Tikrit Journal of Pure Science
ISSN: 1813 – 1662 (Print) --- E-ISSN: 2415 – 1726 (Online)
Journal Homepage: http://tjps.tu.edu.iq/index.php/j

The Role of IL-6 and IL-17 in SARS CoV-2 Patients with Secondary Bacterial Pneumonia

May Raheem Ali [1], Suha Maher Abed [2], Mohanad Hasan Mahmood AL-Izzi [2]
1 Kirkuk Health Directorate, Ministry of Health, Kirkuk, Iraq
2 Biology department, Science College, Tikrit University, Tikrit, Iraq

https://doi.org/10.25130/tjps.v28i1.1260

ARTICLE INFO.

Article history:
-Received: 1 / 10 / 2022
-Accepted: 30 / 10 / 2022
-Available online: 20 / 2 / 2023

Keywords: SARS CoV-2, Secondary bacterial pneumonia, IL-6, IL-17, Mixed bacterial infection.

Corresponding Author:
Name: May Raheem Ali
E-mail: may.r.ali4449@st.tu.edu.iq
Tel:

ABSTRACT

The current study was conducted in Kirkuk city at Al-Shifaa 14 hospital from November 2021 to March 2022, indicated the bacteria causing secondary pneumonia isolated from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) patients and the role of IL-6 and IL-17 in these infection.

Sputum samples were used to obtain the bacterial isolates, and API testing was used to confirm the species level identification. Using an enzyme-linked immunosorbent assay (sandwich ELISA), the levels of IL-6 and IL-17 in the blood were evaluated. The study documented several bacterial species in a single infection (56/87.5%) or mixed bacterial infection (8/12.5%). The most common isolated bacteria species was *Klebsiella pneumoniae* (35.95%) followed by *Staphylococcus aureus* (31.25%), *E. coli* (17.19%), *Pseudomonas aeruginosa* (10.94%), and (1.56%) for each of *Klebsiella oxytoca*, *Acinetobacter baumannii* and *Cronobacter sakazakii*. The study recorded a high significant difference ($P < 0.01$) between the patients (22.2±6.82) pg/mL and the control group (58.39±11.15) pg/ mL concerning IL-6 also a high significant difference ($P < 0.01$) between the patients (101.79±27.13) pg/mL and the control group (58.39±11.15) pg/mL concerning IL-17.

In conclusion, *K. pneumoniae* and *S. aureus* were the predominant isolated bacteria from COVID-19 patient's lung and there was a highly significant increase in IL-6 and IL-17 levels in secondary bacterial pneumonia in COVID-19 patients.

Introduction

The SARS-CoV-2 that causes COVID-19 disease was first detected in December 2019 in Wuhan, China, which has actively spreading throughout the world [1]. Viral respiratory infections lead to clinical deterioration, and a common side effect of secondary bacterial infection, Secondary bacterial infection was a major contributor to morbidity and mortality in earlier, researched influenza pandemics, as well as in seasonal influenza and other respiratory illnesses. [2,3]. Additionally, it is becoming obvious the secondary bacterial infections frequently develop in COVID-19 patients and may be related to worse outcomes [4].

Although the specific nature and source of these infections are still unclear, some evidence suggests that multidrug resistance bacteria are among the microorganisms believed to be responsible for the prevalence of these infections [5,6]. The bacteria *K. pneumoniae*, *S. aureus*, *A. baumannii*, *P. aeruginosa*, and *E. coli* are the most predominant bacterial species that cause secondary bacterial pneumonia related with COVID-19, which eventually results in death despite receiving prophylactic antimicrobial treatment [7,8]. In COVID-19 patients, the development of secondary bacterial infection is enhanced by several risk factors,

including disease severity, recent disease and treatment [9].

