RESEARCH ARTICLE

Relationship between Co-infection and Secondary Bacterial Infection with Opportunistic Fungi in COVID-19 Patients

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ABSTRACT

The outbreak of 2019 novel coronavirus disease (2019-nCOV) in Wuhan city, China, by January 30, 2020. Iraq is one of the countries that diseases have been spread special in Misan province, Iraq. One hundred twenty-five patients suffer from COVID-19 disease with signs and symptoms as high fever, headache, chest pain, dry cough, diarrhea, short breathing, and another complicated lung, renal failure, and death. All samples were collected from Al-Sadder Educational Hospital and depended on auxiliary examinations such as chest X-ray examinations and chest CT-scan. Other diagnoses were taken from throat swabs from throat swabs as sputum, lower respiratory tract secretion, and blood was positive for 2019-nCov. The aim of study and diagnosis of infected with COVID-19 disease by serological tests and biochemical tests as ferritin, c-reactive protein (CRP), lactate dehydrogenase (LDH), Platelets count, and Lymphocytes count. Determinate a secondary bacterial and co-infection with opportunistic fungi in COVID-19 diseases. Detection of the relationships among some parameters associated with COVID-19 and which causes secondary and co-infection. SPSS program version (20) has been used in statistical analysis using different parameters related to COVID-19 diseases.

Keywords: COVID-19 diseases, Co-infection, Opportunistic fungi, Secondary bacterial infection.

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INTRODUCTION

While facing the covid-19 pandemic with over (2.1) million deaths globally, it must deal with co-infection with bacteria and fungi.[1] COVID-19 diseases worldwide pandemic infection caused by documented to cause co-infection in COVID-19 patients and causes high morbidity and mortality.[2] A few days of infection with corona virus occur respiratory tract infection or pulmonary infection and prolonging recorded bacterial infection or fungi infection a few weeks later.[3] Accurate results and raid diagnosis of bacterial and fungi as a pathogenic microorganism or resident factors during COVID-19 infection.[4] Goyal and colleagues were reported a percentage (6%) of bacteremia during hospital admission[5] Wang and colleagues reported that (29/69) patients had bacterial and fungal co-infection.[6] *Acinetobacter*, *Klebsiella*, *Enterobacter* spp, *Aspergillus spp* and *Candida spp* are among the main genera which cause secondary infection in COVID-19 patients.[7]

Bacterial co-infections were recorded (91.8%) over viral (31.5%) and fungal (23.3%) infections and association between co-infection rates and severity or mortality in COVID-19 patients. Secondary bacterial infections with covid-19, *Streptococcus pneumonia*, *Klebsiella pneumonia*, *Heamophilus influenza*, *Escherichia coli*, *Staphylococcus aureus*, *Aspergillus spp*, and Epstein-Barr virus were diagnosis in covid-19 but in *Pseudomonas aeruginosa*, human adenovirus, human rhinovirus, and herpes simplex virus were diagnosis in symptomatic patients according in severity diseases. Influenza A virus, influenza B virus, or coronavirus were not common in COVID-19 patients.[8] The first SARS-CoV outbreak in (2002–2003), was (30%) of patients were infected with secondary bacterial infections and co-infection was associated with disease severity (9–10). Bacterial co-infections are present during regular influenza seasons in (2-65)% and lead to morbidity and mortality.[11,12] In the outbreak of SARS-CoV, analyses of isolates collected from patients present in intensive care unit (ICU) in Prince of Wales Hospital (Hong Kong) recorded that rates of methicillin-resistant *S. aureus* acquisition increased during the outbreak from (3.53%) before being infected with SARS to (25.30%) during SARS outbreak.[13] Some bacteria were isolated from sputum specimens of patients in Hong Kong as *S. aureus, P. aeruginosa, Klebsiella spp.*, and *S. pneumonia*, each of bacteria was highly resistant to a broad spectrum of drugs.[14,15] Some of the pathogens isolated from COVID-19 patients can resist to antibiotic, which less the efficacy of treatments administered to patients.[16,17]

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MATERIAL AND METHODS

Inclusion Criteria and Sampling

About (125) patients of age group (10–89) years and both sexes were included in the study from December 2020 to April 2021. Samples collected from patients included lower respiratory samples, and serum for COVID-19 patients' Sputum, taken from the lower respiratory and endotracheal aspirate.

