

Pattern of Potential Laboratory Markers for COVID-19 in Eastern Sudan

Nazik Sir El Khatim Bakhit Suliman^{1*}, Mohammed Omer Abaker Gibreel²,
Mervat Sir El Khatim Bakhit Suliman³

¹Department of Clinical Chemistry, College of Medical Laboratory Science, Eastern Sudan University of Medical Science and Technology, Port Sudan, Sudan

²Dean of the Secretariat of Academic Affairs, Port Sudan Ahlia University, Port Sudan, Sudan

³Cardiology Department, Cath Lab, Fujaira Hospital, Fujaira, UAE

Email: *naziksuliman18@gmail.com, m_omer8164@yahoo.com, mero-77@hotmail.com

How to cite this paper: El Khatim Bakhit Suliman, N.S., Gibreel, M.O.A. and El Khatim Bakhit Suliman, M.S. (2024) Pattern of Potential Laboratory Markers for COVID-19 in Eastern Sudan. *Open Journal of Epidemiology*, 14, 508-516.
<https://doi.org/10.4236/ojepi.2024.143036>

Received: June 4, 2024

Accepted: August 20, 2024

Published: August 23, 2024

Copyright © 2024 by author(s) and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).
<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Background: Coronavirus disease 2019 (COVID-19) is a recent global health crisis. One of the major issues of COVID-19 is its unpredictable manifestations and serious outcomes. Many hematological parameters are thought to change dramatically during the course of the disease. These include white blood cells, red blood cells, and platelets. This study aimed at evaluating certain laboratory results; peripheral blood lymphopenia, relative neutrophilia, high neutrophil-lymphocyte ratio, and elevated C-reactive protein as potential laboratory markers of COVID-19 in Eastern Sudanese patients. **Methods:** We, retrospectively, aimed at the evaluation of peripheral blood leucocytes count, neutrophil-lymphocyte ratio NLR and C-reactive protein (CRP) levels in confirmed COVID-19 eastern Sudanese patients during the course of the disease. **Results:** The mean total leucocytes count, % neutrophils count, absolute neutrophils count and C-reactive protein (CRP) were significantly higher (P. value = 0.000) in COVID-19 patients than in the control group while the mean % lymphocytes count and % mixed cells count were found to be significantly lower in COVID-19 patients than in the control group (P. value 0.000). **Conclusion:** Peripheral blood leucocyte alterations (simultaneous presence of lymphopenia, relative neutrophilia and high neutrophil lymphocyte ratio (NLR) along with elevated CRP levels may be valuable biomarkers associated with COVID-19 in Port Sudan city, Red Sea state, Sudan. These markers might be important in prediction, inspection of disease progression and prognosis.

Keywords

COVID-19, SARS 2, WBCs, CRP, NLR, Port Sudan

1. Introduction

The name severe acute respiratory coronavirus 2 (SARS2) was applied to the novel b-corona virus discovered in 2019 that is now known to cause respiratory disease that causes mild, moderate or severe life-threatening disorder [1]. Two strains of COVID-19; SARS-CoV and its divergent (the zoonotic positive-strand RNA virus known as SARS-CoV-2) have been associated with high incidences of morbidity and mortality worldwide during the recent decade [2]. The World Health Organization (WHO) declared that COVID-19 is a global pandemic the spread of which has impacted all aspects of life and has negatively affected healthcare, medical activity and research [3]. SARS2 is responsible for the acute respiratory distress syndrome (ARDS) that is associated with multi-organ failure and death experienced in affected patients [1]. Predicting the risk factors for severe COVID-19 infection can greatly help manage critical cases and save lives [4]. It is important that the majority of human populations in the world are at risk of the infection. Alterations that happen in peripheral blood leucocytes including lymphocytes, eosinophils and neutrophils in COVID-19 patients are suggested as a potential indicator for both disease progression and response to therapeutic procedures [2]. In 2020, the WHO declared SARS2 a global health emergency with more than 800,000 confirmed cases, more than 2700 deaths and affecting at least 37 countries at that time [5]. One of the best-recognized leucocytes change in COVID-19 patients is lymphopenia (absolute lymphocytes count less than $1.0 \times 10^9/L$) which is correlated with disease outcome. A more severe course of COVID-19 is often accompanied by leucocytosis with neutrophilia in a majority of patients. As the disease progresses neutrophilia increases and is thus regarded as a marker of respiratory disease and poor outcome. Reversible morphological neutrophil alterations including toxic granulation and hypo-lobulation are also encountered in SARS 2 infected patients [1]. Significant correlations were found between WBCs count and death in hospitalized patients [6]. Neutrophil lymphocyte ratio (NLR) obtained by the division of absolute neutrophil count over the absolute lymphocyte count has been recognized as a useful marker in the prediction of many inflammatory processes including ischemic heart disease, acute pancreatitis along with some malignant conditions. NLR might be a better predictor of COVID-19 infection than neutrophil count alone [1]. COVID-19 pandemic expresses a state of rapid spread that rendered health service providers in all countries to make efforts to provide tools of rapid diagnosis ranging from simple biological markers to DNA analysis. Complete blood Count (CBC) is the most utilized laboratory test worldwide; hence, markers associated with CBC would give valuable information for both detection and prognosis of the disease. C-reactive protein (CRP) is considered a sensitive marker of both infection and inflammation [7]. It is often requested by physicians in the counseling of COVID-19 patients. C-reactive protein can be used to predict the cases that are most susceptible to progress unfavorably [8]. Local researches that assess the sensitivity and specificity of hematology laboratory tests in the diagnosis and prog-