In severe COVID-19 infections, SARS-CoV-2 causes an excessive immune response termed a cytokine storm [4]. A cytokine storm is an immunological condition that has the potential to be devastating and is distinguished by the excessive production of inflammatory cytokines and chemical mediators such as IL-6, IL-7, IL10, 1L17, TNF, INF, CCL2, CCL3, and CXCL10, as well as a high level of immune cell stimulation [10,11].

The study aims to isolate and identify the bacteria causing secondary pneumonia in SARS CoV-2 patients and determine the role of IL-6 and IL-17 in these infections.

Materials and methods

Sample Collection: A total of 186 sputum samples and 60 peripheral blood samples (from positive bacterial infection) were collected from COVID-19 patients attending Al-Shifaa 14 hospital at Kirkuk city during the period from November 2021 to March 2022.

Isolation and Identification: Isolation and identification of bacterial species were performed using sputum samples that were cultured on blood agar, MacConkey agar and chocolate agar. The isolated bacteria were identified on the basis of macroscopic appearance (colour, conistency, texture and shape of colony) microscopic (Gram stain, bacterial morphology) and biochemical tests (catalase, oxidase, urease, IMVIC and KIA) [12] Identification was confirmed at the species level using API test. IL-6 and IL-17 levels were evaluated by using ELISA technique (sandwich ELISA).

Statistical analysis

The data were analyzed statistically by using the test analysis (T. test) at P. value (0.01) and compared averages means using (Duncan Multiple Range) by applying statistical programs SPSS (version 28) and Microsoft Office Excel 2010 [13].

Results

Bacterial isolation and identification

The present study recorded (60/32%) of cases were confirmed to have bacteria as a secondary infection to COVID-19. Also determined various bacterial species in a single infection (56/87.5%) or in a mixed bacterial infection (8/12.5%). as shown in Table (1).

Table 1: Bacterial species isolated from patients with SARS CoV-2 infection

Isolated bacteria	Gram stain	Single 56 (87.5%)		Mixed 8 (12.5%)		TOTAL 60 (32%)	
		No.	%	No.	%	No.	%
K. pneumoniae	Gram-negative	21	32.82	2	3.13	23	35.95
K. oxytoca		1	1.56	0	0	1	1.56
E. coli		9	14. 06	2	3.13	11	17.19
P. aeruginosa		6	9.38	1	1.56	7	10.94
C. sakazakii		1	1.56	0	0	1	1.56
A. baumannii		1	1.56	0	0	1	1.56
S. aureus	Gram-positive	17	26.56	3	4.69	20	31.25

IL-6 level in SARS CoV-2 patients with secondary bacterial pneumonia and control group

The study reported a highly significant increase in IL-6 levels in SARS CoV-2 patients with secondary bacterial infection (22.2±6.82 pg/mL) compared to the control group (13.47±1.85 pg/mL) at (P <0.01). Table (2).

Table 2: IL-6 level in SARS CoV-2 patients with secondary bacterial pneumonia and control group

Patients		Control
No.	60	30
IL-6 (pg/mL)	22.2±6.82	13.47±1.85
P. value: 0.001		**T test:** 6.84

IL-17 level in SARS CoV-2 patients with secondary bacterial pneumonia and control group.

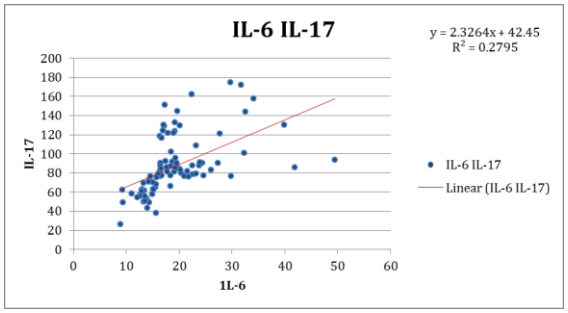
The present study determined that the highest mean level of IL-17 in SARS COV-2 patients with secondary bacterial pneumonia was (101.79±27.13 pg/mL) compared with the control group (58.39±11.15 pg/mL) at (P <0.01). As shown in Table (3).

