D-Dimer levels ≥ 500 ng/ml were found in 42(82%) patients. Serum ferritin ≥250 U/L seen in 44 (88%) patients as summarized in (Table 6).

Table 6. Laboratory Finding - Biochemical parameters of patient with covid-19

Parameters	Results	%
CRP		
normal <10	1	2
High (10-30)	7	14
Extremely high > 30	42	84
D-Dimer		
normal 1-499	8	16
High 500-1000	12	24
Extremely high >1000	30	60
S. Ferritin (20-250 Ug/L)		
normal 20-250	6	12
High 250-500	12	24
Extremely high >500	32	64

Discussion

The present study reveal that the mortality rate among studied patients was (42%) which is in agreements with a study done by the Chinese Center for Disease Control and Prevention found that nearly 44,500 diagnosed infections cases with an detection of disease severity [15]. the Mild for of disease presentation which mean **(mild or nopresence of pneumoniano)** was mentioned in 81 %t, Severe disease (eg, with hypoxia, or >50 percent lung involvement on imaging within 24 to 48 hours, and dyspnea,) was documented in 14 %, and the dangerous serious disease (eg, with shock, or multiorgan dysfunction, and respiratory failure,) was written in 5 %. The total case-fatality rate was 2.3 %; no deaths occurance were reported among non-dangerous cases. SARS-CoV-2 has far outperformed other major respiratory viral diseases in terms of mortality, and bacterial superinfection [16]. SARS-CoV-2 superinfection with other microorganisms, particularly fungi , and bacteria , is a proving risk factor in the determination of COVID-19, which making the diagnosis, the treatment, and lastly the prognosis more specific [17]. In COVID-19 patients presented with , bacterial superinfection is correlated with a disease prognosis, and progression . This phenomena elevates the need for hospital admission in respiratory care units, with antibiotic treatment, and increase the mrtality rate [18].

In the existing study, 50% of the participants having a bacterial superinfection, which is a fairly a high rate when compared to another earlier studies [19]. inspite of that , there is an explaination for the higher rate of antibiotic prescriptions in patients group , which contradicts another recent previous studies in which reveled that the superinfection percentage which was recorded is highly significantly lower than the antibiotics adminstration percentage [20]. many different studies taken in the United States and several European nations and Asian regiones have mentioned avery highly varying frequency of bacterial superinfection in COVID-19 patients, ranging from 1% to 50% , which can be explained by discrepancies in diagnostic procedures and criteria that are utilized.

regarding the clinical characteristics and demographic features related with bacterial superinfection, there is a very a significant correlation was detected with patients aged above 50 years old [in comparsion to those patients aged less than 50 years old], who are suffering from diabetes, hypertension , and having renal failure, which is persistant withthem before the study [21]. This relation ship demonstrates the ergent needs for stratifying this group of patient based on the severity of risk factors associated with the incidence of superinfection and the amount of number . The age-dependent defects in T-cell and B-cell function and the excess production of type 2 cytokines couldl inked with a defect in control of viral replication and more proinflammatory responses prolongation , potentially leading to poor results [22].

The proportion of bacterial co-infection seen in this study (50%) is similar to the findings on bacterial superinfection in COVID-19 infected patients in Colombia [23]. Although this co-infection percentage appears to be high in comparison to another study conducted in the UK in which only 27 out of 836 (3,2 percent) COVID-19 patients were confirmed to have bacterial co-infection at the time of admission, this percentage increased to 6.1 percent throughout admission (0-5 days after admission) [24]. The predominance of Gram Negative Bacteria (GNB) reflects nosocomial infection following prolonged hospitalization and empirical antibiotic use [25].

Klebsiella pneumoniae is the second frequent present gram-negative bacterium, after Escherichia coli, and is related with a avariety of diseases occurance , including intra-abdominal infection, pneumonia, , bloodstream infection (BSI), urinary tract infection (UTI), meningitis, and pyogenic liver abscess. the Infection with the SARS-CoV-19 virus can ead to in a dangerous infection in every person , involving patients without risk factors. The main reason for this phenomena is still unknown unknown, inspite of that it is frequent likely correlated to

socioeconomic determinants variations in the health (e.g , community experience, education, access to health care, economic stability, and living environment) [26].