nosis of COVID-19 are scanty. We have tried in this study to verify hematological changes associated with peripheral blood leucocyte counts and CRP that may add valuable information as laboratory markers for the prediction and prognosis of COVID-19 infection in the Red Sea state, Sudan.

2. Patients and Methods

A total of 50 adult Eastern Sudanese COVID-19 patients (confirmed by RT PCR assay of nasal and pharyngeal swab specimens) living in Port Sudan City and aged between 11 and 90 years old of whom 29 (58%) were males and 21 (42%) were females (**Figure 1**) along with other 50 healthy appearing adults aged between 18 and 82 years of whom 28 (56%) were males and 22 (44%) were females (**Figure 2**) as a control group were enrolled into this cross-sectional retrospective study. Venous blood specimens were collected and analyzed during the period from September to November 2021. All specimens from participants were subjected to the determination of Complete Blood Count (CBC) using the Sysmex XP-300 apparatus in the Hematology department at the Eastern Sudan University of Medical Science and Technology, College of Medical Laboratory Science. CRP level was estimated in patients and the control group using the Biosystems A25 chemistry analyzer. In respect to relative illiteracy, only verbal consent was obtained from patients and was approved by the ethics committee at the Eastern Sudan University of Medical Science and Technology, Port Sudan. Data were statistically analyzed by the Statistical Product and Service Solutions IBM SPSS 24 program. Descriptive statistics in the form of frequencies and percentages were used to facilitate the interpretation of results. Degree of confidence adhered to was 95% where P. values lower than 0.05 considered significant.

3. Results

Of COVID-19 patients included in this study, 64% were vaccinated, 80% were home-isolated, 22% were hospitalized, and 90% had received oxygen supplements. Most of the patients had been suffering from an accompanying chronic illness (**Table 1**). 46% of the individuals in the control group were also vaccinated.

Table 1. Frequency of chronic illness among patients.

Item	COVID-19 patients (N = 50) Frequency	COVID-19 patients (N = 50) Percent
Diabetes Mellitus	24	48
Cardiac disorder	03	06
Hypertension	10	20
Renal disease	04	08
Arteriosclerosis	02	04
Hyperthyroidism	01	02
No chronic disease	06	12
Total	50	100

Statistically significant differences were detected between COVID-19 patients and controls in the measured parameters except for one. The mean total leucocytes count, % neutrophils count, absolute neutrophils count and neutrophil lymphocyte ratio were significantly higher (P. value = 0.000) in the patient group than in the control group while the mean % lymphocytes count and % mixed cells count were found to be significantly lower in the patient group than in the control group (P. value = 0.000) (Table 2).

Table 3 illustrates the clinical presentations observed in the two groups which range from mild to vast distributed symptoms.

Table 2. Comparison between Patients and control based on the measured parameters.