Table 3: IL-17 level in SARS CoV-2 patients with secondary bacterial pneumonia and control group

Patients		Control
No.	60	30
IL-17 (pg/mL)	101.79±27.13	58.39±11.15
P. value: 0.0001		**T test:** 8.39

Correlation between IL-6 and IL-17 in SARS CoV-2 patients with secondary bacterial pneumonia and control group

A significant correlation between IL-6 and IL-17 levels was found by this study, which means that IL-6 levels increase with IL-17 elevation. Figure (1).



r: 0.52 **P. value:** 0.0001

Fig. 1: Correlation between IL-6 and IL-17.

Discussion

The present study determined various bacterial species in a single infection (87.5%) or in a mixed infection (12.5%). The current study agreed with several studies, in a European multicenter study conducted by Rouzé *et al*. [8] it was identified that 83.6% of isolates were Gram-negative bacteria where *P. aeruginosa* was constituted of 22.3%, *Klebsiella* spp. were constituted of 11.5%, followed by *E. coli* 8.4% and *A. baumannii* 7.3%. *S. maltophilia* was accounted for 3.5% and 1% of detected bacteria was for *H. influenzae* and *M. morganii*. It was also revealed that *S. aureus* was isolated in 12.2% of bacterial pneumonia cases, *Enterobacter* spp were accounted for 18.8%, *S. pneumoniae* was detected in 2.8% of cases and 9.8% of cases had mixed growth. [14] demonstrated that *S. aureus* was the most common bacteria involved in secondary bacterial pneumonia (26.2%), followed by *P. aeruginosa* (16.9), *K. pneumoniae* (13.8%) and *E. coli* (12.3%). While *E. cloacae* and *K. aerogenes* were only 7.7% and 3.1% for *E. faecalis* and *H. influenzae*. In other study, *K. pneumoniae* was the most prevalent bacterial species responsible for secondary bacterial pneumonia (73%), followed by *A. baumannii* 57%, *P. aeruginosa* that accounted for only 1.7% of cases, while 24.6% of cases were had mixed bacterial infection [15]

In a study conducted at Kirkuk city in 2021 on COVID-19 patients by Ameen *et al.* [16], reported that the pure single bacterial isolates were 75.55% while mixed isolates accounted for 12.5%. Moreover, they showed that the most common causative agents of secondary bacterial pneumonia in COVID-19 patients were *S. aureus* (31.11%), *S. pneumoniae* (8.8%), *S. pyogenes* (7.4%), *K. pneumoniae* (27.40%), *P. aeruginosa* (11.85%), *H. influenzae* (11.1%), and *K. oxytoca* (2.22%).

With consideration to mixed bacterial infections, Cillóniz *et al*. [17] illustrated that polymicrobial infections are common among patients with pneumonia admitted to the ICU and may lead to inappropriate empiric antimicrobial therapy. Additionally, ARDS and chronic lung illness were predictive factors of polymicrobial pneumonia. They also reported that polymicrobial pneumonia occurs less frequently in general among hospitalized individuals with pneumonia. One common limitation of such research on microbial infections is that not all microbiological tests are performed systematically on all patients, due to this issue, it is possible that a complete microbiological investigation would reveal a greater actual prevalence of polymicrobial etiologies [17].