Serology and Biochemical Tests: These tests are routinely used for detection COVID-19 patients were demonstrated after 5 days to (5–14) day, the serological test used for understanding epidemiology of emerging human COVID-19 and symptomatic infections also hematology parameter as, lymphocytes, platelets and others biochemical parameter as ferritin, hemoglobin, LDH and others by mini VIDAS.[8]

Bacterial Secondary, Co-infection, and Fungal Isolation

One hundred twenty-five of sputum sample was taken from patients suffering from covid-19 were collected from patients attended to the hospitals Al-Saddar Teaching Hospital in Misan. The bacterial isolates were confirmed as colony morphology, motility, pigment production, growth temperature, gram staining, and biochemical tests as Vitek-2, oxidase test, urease test, and catalase test. Sputum specimens were transported into the bacteriology laboratory using transport bacteria media (2 mL) of transport media then inoculated into Macconcy Agar,chocolate agar and blood agar plates. Amphotericin-B (5 mg/mL), to prevent fungi and incubated in aerobic and anaerobic atmosphere bacteria were identified then all bacteria were keep it on brain heart infusion broth. Isolated fungi were diagnosed based on the colony and morphological characteristics like color, shape, and type of spores under a microscope (X10) and then with (X40) objective lens to detect spore, hyphae, and other special structures.[18] All fungi were observed and identify according to appearance. Fungal isolated were firmed by used a Mycological Atlas of Robert and Ellen (1988).[19] Then plated on solidified Potato Dextrose Agar plates, then inoculated plates were incubated at (28°C) for 5 days.

Table 1: Age groups of patients COVID-19 diseases

Age groups (year)	*Frequency*	*Percennt (%)*
Group(A) 15–19	7	5.6
Group (B) 20–29	5	4
Group (C) 30–39	15	11.9
Group (D) 40–49	42	33.3
Group (F) 50–59	29	23
Group (G) 60–69	20	16.7
Group (H) 70–79	7	5.6
Total	125	100%

Table 2: Sex distributions of COVID-19 patients

Sex	*Frequency*	*%*
Male	71	56.3
Female	54	42.9
Total	125	100%

Identification of the fungal Isolates needs (1–4) weeks pure cultures of the fungal isolates was identified using cultural and morphological features such as colony growth, morphology and pigment color by slide culture techniques.[20]

RESULTS AND DISCUSSION

Age groups of patient were arranged into groups, a finding study was based on a set of variables to identify the relationship between COVID-19 disease and these variables and correlated with co-infection and secondary pathogen infection. The sample size of this study was 125 patients with ages ranges from (15–89) year. Some factors such as age, sex, biochemical and hematological parameters and another disease. Age is one of the most important variables closely related to the incidence of COVID-19. A high percentage of Covid-19 diseases was seen in age group D range from (40–49) year as Table 1. In the present study, different age groups. Age group D (40–49) years have a high percentage of 42 (33.3%) related to some factors, such as sample size, ages patients infected with COVID-19, infected with an autoimmune disease like people with diabetes other factors. This is study disagrees with some researches which[21,22] recorded a high rate in age was 56 years, and more than (54.3%) of the patient were men, but this study agree with other previous researches[21] was recorded must case in this age groups. According to age in COVID-19 patients with a mean age was 61 year, 192.78% were recorded male and morality (<1%) in age group (<50) years and highest mortality rate were in age group (>80) year.[23,24] This study disagrees with an accurate study. Korea center of diseases control and prevention documented the morbidity much a higher in elderly (10.9%) in age groups between 70–90 year and 26.6% in patents with age groups (>80) due to age decreases with aging and causes morbidity with chronic diseases like diabetes.[25]

The second variable was sex as in Table 2. Male was recoded a high percentage recorded was 71 (54.3%) more than female 54 (42.9%). According to sex, these results agree with a previous study,[22] they were recorded a man was a high rate 30 (73%) while female 11 (27%) a male was work out more than female, a sample size of the study. Males were smoking which was affected with COVID-19 the leading causes a male more infected than females due to the immune response in females more than males this related to hormone change as progesterone and estrogen level, which increase immunity in males in contrast with males.[26]