Item	Reference Range	Patients Mean ± SD (N = 50)	Control Mean ± SD (N = 50)	P. value
TWBCs count/ μL	4000 - 11000	9364 ± 4446	5958 ± 1818	0.000
% Lymphocytes count	20 - 45	11.25 ± 10.80	38.20 ± 13.53	0.000
% Neutrophils count	40 - 60	79.04 ± 12.62	14.20 ± 08.95	0.000
% Mixed cells count	05 - 20	03.84 ± 02.24	50.38 ± 16.28	0.000
Absolute lymphocytes $\times 10^3/\mu\text{L}$	1.2 - 4.9	05.70 ± 12.85	03.25 ± 01.73	0.186
Absolute neutrophils $\times 10^3/\mu\text{L}$	1.8 - 6.8	06.03 ± 05.13	01.67 ± 01.25	0.000
Neutrophil lymphocyte ratio	1.38 - 1.50	5.43 ± 7.46	0.63 ± 0.59	0.000
C-Reactive protein mg/L	0-5	95.09 ± 1.78	0.84 ± 3.36	0.000

Table 3. Frequencies of clinical remarks.

Symptoms	Patients % (N = 50)	Control % (N = 50)
Fever	68	2
Headache	56	4
Loss of taste	22	0
Cough	100	0
Loss of smell	36	2

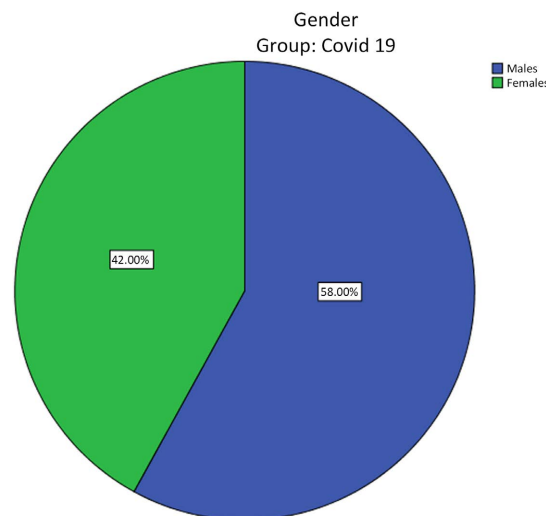


Figure 1. Gender distribution in the patients group.

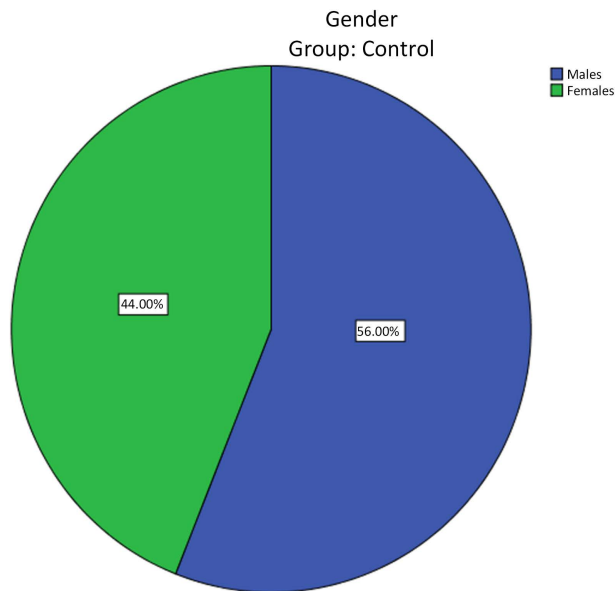


Figure 2. Gender distribution in the control group.

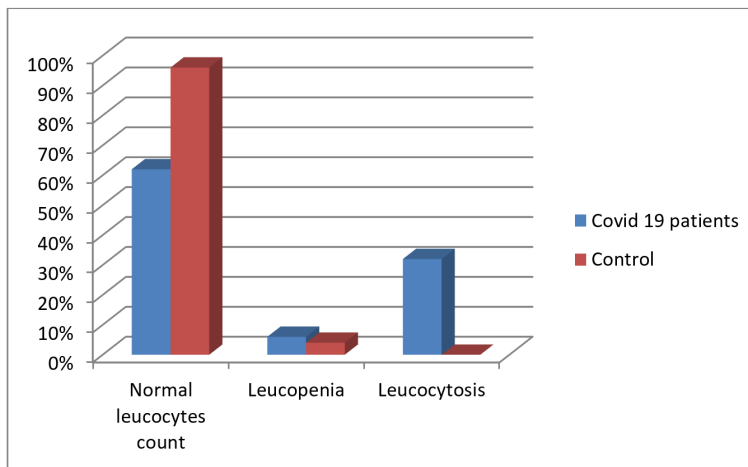


Figure 3. Comparison between the two groups in TWBCs count.

