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Original Article

Evaluation of Serum Interleukin-6 Level among Moderate, Severe and Critical COVID-19 Patients Admitted in a Tertiary Care Hospital

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Abstract

Background: Coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome corona virus -2 (SARS-CoV-2). In COVID-19 patients an exaggerated and excessive release of proinflammatory cytokines (IL-6) occurs and may cause several severe manifestations. High interleukin-6 levels in COVID-19 patients suggest cytokine storm and are considered as a relevant parameter in predicting most severe cases of disease. Objectives: The study is aimed to assess IL-6 levels among hospital admitted COVID-19 patients and evaluate their relationship with disease severity. **Materials and Methods:** Total 136 Rapid antigen test positive or RT-PCR positive COVID-19 patients from Department of Medicine of Sylhet MAG Osmani Medical College and Shahid Shamsuddin Ahmed Hospital, Sylhet from January 2021 to December, 2021 were enrolled in this study by convenient sampling technique. With all aseptic precautions 4ml of venous blood was collected from ante-cubital vein and the serum was separated by centrifuge process at 4000 rpm for 10 minutes and stored in the laboratory at -20°C. Serum IL-6 was assayed by solid-phase chemiluminescent immunoassay. **Results:** In this study among 136 patients, 66(48.5%) were aged between 51-70 years and mean age was 49.59 ± 18.03 years. There were 65 (47.8%) male and 71 (52.2%) female patients. Out of 136 patients, 76(55.9%) were moderate cases, 43 (31.6%) were severe cases and 17 (12.5%) were critical cases. Mean age of moderate cases were 44.36 ± 18.53 years, severe cases were 52.36 ± 14.34 years and critical cases were 64.65 ± 13.90 years. Interleukin-6 level was 6.06 ± 3.69 pg/ml in moderate cases, 44.71 ± 4.49 pg/ml in severe cases and 242.97 ± 21.48 pg/ml in critical cases and it was higher in critical cases than severe and moderate cases. **Conclusion:** This study showed IL-6 level is significantly associate with the severity of illness. So, it can serve as an effective marker for severity of the diseases that can help the physicians to correctly allocate the hospital admitted COVID-19 patients at an early stage and to identify critically ill COVID-19 patients.

Key words: Serum interleukin-6 level, Moderate, Severe and Critical COVID-19 patients.

Introduction

The Corona Virus Disease of 2019 (COVID-19) represents a global crisis caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Corona virus was first isolated and named in the 1960s which belongs to the family Coronaviridae. It is a zoonotic virus that can spread between animals and humans. It is an enveloped virus with a helical nucleocapsid. It contains a nonsegmented, single stranded RNA genome with four classical viral structural proteins, these are: spike (S) protein, envelope (E) protein, membrane (M) protein, and nucleocapsid (N) protein.¹⁻⁴

The novel corona virus (SARS-CoV-2) first broke in Wuhan, China in 31st December 2019. The World Health Organization declared the COVID-19 outbreak as a Public Health Emergency of International Concern on 30 January 2020, and as a pandemic on 11 March 2020. On 8 March 2020, Bangladesh has confirmed its first case of COVID-19 patients caused by SARS-CoV-2 virus.⁵ On, January 2022; there have been 364,191,494 confirmed cases of COVID-19, including 5,631,457 deaths, reported to WHO. Among them, Bangladesh has confirmed a total 1,798,833 cases with 28,394 deaths.

Coronavirus initially undergoes viral replication in the respiratory tract and then spread to other organs and tissues. Then it enters the pulmonary alveolar epithelial cells through angiotensin converting enzyme receptor 2 (ACER2). The main mechanism for inflammation and organ damage is cytokine storm, especially in pulmonary vascular endothelial cells with increased inflammatory cytokines such as interleukin-6 (IL-6), interleukin-10 (IL-10) and interferon- γ (IFN- γ). Exaggerated and excessive synthesized cytokines like IL-6, IL-10 can lead to cytokine storm which is associated with disease severity of COVID-19 patients.⁶⁻¹⁰