The study reported a highly significant increase in IL-6 levels in SARS CoV-2 patients with secondary bacterial infection (22.2 pg/mL) compared to the control group (13.47 pg/mL). The result of this study correspond with Qu *et al*. [18] and Gayam *et al*. [19]. They demonstrated that IL-6 is significantly elevated in patients who experienced secondary bacterial infection associated with SARS CoV-2**.** SARS CoV-2-induced disease is characterized by the excessive production of pro-inflammatory cytokines and the suppression of antiviral innate immune responses [20]. Santa Cruz *et al*. [21] mentioned that due to its strong association with disease severity, likelihood of requiring mechanical ventilation or mortality, and most significantly, the fact that it is a pharmaceutical target, IL-6 plays a special role in the cytokine storm that COVID-19 patients experience. Herold *et al*. [22] proposed that even slightly raised IL-6 levels above 80 pg/mL were adequate to recognize COVID-19 patients who were at a significant risk for respiratory failure. Holub *et al*. [23] and Abed *et al*. [24] revealed that compared to viral infection, the levels of TNF-α, PCT and IL-6 were considerably greater in bacterial infection. The same study showed that high IL 6 and TNF-α levels returned to baseline within three days of initiating antibiotic therapy in the control group, which contained healthy individuals. Moreover, Tocilizumab (IL-6 receptor antagonist) therapy can improve the outcomes in patients hospitalized with serious COVID-19 infection, according to the Randomized Evaluation of COVID-19 Therapy (RECOVERY trial) [25].

It is possible that the viral infection activated the humoral immune response, causing enhanced release of pro-inflammatory cytokines, which would account for the raised IL-6 level in SARS-CoV-2 infection [26]. The virus causes an acute excessive immune response with an abrupt elevation in pro-inflammatory cytokines, which is termed "cytokine storm" [27]. These cytokines may be lead to tissue damage in multiple organs in COVID-19 patients [28]. By generating cytolytic dysfunction, IL-6 may induce cytokine release syndrome. High levels of IL-6 have been found to reduce the cytotoxicity of natural killer (NK) cells, resulting in the inability of T lymphocytes or cytotoxic NK cells to kill target cells, increasing target cell life time and enhancing antigen stimulation. Overall, it leads to the overproduction of proinflammatory cytokines [29,30]. Karwaciak *et al*. [31] suggested that the nucleocapsid and spikes of SARS-CoV-2 can alone stimulate the generation of IL-6 by macrophage and monocytes, and this elevation of IL-6 may be the initial cause of impaired immune response in certain COVID-19 patients.

The present study determined that the highest mean level of IL-17 in SARS COV-2 patients with secondary bacterial pneumonia was (101.79 $\pm$ 27.13 pg/mL) compared with the control group (58.39 $\pm$ 11.15 pg/mL). The researchers [32,33] have demonstrated that COVID-19 patients have higher inflammatory responses due to IL-17 overproduction. Previous research [34] has found that Th17 cells are upregulated in COVID-19 patients. IL-17 promotes neutrophil infiltration into the lungs, which contributes to the pathogenesis of acute respiratory distress syndrome (ARDS) [35]. The severity of ARDS in respiratory syncytial virus illness and Middle East Respiratory Syndrome-

related coronavirus is positively associated with increasing IL-17A activity and elevation of Th17 cells [36,37]. Likewise, Th17-cell over-activation and enhanced cytotoxic effects of CD8+ T cells are at least partially accountable for intense immune impairment in COVID-19 patients [34]. According to De Biasi *et al*. [38], COVID-19 pneumonia patients showed exhausted T-cell profiles and elevated Th17 responses. In viral ARDS, IL-17A is related to pulmonary inflammation and poor recovery rates [39]. Since IL-17A signaling enhances pathological inflammation by inducing pro-inflammatory cytokines including IL-6 and IL-1, it is regarded as a potential target for adjunctive ARDS treatment in COVID-19 patients [35]. IL-17 and acute lung damage in COVID-19 patients are recognized to be related, although the underlying functional processes are not well characterized. There is significant evidence that IL-17 interacts with the SARS-CoV-2 entrance receptor ACE2 [40]

In addition to a pro-inflammatory immune reaction, murine models have shown a connection between lung humans ACE2 expression and COVID-19 progression [41]. Recombinant ACE2 has been found to suppress IL-17A-mediated STAT3 stimulation and reduce lung neutrophil infiltration in a mouse model of severe bacterial pneumonia. This indicates that ACE2 has a protective effect in bacterial lung infections [42]. Despite the complexity of the association between the severity of COVID-19 and the expression of ACE2, the ACE2 is a crucial regulator of IL-17A generation [43,44] Increased levels of alveolar neutrophils and organ failure may result from IL-17A-mediated lung inflammation in COVID-19 patients [31]. It's fascinating to observe that a particular micro-RNA, MIR-155, is primarily activated by influenza infection, decreasing the expression of IL-17 and IL-23, which reduces bacterial clearance and elevates the severity of bacterial pneumonia [45].