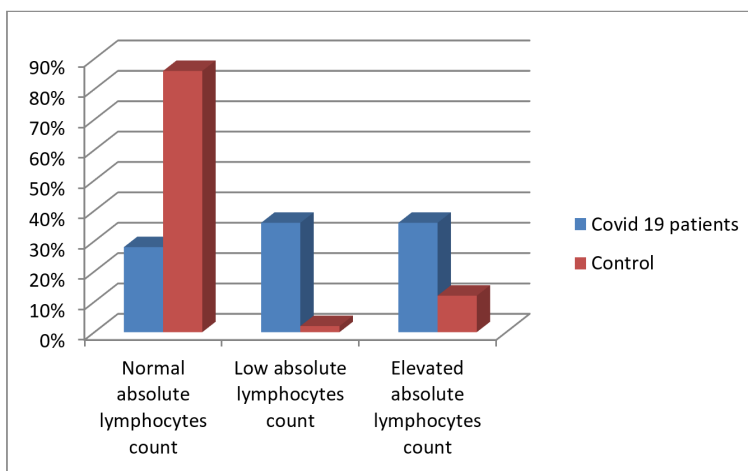


Figure 4. Comparison between the two groups in absolute lymphocytes count.

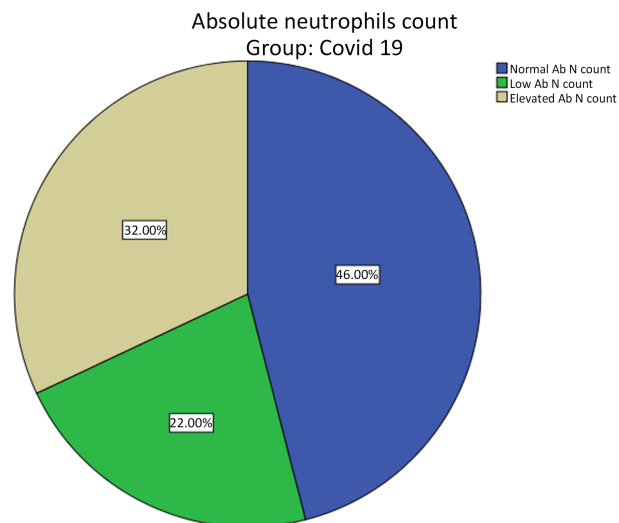


Figure 5. Absolute neutrophils count in the patient group.
(*Ab = Absolute, N = Neutrophils*).

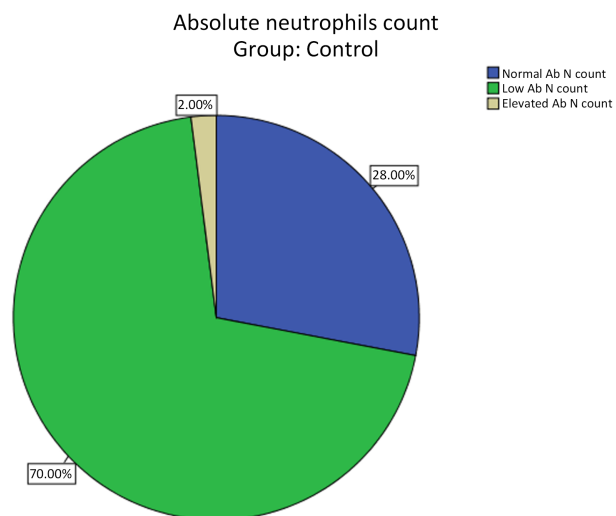


Figure 6. Absolute neutrophils count in the control group.
(*Ab = Absolute, N = Neutrophils*).

Peripheral blood leucocytosis was more prominent in the patient group than in the controls (**Figure 3**). A relatively low percent lymphocytes count was seen most frequently in the patient group (**Figure 4**). Similarly, a relatively elevated absolute neutrophils count was also seen more frequently in the patient group than in the control (**Figure 5** and **Figure 6**).

