

# Neutrophil to lymphocyte ratio and C-reactive protein level markers in severe COVID patients

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**Keywords:**

COVID, CRP, NLR.

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**ABSTRACT**

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Coronavirus infection was described as a highly transmitted strain. COVID is mainly transmitted between people by air droplet and direct contact. COVID is a disease characterized by highly inflammatory changes in the lungs. The complete blood count is the most available, easy, efficient, and economic laboratory test. And, total white blood cell (WBC) count and neutrophil -to-lymphocyte ratio (NLR) are indicators of the systematic inflammatory response. 50 patients were listed as severe infection had developed into severe infection (intensive care unit (ICU) admission) and 30 healthy individual as control group. Data for patients, such as age and gender, were collected. Blood samples s, including CBC with total WBC, differential counts, lymphocyte count, and neutrophil count were performed using 5-parts differential swelab autoanalyzer hematology. 50 COVID cases with mean age of  $52.86 \pm 13.9$  (range: 29-80) years were recruited. Twenty-five (50%) cases were male and 50% were female with 30 normal healthy control group with mean age of  $49.6 \pm 14.8$  years, 17 cases were male and 13 cases were female. There was significant difference between two groups in NLR, CRP. In this study the mean  $\pm$ SD for NLR of the patients found to be very highly significant difference when compared with control group, at the level of significantly ( $<0.001$ ) by student T Test. This study suggest that early identification of critical illness and risk stratification management will reduce mortality and help alleviate the burden on insufficient medical resources. Early diagnosis of patients with status have to worsen may help in get perfect care and optimizing the use of ICU.

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## 1. INTRODUCTION

Coronavirus infection was described as a highly transmitted strain [1], [2]. COVID is mainly transmitted between people by air droplet and direct contact [4]. COVID is a disease characterized by highly inflammatory changes in the lungs [5]. Its pathogenesis, signs, symptoms, and pathological changes are still being discovered, especially in severely infected patients with complicated cases, lung complications, long

disease course, and high mortality [6]. Severe patients are referred to the ICU for treatment, while mild patients can be treated at home [7]. Due to limited information of the virus's spreading and pathology, the mortality rate was high. Subsequent management of COVID has greatly developed despite the absence of antiviral drugs [8]. Predicting severe patients at an early stage is of great clinical importance in reducing clinical morbidity and for the treatment program for COVID disease [9]. Early diagnosis and detection of the severity of COVID infection is important. C-reactive protein (CRP) is a highly useful diagnostic marker specially used to assess acute inflammation. It appears in blood within 6–10 hours of any tissue damaging event and decreases over 18–20 h [10], [11]. The complete blood count is the most available, easy, efficient, and economic laboratory test. And, total white blood cell (WBC) count and neutrophil -to-lymphocyte ratio (NLR) are indicators of the systematic inflammatory response [12], [13]. Previous researches have been done on neutrophils, lymphocytes, and CRP in COVID patients [14], [15], but little is known about their relations with disease severity in Iran. More researchs are indicated to confirm the findings of previous reports in different populations. This study aimed to investigate NLR with CRP in COVID patients to analyze differences among severe COVID patients and control normal patients.

## 2. Patients and Method

This retrospective study was conducted on patients who referred to Al-Hussain medical city Hospital, Karbala, from March 26 to April 21, 2020. Positive COVID patients were diagnosed by RT-PCR and based on clinical symptom categorized into severe infection. According to clinical reports, 50 patients were listed as severe infection had developed into severe infection (intensive care unit (ICU) admission) and 30 healthy individual as control group. Data for patients, such as age and gender, were collected from medical records. Blood samples were collected from each patients and controls for laboratory units, including CBC with total WBC, differential counts, lymphocyte count, and neutrophil count were performed using 5-parts differential swelab autoanalyzer hematology. Inflammatory biochemistry parameters such as CRP were also tested using a CRP on a Dirui automated biochemistry analyzer.

### 2.1 Statistical analysis

Statistical analysis was performed using excel. Measurement data with normal distribution is represented as mean  $\pm$  standard deviation (mean  $\pm$  SD). For continuous variables that were normally distributed, differences between two groups were compared using the t tests.