References

[1] Wang, C., Horby, P. W., Hayden, F. G., and Gao, G. F. (2020). A novel coronavirus outbreak of global health concern. The lancet, 395(10223), 470-473.

[2] Morens, D. M., Taubenberger, J. K., & Fauci, A. S. (2008). Predominant role of bacterial pneumonia as a cause of death in pandemic influenza: implications for pandemic influenza preparedness. The Journal of infectious diseases, 198(7), 962-970.

[3] Morris, D. E., Cleary, D. W., & Clarke, S. C. (2017). Secondary bacterial infections associated with influenza pandemics. Frontiers in microbiology, 8, 1041.

[4] Feng, Y., Ling, Y., Bai, T., Xie, Y., Huang, J., Li, J., ... & Qu, J. (2020). COVID-19 with different severities: a multicenter study of clinical features. American journal of respiratory and critical care medicine, 201(11), 1380-1388.

[5] Bengoechea, J. A., & Bamford, C. G. (2020). SARS- CoV- 2, bacterial co- infections, and AMR: the deadly trio in COVID- 19?. EMBO molecular medicine, 12(7), e12560.

[6] Rawson, T. M., Moore, L. S., Zhu, N., Ranganathan, N., Skolimowska, K., Gilchrist, M., ... & Holmes, A. (2020). Bacterial and fungal coinfection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. Clinical infectious diseases, 71(9), 2459-2468.

[7] Du, R. H., Liang, L. R., Yang, C. Q., Wang, W., Cao, T. Z., Li, M., … & Shi, H. Z. (2020). Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. European Respiratory Journal, 55(5).

[8] Rouzé, A., Martin-Loeches, I., Povoa, P., Makris, D., Artigas, A., Bouchereau, M., … & Nseir, S. (2021). Relationship between SARS-CoV-2 infection and the incidence of ventilator-associated lower respiratory tract infections: a European multicenter cohort study. Intensive care medicine, 47(2), 188-198.

[9] De Bruyn, A., Verellen, S., Bruckers, L., Geebelen, L., Callebaut, I., De Pauw, I., Stessel, B., & Dubois, J. (2022). Secondary infection in COVID-19 critically ill patients: a retrospective single-center evaluation. BioMed Central infectious diseases, 22(1), 1-7.

[10] Teijaro, J. R., Walsh, K. B., Rice, S., Rosen, H., & Oldstone, M. B. (2014). Mapping the innate signaling cascade essential for cytokine storm during influenza virus infection. Proceedings of the National Academy of Sciences, 111(10), 3799-3804.

[11] Merad, M., & Martin, J. C. (2020). Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages. Nature Reviews Immunology, 20(6), 355–362.

[12] Conti, P., D'Ovidio, C., Conti, C., Gallenga, C. E., Lauritano, D., Caraffa, A., Kritas, S. K., & Ronconi, G. (2019). Progression in migraine: role of mast cells and pro-inflammatory and anti-inflammatory cytokines. European journal of pharmacology, 844, 87-94.

[13] Al-Rawi Kh. M., Entrance to Statistics, 2ed ed., 2000, Babylon, Iraq.

[14] d'Humières, C., Patrier, J., Lortat-Jacob, B., Tran-Dinh, A., Chemali, L., Maataoui, N., Rondinaud, E., Ruppé, E., Burdet, C., Ruckly, S., Montravers, P., Timsit, J. F., & Armand-Lefevre, L. (2021). Two original observations concerning bacterial infections in COVID-19 patients hospitalized in intensive care units during the first wave of the epidemic in France. Public library of sience one, 16(4), e0250728.