The third variable was platelet count (Plts) Maryame A., 2020, who reported a normal platelets count was (226×10^9) as an average count range between 187–280. Therefore, this disagrees with current results was 37 (68.5%) in the range between 200–299 with significant p-value as in Table 3 and Figure 1.[26,27] In Table 4 and Figure 2 and 4, a fourth variable was ferritin is a key meditator of immunity dysregulation, and it is a correlation with cytokine storm in covid-19, ferritin was recorded 18 (25.4%) with a significant p value (0.014).In COVID-19 patients, ferritin level is increased like current study.[28] Lymphocytes, immunity cells in peripheral

blood of patients with COVID-19 were significantly reduced in patients with severe COVID-19 diseases.[29] Lymphocytes count was recorded in severe cases was recorded (0.63%). This agrees with a current study recorded 15 (21.1%) with *p-value* (0.001) more significant as in Table 5 and Figure 2. In Table 6 and Figure 3 was LDH level, which is an enzyme responsible for energy production was measure in blood as a monitor tissue damage associated with a wide range of disorder as a liver disorder, intestinal, lung diseases increase of LDH refer to lung destruction or damage such as bacterial pneumonia infection induce by COVID-19, therefore, it used as a biomarker to viral infection or ling damage, this agreement with accurate data was recorded 19 (26.8%).[30]

C-reactive protein levels are associated with inflammation and related to age, sex, and physical condition. CRP activated a complement and phagocytosis for killing any microorganisms

Table 3: Platelets count of serum in infected and non-infected patients

Platelets count (Plts)	*Non infected patients No. (%)*	*Infected patients No. %*	*p-value*
Group A (1–99)	(3.7) 2	2 (2.8)	
Group B (100–199)	(16.7) 9	5 (.7)	
Group C (200–299)	37 (68.5)	14 (9.7)	
Group D (300–399)	5 (9.3)	37 (52.1)	0.00*
Group E (400–499)	0	10 (14.1)	
Group F (500–599)	1.9 (1)	3 (4.2)	
Total	54 (100)	71 (100)	

*p<0.05

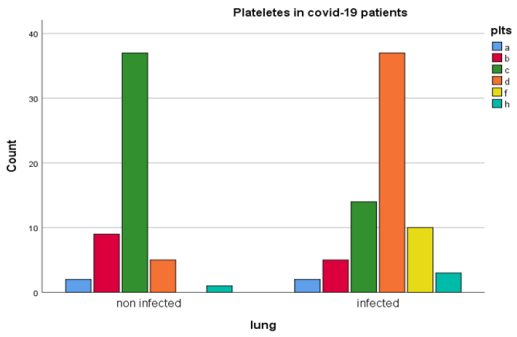

Figure 1: Platelets count in COVID-19 patients

Table 4: Ferritin in serum of infected and non-infected patients

Ferritin count	*Non-infected patients No. (%)*	*Infected patients No. %*	*p-value*
Group A (10-199)	24(44.4)	18 (25.4)	
Group B (200-399)	15 (27.8)	41 (57.7)	
Group C (400-599)	8 (14.8)	9 (12.7)	0.014*
Group D (600-699)	4 (7.4)	2 (2.8)	
Group E (800-999)	3 (5.6)	1 (1.4)	
Total	54 (100)	71 (100)	

*p<0.05

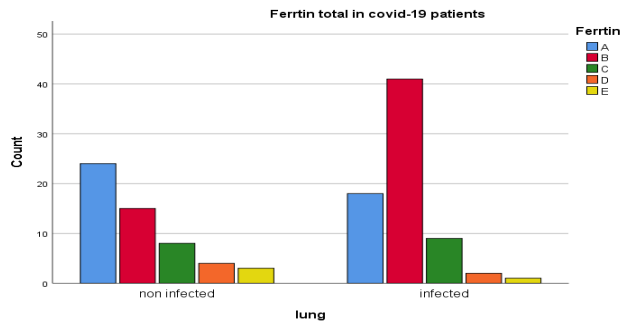

Figure 2: Ferritin level in COVID-19 patients

Table 5: Lymphocytes cells count of serum in infected and non-infected patients

Lymphocytes count (Lymph)	*Non infected patients No. %*	*Infected patients No. %*	*p-value*
Group A (1 - 9)	13 (24.1)	36 (50.7)	
Group B (10-19)	22 (40.7)	15 (21.1)	
Group C (20-29)	7 (13)	10 (14.1)	0.001*
Group D (30-39)	4 (7.3)	9 (12.7)	
Group G (40-49)	8 (14.8)	1 (1.4)	
Total	54 (100)	71 (100)	