The clinical manifestations of COVID-19 are wide-ranging, from asymptomatic, mild, and moderate to severe viral pneumonia such as acute respiratory distress syndrome (ARDS). COVID-19 patients with clinical sings of pneumonia (fever, cough, dyspnoea, fast breathing) but no signs of severe pneumonia ($\text{SpO}_2 \geq 90\%$ on room air) categorized as moderate case, patients with clinical sings of pneumonia (fever, cough, dyspnoea, fast breathing) plus one of the following: severe respiratory distress, respiratory rate > 30 breaths/min or $\text{SpO}_2 < 90\%$ on room air categorized as severe case (Severe Pneumonia) and severe COVID-19 case with any of the following criteria: respiratory failure and requiring mechanical ventilation, sepsis, septic shock, ARDS, any organ failure that requires ICU care categorized as Critical cases (Cases requiring ICU care).¹¹ But some COVID-19 patients experience respiratory deterioration over a short period of time during their clinical course. Thus, it is essential to identify patients who are likely to develop severe condition as early as possible.^{6,7,12} Several blood markers could predict respiratory failure in COVID-19 patients. Some inflammatory cytokines could distinguish disease severity in COVID-19. In some patients, the general condition dramatically worsens within a couple of days with severe respiratory failure. Therefore, it is of high priority to identify reliable blood markers which could predict respiratory illness in the short term in clinical settings. In COVID-19 patients with cytokine release syndrome (CRS), interleukin-6 (IL-6), IL-10,

and interferon (IFN)- γ are consistently elevated. In COVID-19 patients IL-6 contributes to many of the symptoms, such as the production of acute phase reactants by hepatocytes, activation of the extrinsic coagulation pathway and production of vascular endothelial growth factor (VEGF), leading to endothelial inflammation. IL-6 play a pivotal role in the pathophysiology of lung damage in COVID-19 patients. High level of serum IL-6 have been observed in many patients with cytokine storm in severe COVID-19. COVID-19 patients with comorbidities with high IL-6 levels at admission are at increased risk of developing a severe from of the diseases, requiring mechanical ventilation and ICU and progressing to respiratory distress syndrome and multiorgan failure.¹³⁻¹⁷ In a meta-analysis including nine studies reporting that mean IL-6 levels were more than three times higher in patients with complicated COVID-19 compared with mild or moderate diseases. The concentration of IL-6 $> 24\text{pg/ml}$ at initial assessment predicted the development of hypoxemia requiring hospitalization.¹⁸ So, by this study we can evaluate serum IL-6 level among hospital admitted COVID-19 patients and can make an association of IL-6 with severity of the diseases in hospital admitted COVID-19 patients and can help in further management of patients.

Materials and Methods

This cross-sectional observational study was conducted in the department of Microbiology and Virology in collaboration with Department of Medicine of Sylhet MAG Osmani Medical College and Shahid Shamsuddin Ahmed Hospital, Sylhet from January 2021 to December 2021. After obtaining ethical clearance, total 136 Rapid antigen test positive or RT-PCR positive COVID-19 patients were enrolled in this study by convenient sampling technique. With all aseptic precautions 4ml of venous blood was collected from ante -cubital vein. Then serum was separated by centrifuge process at 4000 rpm for 10 minutes and stored in the laboratory at -20°C . Serum IL-6 was assayed by solid-phase chemiluminescent immunoassay. Data were recorded in a pre-designed

structured data collection form. One way ANOVA and unpaired t-test was applied to analyse the data by using SPSS version 26.

Results

In this study the age of the patients ranged from 18 years to 90 years. The mean age of the patients was 49.59 (SD± 18.03) years.

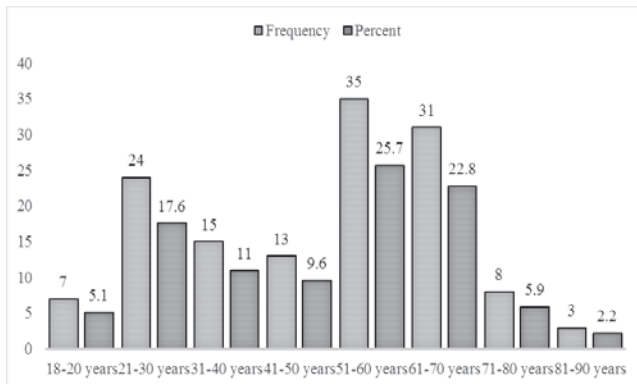


Figure-1: Distribution of the patients according to age group (n=136)

Figure 1: Shows out of 136 patients, majority 35(25.7%) were aged between 51-60 years followed by 31 (22.8%) were in the age group of 61-70 years.