4. Discussion

The clinical and laboratory spectrum of COVID-19 is not yet totally verified despite the huge data concerning the documentation of epidemiological and clinical characteristics. The state of dramatically rapid human-to-human spread of the virus and that both middle-aged and elderly patients are susceptible to acute respiratory failure associated with poor prognosis [6] necessitate the provision of

further markers to predict the disease. The provision of biomedical and/or statistical markers will help physicians to make proper decisions concerning the prediction, progression and prognosis of the disease. Our present study tried to assess the alterations in peripheral blood leucocytes count and CRP levels in COVID-19 patients as compared to healthy-appearing adult controls. Lymphopenia and neutrophilia which are significantly associated with our patient group (P. value = 0.000), is in concordance to [1] and [2] who both reported results that are associated with COVID-19 infection and severity among an Italian and Saudi Arabian patient populations, respectively. Furthermore, neutrophilia detected in our present study in COVID-19 patients are in concordance with [9], [10] and [11] where white cell alterations in COVID-19 patients were evaluated retrospectively. The fact that patients with higher white blood cells at admission were facing a much higher death possibility, [6], makes our present study which aims at searching for biological markers linked to peripheral blood white cell alterations valuable. Moreover, the whole clinical and diagnostic picture for COVID-19 is not yet completed owing to the continuous evolvement of new convergent copies of the virus. These facts, collectively, necessitate the presence of close open eye inspection concerning COVID-19 infection. Much remains unknown about COVID-19 in spite of the information emerged on the viral genome and epidemiology. Liu *et al.* [12] reported that lymphocytopenia was detected in about 72.3% of patients while nearly 80% had normal or decreased WBCs counts. Again these findings agree with our observations. Our findings regarding CRP are matched with what was reported by Manalu E. *et al.* [7] who reported that the average CRP levels in patients with moderate symptoms was 63.705 mg/l while the average level in patients with severe symptoms was 132.050 mg/l. A strong association (P value < 0.001) between first CRP level and mortality had been reported by [13] in records of 10 hospitals at Common Spirit Health, USA. Again, statistically significant difference in CRP levels (P. value 0.000) between COVID-19 patients and the healthy control group was detected by Kurt N. *et al.*, [14]. Chandran RT. and Vadhul PB, [15] have also reported that elevated levels of CRP was associated with high ICU mortality in COVID-19 infected (Adult Respiratory Distress Syndrome (ARDS)) patients. We greatly hope that our results might provide significant local medical data that will help physicians to predict COVID-19 through these laboratory markers. Nonetheless, some limitations are to be noticed such as our smaller sample size and relatively heterogeneous group of patients. So, future research is needed to investigate more biological and laboratory markers associated with COVID-19 infection.

Limitations

This study was primarily conducted in an Eastern Sudanese patient population. So, geographical, environmental and ethnic considerations may differ from other areas. Further studies with larger sample sizes are recommended that clarify the correlation between COVID-19 infection and other dynamic hematological

changes.

Ethical approval and consent to participate

Permission for this study was obtained from the Medical Laboratory Science College, Eastern Sudan University of Medical Science and Technology and Ministry of Health issued by the local ethics committee. Verbal consent was also obtained from participants.

Conclusion

The hematopoietic system is one of the organs that are affected by COVID-19 manifestation. Many alterations in the components of the hematopoietic system occur including lymphopenia, neutrophilia, raised neutrophil lymphocyte ratio NLR and elevated levels of CRP in COVID-19 patients. To some extent, these alterations may act as laboratory markers that assist prediction and/or prognosis of the disease.

Conflict of Interest

No conflict of interest is declared.