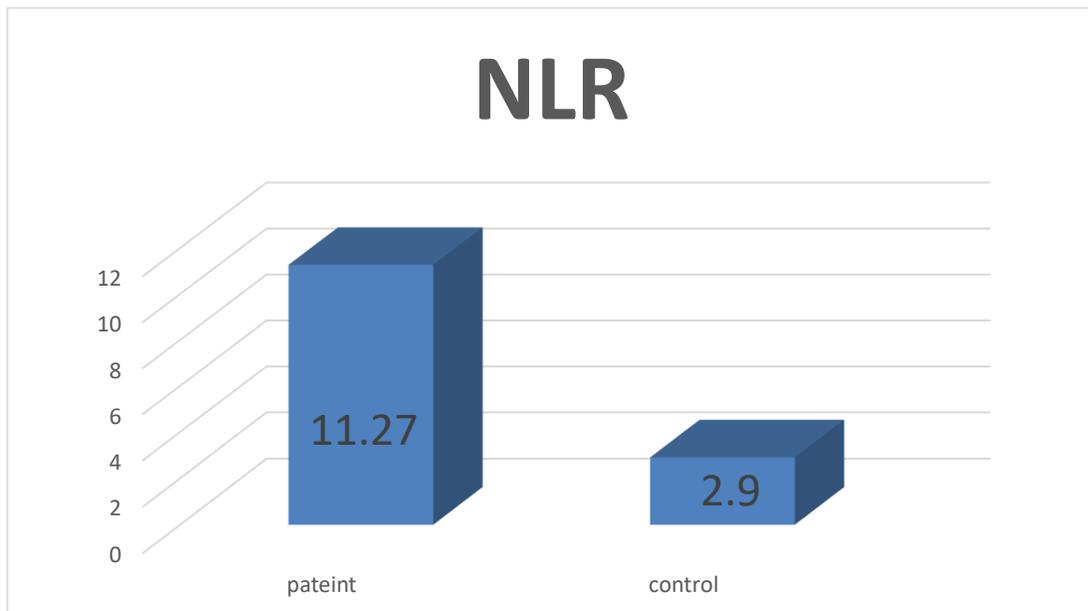
## 3. Results

50 COVID cases with mean age of  $52.86 \pm 13.9$  (range: 29-80) years were recruited. Twenty-five (50%) cases were male and 50% were female with 30 normal healthy control group with mean age of  $49.6 \pm 14.8$  years, 17 cases were male and 13 cases were female. Table 1 show the distributions of WBC, Neutrophile count, Lymphocyte count, CRP and NLR between the two groups (patients and control). There was significant difference between two groups in NLR, CRP.

**Table 1.** Laboratory findings of COVID patients and control group.

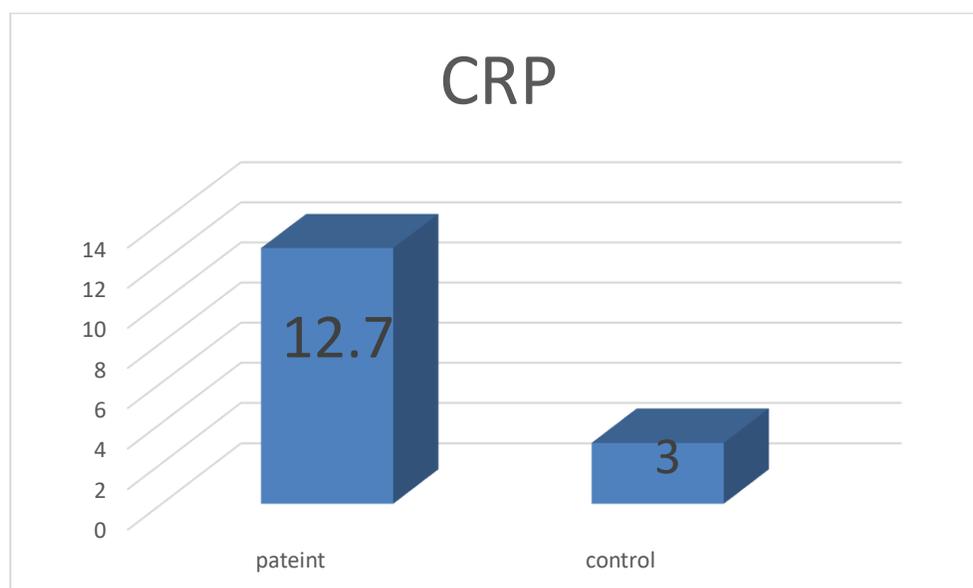
Variables (M $\pm$ SD)	COVID patients (n=50)	control (n=30)	P
Male	25 (50%)	17 (56.6%)	