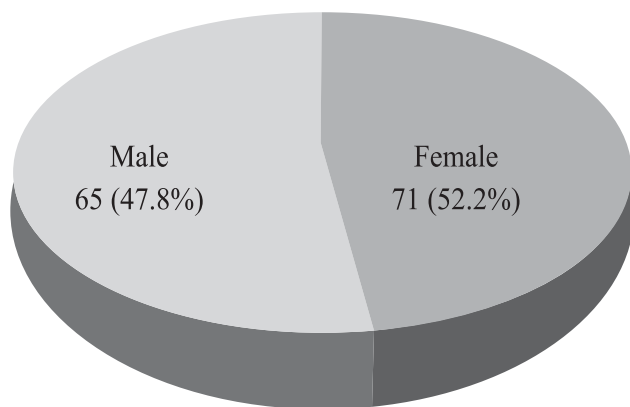


Figure-2: Distribution of the patients according to Gender (n=136)

Figure 2: Shows out of 136 COVID-19 patients, male patients were 65 (47.8%) and female patients were 71 (52.2%).

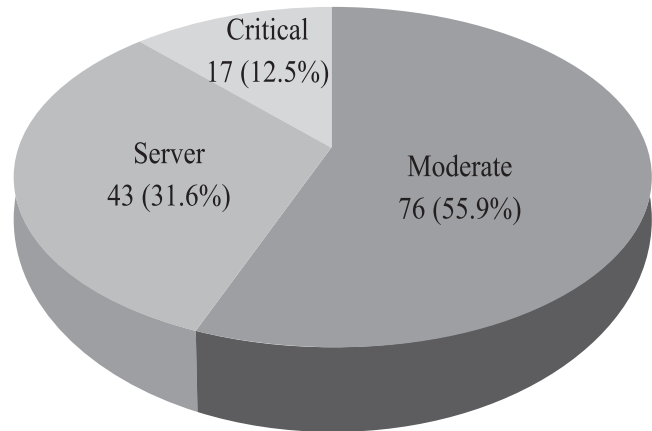


Figure-3: Distribution of the COVID-19 patients according to disease severity.

Figure 3: Shows out of 136 patients, moderate cases were 76 (55.9%), severe cases were 43 (31.6%) and critical cases were 17 (12.5%).

Table-I: Distribution of age of the COVID-19 patients among severity of the diseases

Age (year)	Severity			*p-value
	Moderate	Severe	Critical	
Mean	44.36	52.36	64.65	p<0.001
± SD	± 18.53	±14.34	± 13.90	

*One way ANOVA was applied to analyse the data

Table I: Shows the mean age of moderate cases was 44.36 ± 18.53 years, severe cases was 52.36 ±14.34 years and critical cases was 64.65 ± 13.90 years and the difference of the age of the patients of different group was statistically significant (F=11.360; p<0.001).

Table-II: Comparison of IL-6 level among moderate, severe and critical COVID-19 patients:

Interleukin-6 level (pg/ml)	Severity			*p-value
	Moderate (76)	Severe (43)	Critical (17)	
Mean	6.06	44.71	242.97	p<0.001
± SD	± 3.69	± 4.49	± 21.48	

*One way ANOVA was applied to analyse the data

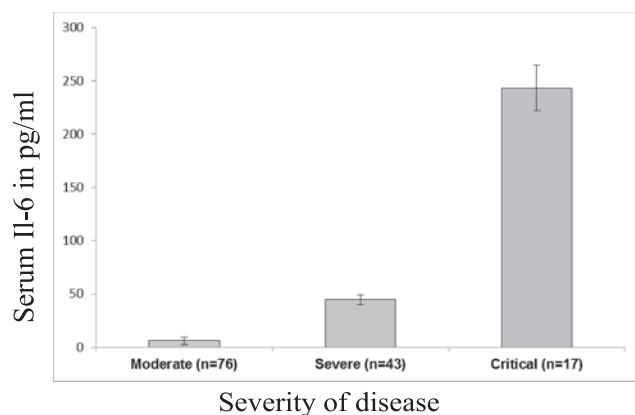


Figure-4: Comparison of interleukin-6 level among severity of COVID-19 patients

Table II and figure 4: Shows IL-6 level were 6.06 (SD± 3.69) pg/ml, 44.71 (SD± 4.49) pg/ml and 242.97 (SD± 21.48) pg/ml in moderate, severe and critical cases of COVID 19 patients respectively. IL-6 level was significantly differed among the severity of cases ($F=318.641$; $p<0.001$) and the difference was statistically significant.