[15] Pourajam, S., Kalantari, E., Talebzadeh, H., Mellali, H., Sami, R., Soltaninejad, F., ... & Solgi, H. (2022). Secondary Bacterial Infection and Clinical Characteristics in Patients With COVID-19 Admitted

to Two Intensive Care Units of an Academic Hospital in Iran during the First Wave of the Pandemic. Frontiers in cellular and infection microbiology, 141.
[16] Ameen, H. M., Mahdi, N. B., & Eldin, A. M. K. (2021). 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. NVEO-NATURAL VOLATILES & ESSENTIAL OILS Journal| NVEO, 9153-9161.
[17] Cillóniz, C., Ewig, S., Ferrer, M., Polverino, E., Gabarrús, A., Puig de la Bellacasa, J., ... & Torres, A. (2011). Community-acquired polymicrobial pneumonia in the intensive care unit: aetiology and prognosis. Critical care, 15(5), 1-10.
[18] Qu, J., Cai, Z., Liu, Y., Duan, X., Han, S., Liu, J., ... & Yang, L. (2021). Persistent bacterial coinfection of a COVID-19 patient caused by a genetically adapted *Pseudomonas aeruginosa* chronic colonizer. Frontiers in cellular and infection microbiology, 129.
[19] Gayam, V., Konala, V. M., Naramala, S., Garlapati, P. R., Merghani, M. A., Regmi, N., ... & Adapa, S. (2020). Presenting characteristics, comorbidities, and outcomes of patients coinfected with COVID- 19 and *Mycoplasma pneumoniae* in the USA. Journal of medical virology, 92(10), 2181-2187.
[20] Blanco-Melo, D., Nilsson-Payant, B. E., Liu, W. C., Uhl, S., Hoagland, D., Møller, R., … & Albrecht, R. A. (2020). Imbalanced host response to SARS-CoV-2 drives development of COVID-19. Cell, 181(5), 1036-1045
[21] Santa Cruz, A., Mendes-Frias, A., Oliveira, A. I., Dias, L., Matos, A. R., & Carvalho, A. (2021). Interleukin-6 is a biomarker for the development of fatal severe acute respiratory syndrome coronavirus 2 pneumonia. Frontiers in Immunology. 2021; 12: 613422.
[22] Herold, T., Jurinovic, V., Arnreich, C., Hellmuth, J. C., von Bergwelt-Baildon, M., Klein, M., & Weinberger, T. (2020). Level of IL-6 predicts respiratory failure in hospitalized symptomatic COVID-19 patients. MedRxiv.
[23] Holub, M., Lawrence, D. A., Andersen, N., Davidová, A., Beran, O., Marešová, V., & Chalupa, P. (2013). Cytokines and chemokines as biomarkers of community-acquired bacterial infection. Mediators of inflammation, 2013.
[24] Abed, S. M., Al Boraqy, M. M., & Fatlawi, S. N. A. (2018). Role of Procalcitonin in Detection of Bacterial Pneumonia. EXECUTIVE EDITOR, 9(12), 12638.
[25] Recovery Collaborative Group. (2021). Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. The Lancet, 397(10285): 1637-1645.
[26] Yang, L., Liu, S., Liu, J., Zhang, Z., Wan, X., Huang, B., Chen, Y., & Zhang, Y. (2020). COVID-19: immunopathogenesis and Immunotherapeutics. Signal transduction and targeted therapy, 5(1), 1-8.
[27] Ragab, D., Salah Eldin, H., Taeimah, M., Khattab, R., & Salem, R. (2020). The COVID-19 cytokine storm; what we know so far. Frontiers in immunology, 1446.
[28] Shin, Y. H., Shin, J. I., Moon, S. Y., Jin, H. Y., Kim, S. Y., Yang, J. M., … & Yon, D. K. (2021). Autoimmune inflammatory rheumatic diseases and COVID-19 outcomes in South Korea: a nationwide cohort study. The Lancet Rheumatology, 3(10), e698-e706.
[29] Liu, X., Wang, H., Shi, S., & Xiao, J. (2021). Association between IL-6 and severe disease and mortality in COVID-19 disease: a systematic review and meta-analysis. Postgraduate Medical Journal.
[30] Abbas, H. A.; Abed, S.M.; Iqbal, M. N. (2022) Levels of IL-37 and IgA among pneumonia patients. Biochem. Cell. Arch. 22, 319-324.
[31] Karwaciak, I., Sałkowska, A., Karaś, K., Dastych, J., & Ratajewski, M. (2021). Nucleocapsid and spike proteins of the coronavirus SARS-CoV-2 induce il6 in monocytes and macrophages-Potential implications for cytokine storm syndrome. Vaccines, 9(1), 54.
[32] Orlov, M., Wander, P. L., Morrell, E. D., Mikacenic, C., & Wurfel, M. M. (2020). A case for targeting Th17 cells and IL-17A in SARS-CoV-2 infections. The Journal of Immunology, 205(4), 892-898.
[33] Kang, Y. W., Lee, S. C., Jeon, S. M., & Jo, E. K. (2021). Roles of Interleukin-17 and Th17 Responses in COVID-19. Journal of Bacteriology and Virology, 51(3), 89-102.
[34] Xu, Z., Shi, L., Wang, Y., Zhang, J., Huang, L., Zhang, C., … & Wang, F. S. (2020). Pathological findings of COVID-19 associated with acute respiratory distress syndrome. The Lancet respiratory medicine, 8(4), 420-422.
[35] Salinas, T. R. W., Zheng, B., Routy, J. P., & Ancuta, P. (2020). Targeting the interleukin- 17 pathway to prevent acute respiratory distress syndrome associated with SARS- CoV- 2 infection. Respirology (Carlton, Vic.).
[36] Mangodt, T. C., Van Herck, M. A., Nullens, S., Ramet, J., De Dooy, J. J., Jorens, P. G., & De Winter, B. Y. (2015). The role of Th17 and Treg responses in the pathogenesis of RSV infection. Pediatric Research, 78(5), 483-491.
[37] Mahallawi, W. H., Khabour, O. F., Zhang, Q., Makhdoum, H. M., & Suliman, B. A. (2018). MERS-CoV infection in humans is associated with a pro-inflammatory Th1 and Th17 cytokine profile. Cytokine, 104, 8-13.
[38] De Biasi, S., Meschiari, M., Gibellini, L., Bellinazzi, C., Borella, R., Fidanza, L., … & Cossarizza, A. (2020). Marked T cell activation, senescence, exhaustion and skewing towards TH17 in patients with COVID-19 pneumonia. Nature communications, 11(1), 1-17.