Variables (M ± SD)	COVID patients (n=50)	control (n=30)	P
Female	25 (50%)	13 (43.3%)	
Age	52.68 ± 13.9	49.6 ± 14.8	0.362
WBC (cells/mm <sup>3</sup> )	10.84 ± 4.32	7.03 ± 1.75	<0.001
N, 10 <sup>9</sup> /L	8.8 ± 3.8	3 ± 0.4	<0.001
L, 10 <sup>9</sup> /L	1.27 ± 0.8	2.4 ± 0.43	<0.001
CRP (mg/L)	12.7 ± 13.6	3.07 ± 1.15	<0.001
NLR	11.27 ± 6.4	2.9 ± 3.04	<0.001



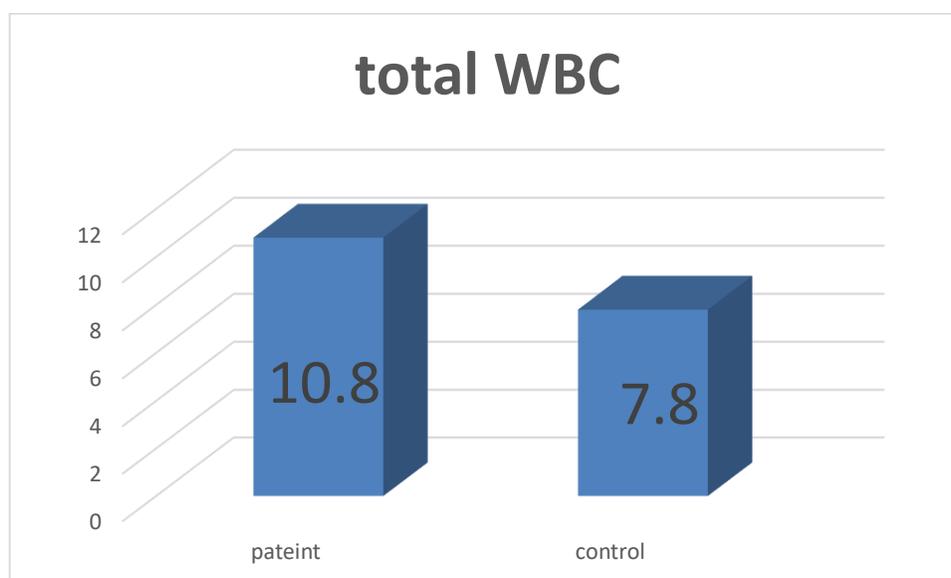
**Figure 1** shows mean NLR in patients and control

In this study the mean  $\pm$ SD for NLR of the patients ( $11.27 \pm 6.4$ ) found to be very highly significant difference when compared with control group ( $2.9 \pm 3.04$ ), at the level of significantly ( $<0.001$ ) by student T Test as shown in the figure 1