Discussion

The present study conducted to assess IL-6 level of moderate, severe and critical COVID-19 patients. In this study the age of the patients ranged from 18 years to 90 years and the mean age was 49.59 (SD± 18.03) years. In Cruz⁶ mean age was 45.24 (SD± 13.97) years and in Vultaggio¹⁹ the mean age was 63 (SD± 15) years. The majority 66 (48.5%) of the patients were aged between 51-70 years.

There were 65 (47.8%) male and 71 (52.2%) female cases with a ratio of male and female 1:1.1 in this study. Gender distribution was reported by Liu¹⁴ in China, where 46.98% male and 53.02% female and in Cruz⁴ where male patients 52%, female patients 48%. The gender ratio of the study subjects was almost same. Men and women had the same prevalence in COVID-19 in Jiang⁹.

In the present study out of 136 patients 76 (55.9%) were moderate cases, 43 (31.6%) were severe cases and 17 (12.5%) were critical cases of COVID-19. (Patient's categorization: moderate, severe and critical

case according to national guideline 9th edition: page 1 & 2). The case distribution was reported by Azmy²⁰ in New Haven, USA where moderate case was 48%, severe case was 30% and critical case was 22%.

In this study the mean age of moderate cases was 44.36 ± 18.53 years, severe cases were 52.36±14.34 years and critical cases was 64.65±13.90 years. Similar observation was recorded by Gong¹² in China where the mean age of moderate cases was 45.29±13.08 years, severe cases was 60.41±9.80 years and critical cases was 65.88±13.61 years. So, mean age of patients was higher in critical case, than severe and moderate cases.

In the present study interleukin-6 level were 6.06± 3.69 pg/ml in moderate cases, 44.71±4.49 pg/ml in severe cases and 242.97±21.48 pg/ml in critical cases of COVID 19 patients respectively. Mean value of IL-6 was higher in critical cases, than severe and moderate cases. A study Vultaggio²¹ in Chin showed the mean interleukin-6 level was 15.7±15.60 pg/ml in moderate cases, and 53.63±63.8 pg/ml in severe and critical cases, 27±40.9 pg/ml in all cases of COVID-19 patients respectively. Another study Azmy²⁰, in New Haven, USA showed interleukin-6 level was 19.5pg/ml in moderate cases, 21.20 pg/ml in severe cases of COVID 19 patients respectively. IL-6 values in critically ill COVID-19 patients were admitted to the ICU was 336 pg/ml in Gorham, California. So, IL-6 level was significantly higher in critical cases compared to moderate and severe cases.

Conclusion

Coronavirus disease 2019 (COVID-19) was caused by a new strain of beta coronavirus, SARS-CoV-2. Worldwide it is emerging as a huge threat to human health and the mortality rate is higher among severe and critical cases. Cytokine storm causes systemic inflammation, ARDS and multi-organ dysfunction in COVID-19 patients. The current study indicates that high IL-6 levels suggest a cytokine storm which may play a major role in the pathophysiology of this disease and are considered as a relevant parameter in predicting most severe cases of disease. In this study

IL-6 level was significantly higher in critical cases compared to moderate and severe cases who needed more intensive care and treatment, due to severe lung damage. IL-6 level was significantly differed among the moderate, severe and critical COVID-19 patients. Therefore, IL-6 could be a potential marker for disease monitoring in hospital admitted COVID-19 patients. Targeting IL-6 may be effective in treating inflammatory cytokine storm by using anticytokine therapeutic during disease progression. A better understanding of IL-6 in the pathogenesis of COVID-19, especially in the critical cases, may help us to manage the disease.

Limitations of the study

1. Association and correlation with other inflammatory markers were not included in this study.
2. A more detailed recording of IL-6, as well as its upstream and downstream parameters, may help clarify this ambiguity.