*p <0.05

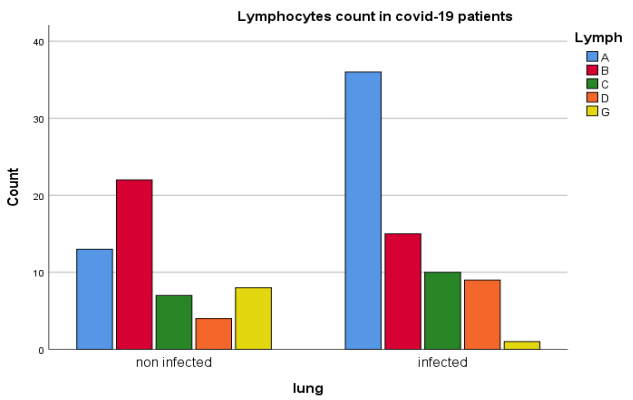

Figure 3: Lymphocytes count in serum COVID-19 patients

Table 6: Lactate dehydrogenase of serum of infected and non-infected patients

Lactate dehydrogenase (LDH)	*Non infected patients No. (%)*	*Infected patients No. (%)*	*p-value*
Group A (1-199)	18 (33.3)	19 (26.8)	
Group B (200-299)	17 (31.5)	22 (31)	
Group C (300-399)	7 (13)	13 (18.3)	
Group D (400-499)	6 (11.1)	5 (7)	
Group E (500-599)	4 (7.4)	4 (5.6)	0.000*
Group F (600-699)	0	4 (5.6)	
Group G (700-799)	0	2 (2.8)	
Group H (800-899)	2 (3.7)	2 (2.8)	
Total	54 (100)%	71 (100)%	

*p<0.05

as corona-virus. CRP level was diagnosis in the early stage of bacterial pneumonia in COVID-19 patients and increases with the severity of COVID-19 diseases. A current study was documented 12(16.9%) with no significance p-value (0.32) as in Table (3–10) and Figures 3–10.[31]

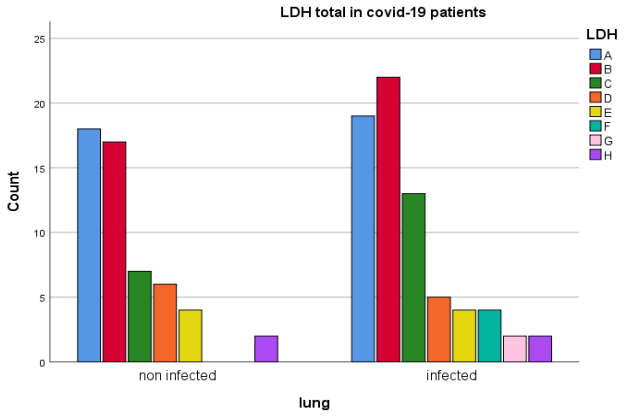

Figure 4: Lactate dehydrogenase (LDH) in COVID-19 patients

Table 7: C-reactive protein(CRP) level in infected and non-infected patients

C-reactive protein (CRP)	*Non-infected patients No. (%)*	*Infected patients No. (%)*	*p-value*
Group A (1 - 9)	18 (33.3)	12 (16.9)	
Group B (10-19)	8 (14.8)	12 (16.9)	
Group C (20-29)	1 (1.9)	1 (1.4)	
Group D (30-39)	5 (9.3)	17 (23.9)	
Group E (40-49)	7 (13)	7 (9.9)	
Group F (50-59)	16.7(9)	10 (4.2)	0.025*
Group K (60-69)	5(9.3)	8 (11.3)	
Group G (70-79)	1 (1.9)	4 (5.6)	
Total	54 (100)	71 (100)	
Total	54 (100)	71 (100)	
Group G (40-49)	8 (14.8)	1 (1.4)	
Total	54 (100)	71 (100)	