[39] Mikacenic, C., Hansen, E. E., Radella, F., Gharib, S. A., Stapleton, R. D., & Wurfel, M. M. (2016). IL-17A is associated with alveolar inflammation and poor outcomes in acute respiratory distress syndrome. Critical care medicine, 44(3), 496.
[40] Gonzalez, S. M., Siddik, A. B., & Su, R. C. (2021). Regulated Intramembrane proteolysis of ACE2: a potential mechanism contributing to COVID-19 pathogenesis?. Frontiers in Immunology, 12, 612807.
[41] Han, K., Blair, R. V., Iwanaga, N., Liu, F., Russell-Lodrigue, K. E., Qin, Z., … & Qin, X. (2021). Lung expression of human angiotensin-converting enzyme 2 sensitizes the mouse to SARS-CoV-2 infection. American journal of respiratory cell and molecular biology, 64(1), 79-88.
[42] Sodhi, C. P., Nguyen, J., Yamaguchi, Y., Werts, A. D., Lu, P., Ladd, M. R., … & Jia, H. (2019). A dynamic variation of pulmonary ACE2 is required to modulate neutrophilic inflammation in response to Pseudomonas aeruginosa lung infection in mice. The Journal of Immunology, 203(11), 3000-3012.
[43] Bourgonje, A. R., Abdulle, A. E., Timens, W., Hillebrands, J. L., Navis, G. J., Gordijn, S. J., … & van Goor, H. (2020). Angiotensin- converting enzyme 2 (ACE2), SARS- CoV- 2 and the pathophysiology of coronavirus disease 2019 (COVID- 19). The Journal of pathology, 251(3), 228-248
[44] Song, J., Zeng, M., Wang, H., Qin, C., Hou, H. Y., Sun, Z. Y., … & Liu, Z. (2021). Distinct effects of asthma and COPD comorbidity on disease expression and outcome in patients with COVID- 19. Allergy, 76(2), 483-496.
[45] Gurczynski, S. J., & Moore, B. B. (2018). IL-17 in the lung: the good, the bad, and the ugly. American Journal of Physiology-Lung Cellular and Molecular Physiology, 314(1), L6-L16.