**Figure 2** shows mean CRP in patients and control

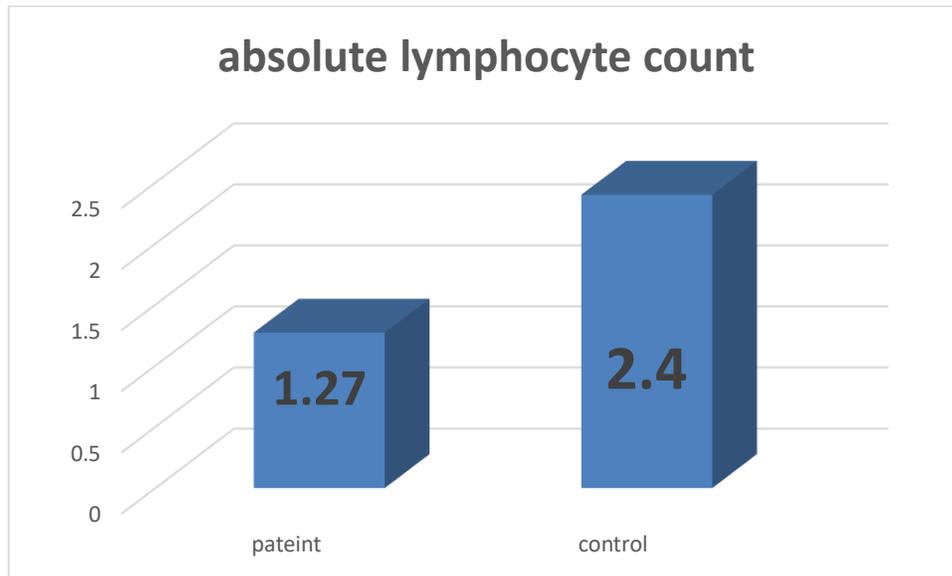
Plasma CRP levels were higher in COVID cases than in control group, and this difference was very high significant difference. The mean $\pm$ SD for CRP of the patients ( $12.7 \pm 13.6$ ) found to be when compared with control group ( $3.07 \pm 1.15$ ), at the level of significantly ( $<0.001$ ) by student T Test as shown in the figure 2



**Figure 3** show the total WBC values in COVID patients and healthy controls

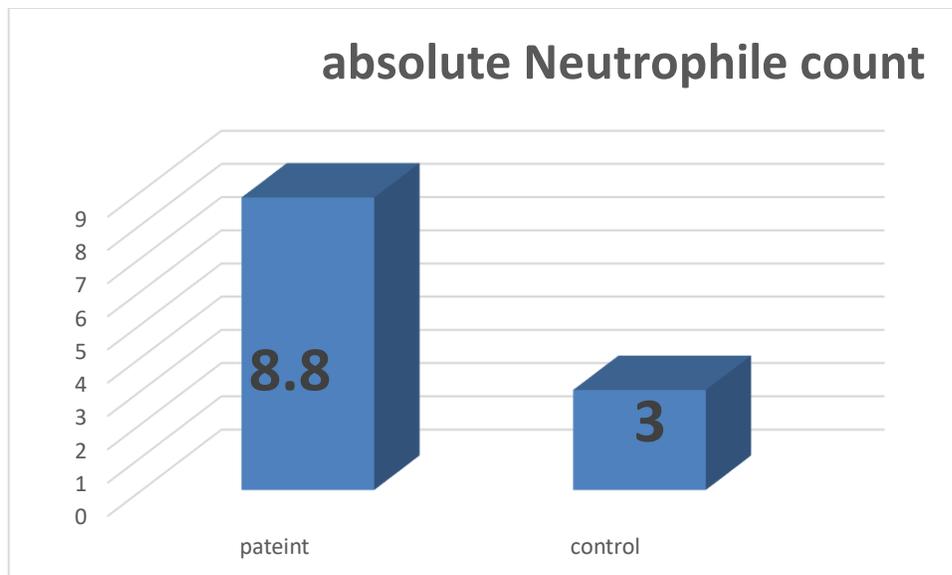
The mean WBC of severe patients were significantly higher than those of control group ( $p<0.001$ ). In this study the mean  $\pm$ SD for WBC of the patients ( $10.84 \pm 4.32$ ) found to be very highly significant difference when compared with control group ( $7.03 \pm 1.75$ ), at the level of significantly ( $<0.001$ ) by student T Test as