References

- [1] Palladino, M. (2021) Complete Blood Count Alterations in COVID-19 Patients. *Biochemia Medica*, **31**, 403-415. <https://doi.org/10.11613/bm.2021.030501>
- [2] Elderderly, A.Y., Elkhalfifa, A.M.E., Alsrhani, A., Zawbaee, K.I., Alsurayea, S.M., Escandarani, F.K., *et al.* (2022) Complete Blood Count Alterations of COVID-19 Patients in Riyadh, Kingdom of Saudi Arabia. *Journal of Nanomaterials*, **2022**, Article ID: 6529641. <https://doi.org/10.1155/2022/6529641>
- [3] Fois, S.S., Zinellu, E., Zinellu, A., Merella, M., Pau, M.C., Carru, C., *et al.* (2022) Comparison of Clinical Features, Complete Blood Count Parameters, and Outcomes between Two Distinct Waves of COVID-19: A Monocentric Report from Italy. *Healthcare*, **10**, Article 2427. <https://doi.org/10.3390/healthcare10122427>
- [4] Mahmood Edan, L., Samein, L.H. and Salih, K.S. (2022) Prognostic Value of C-Reactive Protein and Platelet Lymphocyte Ratio in Coronavirus Disease 19. *Bionatura*, **7**, 1-5. <https://doi.org/10.21931/rb/2022.07.02.53>
- [5] Yuen, K., Ye, Z.-W., Fung, S., Chan, C. and Jin, D. (2020) SARS-CoV-2 and COVID-19: The Most Important Research Questions. *Cell & Bioscience*, **10**, Article No. 40. <https://doi.org/10.1186/s13578-020-00404-4>
- [6] Zhu, B., Feng, X., Jiang, C., Mi, S., Yang, L., Zhao, Z., *et al.* (2021) Correlation between White Blood Cell Count at Admission and Mortality in COVID-19 Patients: A Retrospective Study. *BMC Infectious Diseases*, **21**, Article No. 574. <https://doi.org/10.1186/s12879-021-06277-3>
- [7] Manalu, E., Winanda, A. and Luhulima, D.E.J. (2022) C-Reactive Protein (CRP) Medium and Severe Symptoms Levels of Covid-19. *Journal of Drug Delivery and Therapeutics*, **12**, 152-156. <https://doi.org/10.22270/jddt.v12i6.5687>
- [8] Bouayed, M.Z., Laaribi, I., Chatar, C.E.M., Benaini, I., Bouazzaoui, M.A., Oujidi, Y., *et al.* (2022) C-Reactive Protein (CRP): A Poor Prognostic Biomarker in Covid-19. *Frontiers in Immunology*, **13**, Article 1040024.

- <https://doi.org/10.3389/fimmu.2022.1040024>
- [9] Chen, N., Zhou, M., Dong, X., Qu, J., Gong, F., Han, Y., *et al.* (2020) Epidemiological and Clinical Characteristics of 99 Cases of 2019 Novel Coronavirus Pneumonia: A Descriptive Study. *The Lancet*, **395**, 507-513. [https://doi.org/10.1016/s0140-6736\(20\)30211-7](https://doi.org/10.1016/s0140-6736(20)30211-7)
- [10] Pozdnyakova, O., Connell, N.T., Battinelli, E.M., Connors, J.M., Fell, G. and Kim, A.S. (2020) Clinical Significance of CBC and WBC Morphology in the Diagnosis and Clinical Course of COVID-19 Infection. *American Journal of Clinical Pathology*, **155**, 364-375. <https://doi.org/10.1093/ajcp/aqaa231>
- [11] Fan, B.E. (2020) Hematologic Parameters in Patients with Covid-19 Infection: A Reply. *American Journal of Hematology*, **95**, E215. <https://doi.org/10.1002/ajh.25847>
- [12] Liu, K., Fang, Y., Deng, Y., Liu, W., Wang, M., Ma, J., *et al.* (2020) Clinical Characteristics of Novel Coronavirus Cases in Tertiary Hospitals. *Chinese Medical Journal*, **133**, 1025-1031. <https://doi.org/10.1097/cm9.0000000000000744>
- [13] Lentner, J., Adams, T., Knutson, V., Zeien, S., Abbas, H., Moosavi, R., *et al.* (2021) C-Reactive Protein Levels Associated with COVID-19 Outcomes in the United States. *Journal of Osteopathic Medicine*, **121**, 869-873. <https://doi.org/10.1515/jom-2021-0103>
- [14] Kurt, N. (2022) Evaluation of Fetuin-A, CRP and CRP/Fetuin-A Values in COVID-19 Patients. *International Journal of Medical Biochemistry*, **5**, 125-131. <https://doi.org/10.14744/ijmb.2022.83097>
- [15] Chandran, R.T. and Vadhul, P.B. (2022) Correlation of C-Reactive Protein (CRP) with ICU Covid-19 Ards Mortality in Adults. *Chest*, **162**, A725. <https://doi.org/10.1016/j.chest.2022.08.571>