دور IL-6 و IL-17 في مرضى SARS CoV-2 المصابين بالتهاب رئوي بكتيري ثانوي

مي رحيم علي[1]، سهى ماهر عبد[2]، مهند حسن محمود العزي[2]

[1] *صحة كركوك ، وزارة الصحة ، كركوك ، العراق*

[2] *قسم علوم الحياة ، كلية العلوم ، جامعة تكريت ، تكريت ، العراق*

الملخص

أنجزت الدراسة في مدينة كركوك في مستشفى الشفاء 14 خلال الفترة من تشرين الثاني 2021 إلى آذار 2022. تضمنت الدراسة البكتيريا المسببة للالتهاب الرئوي الثانوي المعزولة من مرضى فيروس كورونا 2 (SARS-CoV-2) و دور IL-6 و IL-17 في هذه العدوى.

تم عزل وتحديد الأنواع البكتيرية بأستخدام عينات القشع. تمت عملية تشخيص العزلات البكتيرية بأستخدام نظام API. تم قياس مستويات الانترليوكينات IL-6 و IL-17 في الدم باستخدام تقنية الاليزا (sandwich ELISA). سجلت الدراسة اصابات بكتيرية مفرده (56) بنسبة (87.5٪) بينما كانت الإصابة المختلطه بأكثر من نوع بكتيري (8) بنسبة (12.5٪). كما كانت *Klebsiella pneumoniae* من اكثر البكتريا المعزوله شيوعا بنسبة (35.95٪) تبعتها بكتريا *Staphylococcus aureus* بنسبة (31.25)، *E. coli* (17.19)، *Pseudomonas aeruginosa* (10.94)، ونسبة (1.56) لكل من*Klebsiella oxytoca*، *Acinetobacter baumannii* و *Cronobacter sakazakii*.

سجلت الدراسة فرقاً معنوياً عالياً ($P<0.01$) بين المرضى (**6.82**±22.2)pg/mL ومجموعة السيطرة (11.15±58.39)pg/mL فيما يتعلق بـ IL-6 وكذالك سجلت الدراسة فرقاً معنوياً عالياً ($P<0.01$) بين المرضى (27.13±101.79)pg/mL ومجموعة السيطرة (11.15±58.39)pg/mL فيما يتعلق بـ IL-17 .

استنتجت الدراسة ان بكتيريا *Klebsiella pneumoniae* و *Staphylococcus aureus* هي البكتيريا السائدة المعزولة من رئة مرضى COVID-19 وكانت هناك زيادة كبيرة في مستويات IL-6 و IL-17 في الالتهاب الرئوي البكتيري الثانوي في مرضى COVID-19.