shown in the figure 3



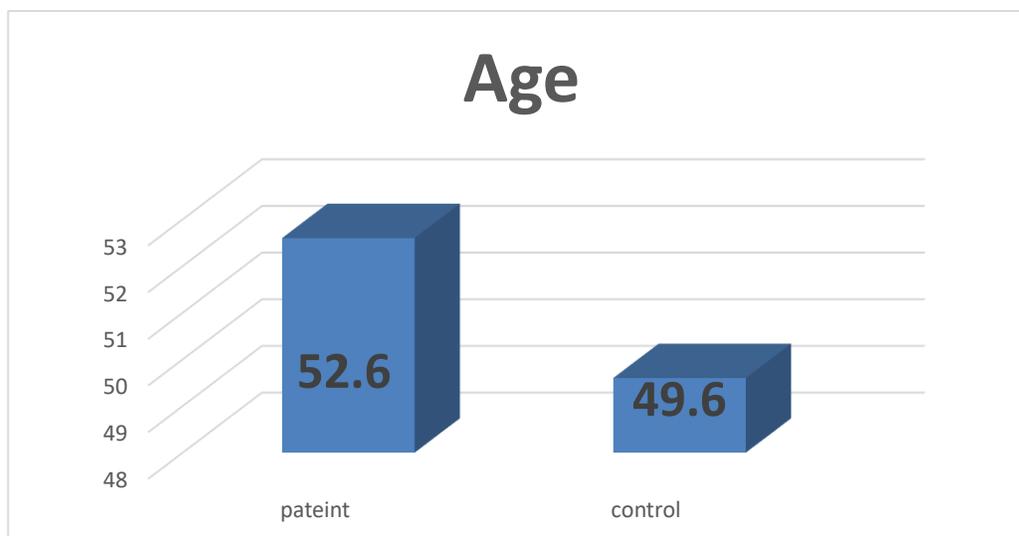
**Figure 4** show the Absolute lymphocyte count values in COVID patients and healthy controls.

The Absolute lymphocyte count values were lower than those of the healthy controls, the mean  $\pm$ SD for Absolute lymphocyte count of the patients ( $1.27 \pm 0.8$ ) found to be very highly significant difference when compared with control group ( $2.4 \pm 0.43$ ) at the lever of ( $<0.001$ ).



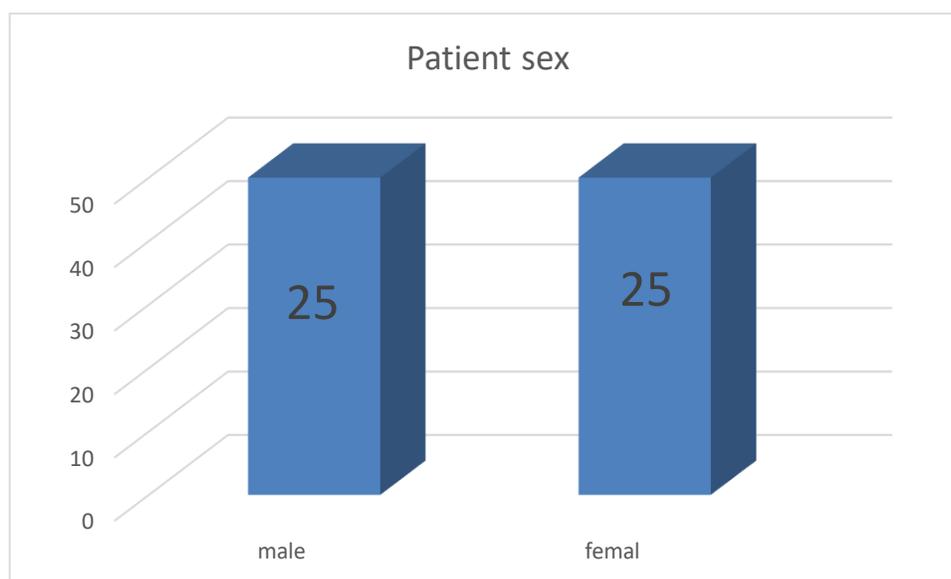
**Figure 5** show the mean Absolute Neutrophile count values in COVID patients and healthy controls

In this study the mean  $\pm$ SD for Absolute Neutrophile count of the patients ( $8.8 \pm 3.8$ ) found to be very highly significant difference when compared with control group ( $3 \pm 0.4$ ), at the level of significantly ( $<0.001$ ) by student T Test as shown in the figure 5