In the present study, the important laboratory markers wrk in at the hospital referred to leukocytosis and severe lymphopenia in the most of the patients, which aggreed with another earlier studies' findings [27]. the Levels of D-dimer, C reactive protein and serum ferritin were obivously increaed like another study of serum levels of interleukin-6, ferritin, C-reactive protein, lactate dehydrogenase, D-dimer, and thenblymphocytes and neutrophils count in COVID-19 patients: Its quitly related to the severity of the disease which is done in Iraq [28]. This result suggested that SARS-CoV-19 preform on lymphocytes, especially T-lymphocytes, virus can distrubuted and spread through respiratory mucosa and infect other body cells through pro- inflammatory and inflammatory mediators which are elevated forming cytokine storm which lead to sever damage of T-lymphocytes that is a dangerous strong factor playing a role in the aggrevation of the patients clinical condition

According to the grading system and guide line which are used to assess the lung alterations and infiltration with inclusion by the COVID-19 (CT severity score index), the study reeled that a high relation between illness severity and increasing the CT chest score [29]. In terms of antibiotic therapy, several of the criteria were reported from the international guidelines recommendations made for cases of bacterial superinfection in influenza pneumonia [30]. for this purposes , this study found that 50(100%) of the patients received antibiotics, espically monotherapy with Meropenem, Levofloxacin, Piperacillin/tazobactam, Ceftriaxone, and Vancomycin, which is in a greemnt with those documented in other similar studies [31]. inspite of that , other investigations suggested that the lower rates of superinfection than the one identified in this study, but despite this, they utilized ahighly significant number of medicationsand treatment therapy focused on bacterial infections, which they eventually failed to explained . This fact should lead us to reconsider how we approach syndromic infections of this type; and accordingly , it is serious to implement and develop programs to rationalizeand importanize the use of antibiotics in COVID-19 patients in order to prevent an increase in the use of these resources and the future results on nosocomial microbiota resistance [32].

Conclusion

Secondary bacterial infection is commenly present with COVID-19 patients and lead to significant morbidity and mortality. Mono-therapy treatment is more prevalence in patients with Covid-19. Chest infection is extensively damaged by Covid-19 virus.

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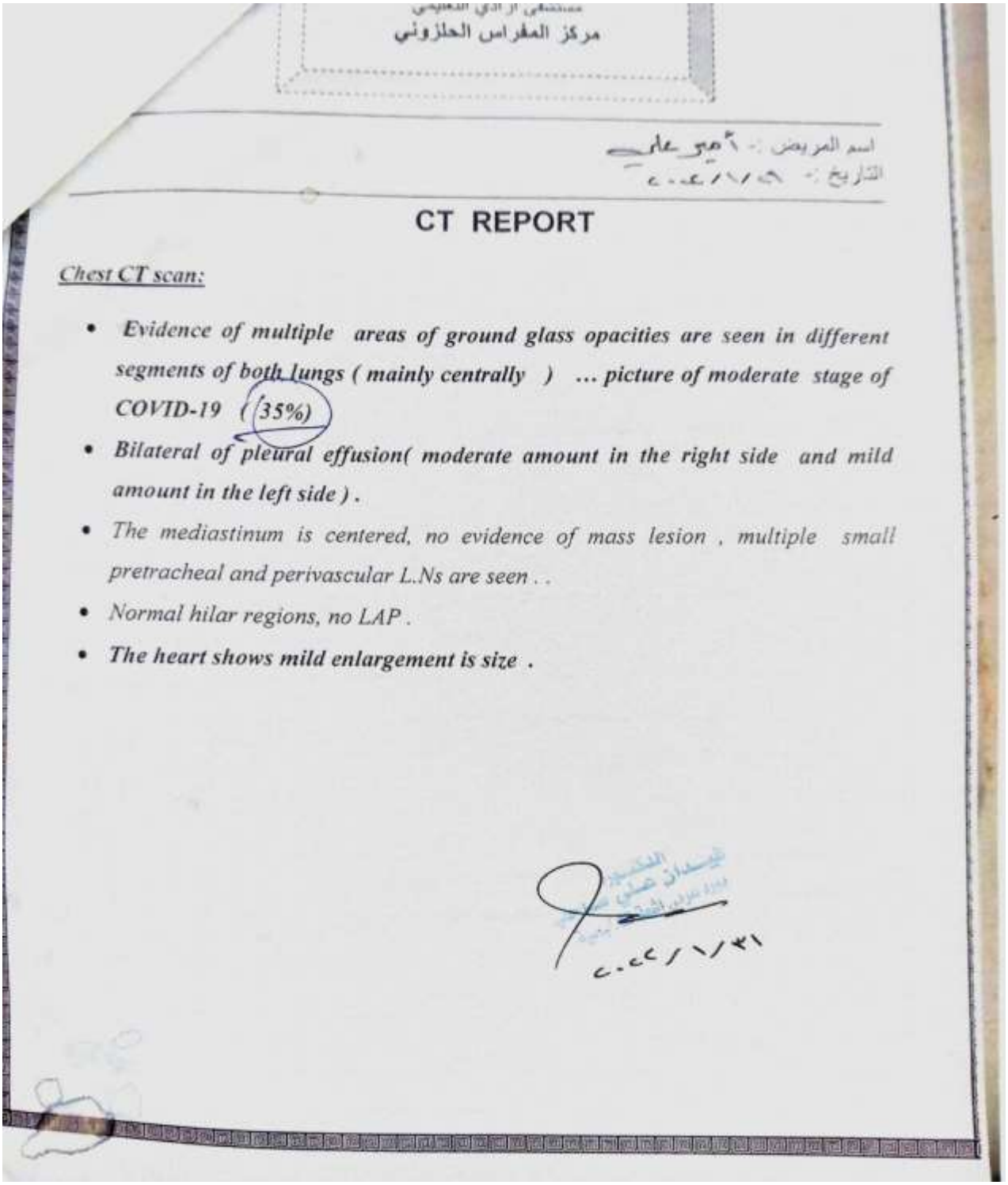
Picture of CT report