References

1. Alsaadi, E.A.J. and Jones, I.M. 'Membrane binding proteins of coronavirus', *Journal of Future Virology*, 2019; 14(4):275-286.
2. Bergmann, C.C., Silvermann. 'COVID-19: Coronavirus replication, pathogenesis, and therapeutic strategies', *Cleveland Clinic Journal of Medicine*, 2020;87(6):321-327.
3. Masters, P.S. 'The molecular biology of coronaviruses', *Advances in Virus Research*, 2006; 66:193-292.
4. Matthay, M.A., Zemans, R.L., Zimmerman, G.A., Arabi, Y.M., Beitler, J.R., Herridge, M. et al. 'Acute respiratory distress syndrome', *Nature Reviews Disease Primers*, 2019 ;5(1):18.
5. Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., et al. 'A Novel Coronavirus from Patients with Pneumonia in China, 2019', *New England Journal of Medicine*, 2020;382(8):727-733.
6. Cruz, A.S., Mendes-Frias, A., Oliveira, A.I., Dias, L., Matos, A.R., Carvalho, A. et al. 'Interleukin-6 Is a Biomarker for the Development of Fatal Severe Acute Respiratory Syndrome Coronavirus 2 Pneumonia', *Frontiers in Immunology*, 2021; 12:613422.
7. Ghazavi, A., Ganji, A., Keshavarzian, N., Rabiemajd, S. & Mosayebi, G. 'Cytokine profile and disease severity in patients with COVID-19', *Cytokine*, 2021;137:155-157.
8. Han, H., Ma, Q., Li, C., Liu, R., Zhao, L., Wang, W. et al. 'Profiling serum cytokines in COVID-19 patients reveals IL-6 and IL-10 are diseases severity predictors', *Emerging Microbs & infections*, 2020;9 (10):1080.
9. Jiang, F., Deng, L., Cai, Z Y., Cheung, C.W. & Xia, Z. 'Review of the Clinical Characteristics of Coronavirus Disease 2019 (COVID-19)', *Journal of General Internal Medicine*, 2020; 35(5):1545-1549.
10. Wan, S., Xiang, Y.I., Fang, W., Zheng, Y., Li, B., Hu, Y., Lang, C. et al. 'Clinical features and treatment of COVID -19 patients in northeast Chongqing', *Journal of medical virology*, 2020; 92(7):797-806.
11. National Guidelines on Clinical Management of COVID-19, 9th edition 2021, pp. 1-2.
12. Gong, J., Dong, H., Xia, Q-S., Huang, Z., Wang, D-K., Zhao, Y. et al. 'Correlation analysis between disease severity and inflammation-related parameters in patients with COVID-19: a retrospective study', *BMC Infectious Diseases*, 2020; 20(1): 963-972.
13. Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y. et al. 'Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China', *Lancet*, 2020;395 (10223): 497-506.

14. Liu, T., Zhang, J., Yang, Y., Ma, H., Li, Z., Zhang, J. et al. 'The role of interleukin-6 in monitoring severe case of coronavirus disease 2019', *EMBO Molecular Medicine Impact Factor*, 2019;12(7).
15. Lucas, C., Wong, P., Klein, J., Castro, T.B.R., Silva, J., Sundaram, M. et al. 'Longitudinal analyses reveal immunological misfiring in severe COVID-19', *Nature*, 2020;584 (7821): 463–469.
16. Rothan, H.A., Byrareddy, S.N. 'The epidemiology and pathogenesis of Coronavirus Disease (COVID-19) outbreak', *Journal of Autoimmun*, 2020; 109:102433.
17. Short, K.R., Veeris, R., Leijten, L.M., Brand, J.M., Jong, V.L., Stittelaar, K. et al. 'Proinflammatory Cytokine Responses in Extra-Respiratory Tissues During Severe Influenza', *The Journal of Infectious Diseases*, 2017;216(7):829–833.
18. Mojtavavi, H., Saghazadeh, A. & Rezaei, N. Interleukin-6 and severe COVID-19: a systematic review and meta-analysis', *European Cytokine Network*, 2020;31(2): 44–49.
19. Vultaggio, A., Vivarelli, E., Virgili, G., Lucenteforte, E., Bartoloni, A., Nozzoli, C. et al. 'Prompt Predicting of Early Clinical Deterioration of Moderate-to-Severe COVID-19 Patients: Usefulness of a Combined Score Using IL-6 in a Preliminary Study', *Journal of Allergy and Clinical Immunology in Practice*, 2020;8(8): 2575-2581.
20. Azmy, V., Kaman, K., Tang, D., Zhao, H., Cruz, C.D., Topal, J. E. et al. 'Cytokine Profiles Before and After Immune Modulation in Hospitalized Patients with COVID-19', *Journal of Clinical Immunology*, 2021; 41(4):738–747.
21. Tanaka, T., Narazaki, M. & Kishimoto, T. 'Interleukin (IL-6) immunotherapy,' *Cold Spring Harbor Perspective in Biology*, 2018; 10(8):2845.
22. Zhou, J., Chu, H., Li, C., Wong, B.H.-Y., Cheng, Z.-S., Poon, V.K.-M., et al. 'Active replication of Middle East respiratory syndrome coronavirus and aberrant induction of inflammatory cytokines and chemokines in human macrophages: implications for pathogenesis', *Journal of Infectious Diseases*, 2014; 209(9): 1331–42.

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