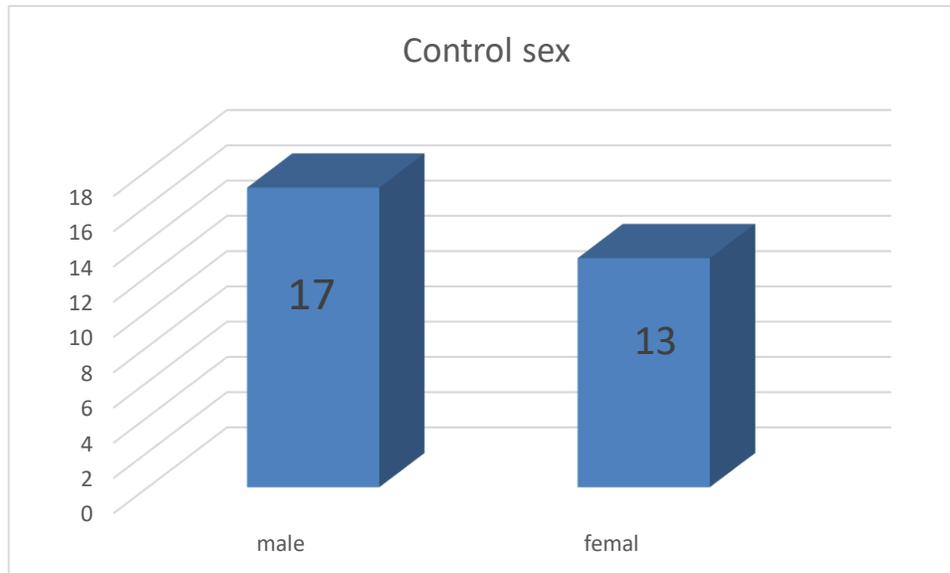
**Figure 6** shows mean age in both patients and control

In this study the mean  $\pm$ SD for age of the patients ( $52.68 \pm 13.9$ ) found to be non-significantly difference when compared with control group ( $49.6 \pm 14.8$ ), at the level of significantly ( $P=0.362$ ) by student T Test as shown in the figure 6



**Figure 7** shows sex distribution in patients group.

In this study the distribution of the patient's sex is equal, 25 patients are male and 25 patients are female as shown in the figure 7, while the distribution of the control's sex is unequal, 17 patients were male and 13 patients were female as shown in the figure 8.



**Figure 8** shows sex distribution in control group.

#### 4. Discussion

COVID has appeared a rapid spread of virus through direct transmission, with an average incubation period of 5-6 days [15]. Recent research has shown that 26% of patients received ICU care, and the mortality rate was less than 5% [16], [17]. The evidence suggests that early identification of critical illness and risk stratification management will reduce mortality and help alleviate the burden on insufficient medical resources. Recent studies have reported that low lymphocyte-to-C-reactive protein ratio and CRP could be predictive biomarkers for COVID-19 severity [18], [19]. Early diagnosis of patients with status have to worsen may help in get perfect care and optimizing the use of ICU [20]. CRP is an acute-phase protein responsible for the clearance of microorganism through interact to pathogens and help elimination by phagocytic cells. A positive correlation between CRP levels and lung lesions, kidney damage, and cardiac injury has been demonstrated; when the inflammation or tissue damage is resolved, CRP concentration decrease [21], [22]. In this study, a significantly higher CRP level ( $p=0.001$ ) was observed in severe COVID patients compared with the control group, as previously reported by other studies [23- 25]. As the first line of innate host defenses for get rid of viral infections, CRP might be attached to the secretion of inflammatory cytokines in severe patients and may lead to damage of various organs in infected patients [26], [27].

NLR is highly useful marker and defined by neutrophil count divided by lymphocyte count. The NLR index was to be an indicator of prognosis in patients with lung inflammation and tumors [28], [29]. The findings have proven the hypothesis of the present study and suggest that elevated NLR is a functional biomarker that affects the development of pneumonia in COVID patients. These findings are supported by previous studies that have the prognostic value of NLR in COVID patients [30], [31]. Neutrophil is a major type of the total white blood cell and can kill pathogens by releasing reactive oxygen species, producing effector molecules [32]. Thus, because of the human immune response and cytokines produced by lymphocyte and endothelial cells, elevated NLR values may be seen following COVID complication [33].