مركز المفراس الحلزوني

اسم المريض :- أمير علي

التاريخ :- ٢٠٠٤/١/٢٩

CT REPORT

Chest CT scan:

- *Evidence of multiple areas of ground glass opacities are seen in different segments of both lungs (mainly centrally) ... picture of moderate stage of COVID-19 (35%)*
- *Bilateral of pleural effusion(moderate amount in the right side and mild amount in the left side) .*
- *The mediastinum is centered, no evidence of mass lesion , multiple small pretracheal and perivascular L.Ns are seen . .*
- *Normal hilar regions, no LAP .*
- *The heart shows mild enlargement is size .*

٢٠٠٤/١/٣١

Picture of Vitek result

bioMérieux Customer:
System#:
Patient Name: 1
Isolate: 1-1 (Approved)
Card Type: GN Bar code: 2411765503587660 Testing Instrument:000015F142EC (Hawler HospitalLAB)
Setup Technologist. Laboratory Administrator (labadmin)

Laboratory Report

Autoprint
Patient ID: 1

Bionumber: 2607734453124210
Organism Quantity:

Selected Organism: Klebsiella pneumoniae ssp pneumoniae

Comments:	

Identification Information	**Card:** GN	**Lot Number:** 2411765503	Expires: Sep 26, 2022 1200 AST	
	Status: Final	**Analysis Time:** 14.85hours	Completed: Mar 19. 2022 22:48 AST	
Organism Origin	VITEK 2			
Selected Organism	99% Probability	**Klebsiella pneumoniae ssp pneumoniae**		
	Bionumber: 2607734453124210		Confidence: Excellent identification	
Analysis Organisms and Tests to Separate:				
Analysis Messages:				
Contraindicating Typical Biopattern(s) Klebsiella pneumoniae ssp pneumoniae	URE(76),			

Biochemical Details

2	APPA	-	3	ADO	+	4	PyrA	-	5	IARL	-	7	dCEL	+	9	BGAL	+
10	H2S	-	11	BNAG	-	12	AGLTp	-	13	dGLU	+	14	GGT	+	15	OFF	+
17	BGLU	+	18	dMAL	+	19	d.MAN	+	20	d,MNE	+	21	BXYL	+	22	BAIap	-
23	ProA	-	26	LIP	-	27	PLE	+	29	TyrA	-	31	URE	-	32	dSOR	+
33	SAC	+	34	dTAG	-	35	dTRE	+	36	CIT	+	37	MNT	+	39	5KG	-
40	ILATk	+	41	AGLU	-	42	SUCT	-	43	NAGA	-	44	AGAL	+	45	PHOS	-
46	GlyA	-	47	ODC	-	48	LDC	+	53	IHISa	-	56	CMT	+	57	BGUR	-
58	0129R	+	59	GGAA	-	61	IMLTa	-	62	ELLM	-	64	ILATa	-			

Installed VITEK 2 Systems Version: 9.02
MIC Interpretation Guideline:
AES Parameter Set Name:

Therapeutic Interpretation Guideline:
AES Parameter Last Modified.
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