*p<0.05

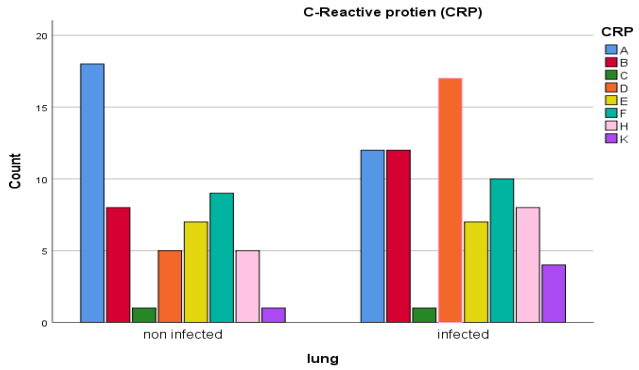

Figure 5: C-reactive protein level in covid-19 patients

Bacterial Secondary Infection, Co-infection and Opportunistic Fungi

This accurate study was focused on co-infection and secondary infection associated with COVID-19 patients. Bacterial and fungal is little recorded in (15%) of hospitalized patients.[32] This finding reported high rate of secondary bacterial infection was *S. aureus* 120/15(20.83%) and lower rate with *Pneumocystis jiroveci* as in Table 8. Co-infection was recored *pseudomonas aeruginosa* a high rate 10 (23.25) as in Table 9, these agree with Clark *et al.,* 2021 recorded a high rate of secondary bacterial infection as 919/1082(84.9%) and in co-infection, *S. aureus* 21(17.8%) as a high rate.[33] Langfod and Colleagues were documented a secondary bacterial infection in COVID-19 patient was recorded and co-infection a (4.9%),[34] therefore, this

Table 8: Secondary respiratory infection isolates from samples of covid-19 patients

Bacterial secondary infection isolates	Number of isolated	%
Streptococcus pneumonia	*10*	*13.88*
Staphylococcus aureus	15	20.83
Heamophilus influenza	5	6.94
Pseudomonas aeruginosa	10	13.88
Enterobacter cloacae	10	13.88
Streptococcus oralis	6	8.33
Acinetobacter spp	8	11.11
Klebsiella spp	8	11.11
Serratia spp	2	2.77
Total	72	100
Fungal secondary infection isolates		
Aspergillus fumigatus	8	44.44
Candida albicans	7	38.88
Penicillium notutum	2	11.11
Pneumocystis jiroveci	1	5.55
Total	18	100

*p<0.05

Table 9: Co-infection with bacterial and opportunistic fungi

Co-infection isolates	*Number of isolated*	*%*
Streptococcus pneumonia	5	12.19
Staphylococcus aureus	7	16.27
Pseudomonas aeruginosa	10	23.25
Acinetobacter spp	4	9.30
Klebsiella spp	4	9.30
Serratia spp	1	2.35
Aspergillus spp	1	2.35
Candida albicans	4	9.30
Penicillium notatum	2	4.65
Monilia	3	11.62
Total	41	100

finding agrees with this results of C-reactive protein and x-ray show infiltration or bacterial infection in COVID-19 patients.[35] Some cause lead to infected covid-19 patients with secondary infection and co-infection as stay along time in hospital, low immunity due to steroid drugs, antibiotics bacterial resistant, autoimmune diseases as diabetics and contamination. Data regarding secondary respiratory infection by bacteria and fungi infection associated with covid-19 (4) who selected 41 and 191 COVID-19 patients in china Wuhan city and observed the 10% and 15% of covid-19 patients with a secondary bacterial infection.[36,37] Zhou *et al*., 2020 reported that about 50% of patients COVID-19 pandemic who died had secondary bacterial infections, while another study recorded the presence of bacterial and fungal infection.[37] Secondary pathogen isolation increases the risk of death in patients with cardiovascular disease, diabetes, obesity, and invasive mechanical ventilation.[38]

CONCLUSIONS

The present study concluded that males more infected with Covid-19 diseases than females were 71 (56.3%). Age was more important parameters associated with COVID-19 group range from 40–49 year was recorded 42 (33.3)%. Study some parameters which was detected a coronavirus as biochemical and hematology parameters. Patients with autoimmune diseases, which more affected with COVID-19. This is study a first study in Misan governorate.

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