The findings of this study indicate that the integration of NLR and CRP may lead to improved prediction and is thus recommended as a valuable early marker to assess prognosis and evaluate the severity of clinical symptoms in COVID patients. Further research is needed to confirm the current findings and to compare the predictive ability of baseline NLR and the change in NLR under treatments.

**5. References**

- [1] Alhusam, . S.. (2021). Clinical Conditions and Risk Factors of *Acinetobacter Baumannii* Producing Metallo Beta-Lactamases Among Hospitalized Patients. *Journal of Scientific Research in Medical and Biological Sciences*, 2(4), 11-17. <https://doi.org/10.47631/jsrmb.v2i4.372>
- [2] Zhu H, Wei L, Niu P. The novel coronavirus outbreak in Wuhan, China. *Glob Health Res Policy*. 2020;5:1–3.
- [3] Zheng J. SARS-CoV-2: an emerging coronavirus that causes a global threat. *Int J Biol Sci*. 2020;16:1678.
- [4] Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. *Nat Microbiol*. 2020;5:536–44.
- [5] Zhang DX. SARS-CoV-2: air/aerosols and surfaces in laboratory and clinical settings. *J Hosp Infect*. 2020;105:577–9.
- [6] Mackenzie JS, Smith DW. COVID-19: a novel zoonotic disease caused by a coronavirus from China: what we know and what we don't. *Microbiol Aust*. 2020;41:45–50.
- [7] Polak SB, Van Gool IC, Cohen D, von der Thüsen JH, van Paassen J. A systematic review of pathological findings in COVID-19: a pathophysiological timeline and possible mechanisms of disease progression. *Mod Pathol*. 2020:1–11.
- [8] Luo X, Zhou W, Yan X, Guo T, Wang B, Xia H, et al. Prognostic value of C-reactive protein in patients with COVID-19. *Clin Infect Dis*. 2020:ciaa641.
- [9] Liu M, Gao Y, Yuan Y, et al. Efficacy and Safety of Integrated Traditional Chinese and Western Medicine for Corona Virus Disease 2019 (COVID-19): a systematic review and meta-analysis. *Pharmacol Res*. 2020;158:e104896.
- [10] Gao Y, Li T, Han M, Li X, Wu D, Xu Y, et al. Diagnostic utility of clinical laboratory data determinations for patients with the severe COVID-19. *J Med Virol*. 2020;92:791–6.
- [11] Hamza , R. T. ., Hamed , A. I. ., Hassan , B. B. B. ., & Ahmed , W. O. . (2021). Assessment of Thyroid Functions in Late Preterm Infants of Mothers on Antenatal Steroids. *Journal of Scientific Research in Medical and Biological Sciences*, 2(4), 18-29. <https://doi.org/10.47631/jsrmb.v2i4.365>
- [12] Ragab D, Salah Eldin H, Taeimah M, Khattab R, Salem R. The COVID-19 cytokine storm; what we know so far. *Front Immunol*. 2020;11:1446.
- [13] Potempa LA, Rajab IM, Hart PC, Bordon J, Fernandez-Botran R. Insights into the Use of C-Reactive Protein as a Diagnostic Index of Disease Severity in COVID-19 Infections. *Am J Trop Med Hyg*. 2020;103:561–3.
- [14] Feng Z, Yu Q, Yao S, Luo L, Duan J, Yan Z, et al. Early prediction of disease progression in 2019

novel coronavirus pneumonia patients outside Wuhan with CT and clinical characteristics. *MedRxiv*. 2020;36

[15] Russell CD, Parajuli A, Gale HJ, Bulteel NS, Schuetz P, de Jager CP, et al. The utility of peripheral blood leucocyte ratios as biomarkers in infectious diseases: A systematic review and meta-analysis. *J Infect*. 2019;78:339–48.

[16] Wang LS, Wang YR, Ye DW, Liu QQ. A review of the 2019 Novel Coronavirus (COVID-19) based on current evidence. *Int J Antimicrob Agents*. 2020:105948.

[17] Zhou M, Zhang X, Qu J. Coronavirus disease 2019 (COVID-19): a clinical update. *Front Med*. 2020;2:1–10.

[18] Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020;395:1033–4.

[19] Ponti G, Maccaferri M, Ruini C, Tomasi A, Ozben T. Biomarkers associated with COVID-19 disease progression. *Crit Rev Clin Lab Sci*. 2020;57:389–99.

[20] Kermali M, Khalsa RK, Pillai K, Ismail Z, Harky A. The role of biomarkers in diagnosis of COVID-19—A systematic review. *Life Sci*. 2020;254:117788.

[21] Wang L. C-reactive protein levels in the early stage of COVID-19. *Med Mal Infect*. 2020;50:332–4.

[22] Liang WH, Liang HR, Ou LM, et al. Development and validation of a clinical risk score to predict the occurrence of critical illness in hospitalized patients with COVID-19. *JAMA Intern Med*. 2020;180:e202033.

[1] 21. Tan C, Huang Y, Shi F, Tan K, Ma Q, Chen Y, et al. C-reactive protein correlates with computed tomographic findings and predicts severe COVID-19 early. *J Med Virol*. 2020;92:856–62.

[23] Chen W, Zheng KI, Liu S, Yan Z, Xu C, Qiao Z. Plasma CRP level is positively associated with the severity of COVID-19. *Ann Clin Microbiol Antimicrob*. 2020;19:18.

[24] Li Q, Ding X, Xia G, Chen HG, Chen F, Geng Z, et al. Eosinopenia and elevated C-reactive protein facilitate triage of COVID-19 patients in fever clinic: a retrospective case-control study. *Clin Med*. 2020;23:100375.

[25] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020;382:1708–20.

[26] Feng X, Li S, Sun Q, Zhu J, Chen B, Xiong M, Cao G. Immune-Inflammatory Parameters in COVID-19 Cases: A Systematic Review and Meta-Analysis. *Front Med*. 2020;7:301

[27] 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 disease severity predictors. *Emerg Microbes Infect*. 2020;9:1123–30.

- [28] Ciccullo A, Borghetti A, Dal Verme LZ, Tosoni A, Lombardi F, Garcovich M, et al. Neutrophil-to-lymphocyte ratio and clinical outcome in COVID-19: a report from the Italian front line. *Int J Antimicrob Agents*. 2020;56:106017.
- [29] Liu J, Liu Y, Xiang P, Pu L, Xiong H, Li C, et al. Neutrophil-to-lymphocyte ratio predicts critical illness patients with 2019 coronavirus disease in the early stage. *J Transl Med*. 2020;18:206.
- [30] Liu Y, Du X, Chen J, Jin Y, Peng L, Wang HH, et al. Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19. *J Infect*. 2020;81:e6–12.
- [31] Sahu BR, Kampa RK, Padhi A, Panda AK. C-reactive protein: a promising biomarker for poor prognosis in COVID-19 infection. *Clin Chim Acta*. 2020;509:91–4.
- [32] Yang AP, Liu JP, Tao WQ, Li HM. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. *Int Immuno Pharmacol*. 2020;84:106504.
- [33] Catanzaro M, Fagiani F, Racchi M, Corsini E, Govoni S, Lanni C. Immune response in COVID-19: addressing a pharmacological challenge by targeting pathways triggered by SARS-CoV-2. *Sig Transduct Target Ther*. 2020;5:84.
- [34] Sharaf , M. A. ., Hashem, H. E., & Ahmed , W. O. (2021). Simultaneous Use of Factor XIII and Fibrin Degradation Products in Diagnosing Early Cases of NEC and Neonatal SEPSIS. *Journal of Scientific Research in Medical and Biological Sciences*, 2(4), 1-10. <https://doi.org/10.47631/jsrmb.v2i4.346>
- [35] Yufei Y, Mingli L, Xuejiao L, Xuemei D, Yiming J, Qin Q, et al. Utility of the neutrophil-to-lymphocyte ratio and C-reactive protein level for coronavirus disease 2019 (COVID-19) *Scand J Clin Lab Invest*. 2020;14:1–5.