PROGNOSTIC ROLE OF C - REACTIVE PROTEIN (CRP) IN CORONAVIRUS DISEASE 2019 (COVID-19) INFECTED PATIENT: A CASE REPORT

Dr. Aruna Kumar Ch (M. Pharm PhD)[a*], Dr GMV Kasiram MD(Pulmonary Medicine)[a], Dr. P. Krishna Sarvanth, MBBS, DNB (Orthopedic Surgeon)[a], Dr. Suryadevara Vidyadhara (M. Pharm PhD)[b], Dr.S.Ramya Krishna(M. Pharm PhD)[b], Dr.D.Sandeep (M. Pharm PhD)[c], R Sai Reshma (M. Pharm)[c]

Abstract

In this article, we described a case report of a hospitalized patient with coronavirus disease 2019 (COVID-19) who had an elevated levels of C - reactive protein (CRP), which was later been identified as one of the diagnostic parameters that hasan established direct relationship with the disease severity during the course of the pharmacotherapy.

Keywords: C - reactive protein (CRP), COVID-19

[a]Department of Physiology and Pharmacology, Chebrolu Hanumaiah Institute of Pharmaceutical Sciences, Chowdavaram, Guntur, Pincode-522013, India

[a]Aditya Multi Speciality Hospital, Guntur, Andhra Pradesh, Pincode-522001, India

[b]Department of Pharmaceutics, Chebrolu Hanumaiah Institute of Pharmaceutical Sciences, Chowdavaram, Guntur, Pincode-522013, India

[c]Department of Physiology and Pharmacology, Chebrolu Hanumaiah Institute of Pharmaceutical Sciences, Chowdavaram, Guntur, Pincode-522013, India

[*]**Corresponding Author:** Dr. Aruna Kumar Ch

[*]Department of Physiology and Pharmacology, Chebrolu Hanumaiah Institute of Pharmaceutical Sciences, Chowdavaram, Guntur, Pincode-522013, India

DOI:

Introduction

The corona virus disease 2019 (COVID-19) is a global pandemic infectious disease caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), demographics shows that it affects human populations in different ways, majority are developing acute illness with common symptoms such as drug cough, fever and tiredness, other less common symptoms include sore throat, diarrhea, headache, conjunctivitis, but some people are developing serious symptoms shortness of breath, chest pain, loss of speech or movement [1]. It has been estimated that on an average it will take 6-14 days to show symptoms when some is infected with COVID-19 [2]. There are many ongoing clinical trials evaluating the effectiveness of available single and combination therapies with indirectly active SARS-CoV-2 therapeutics, such as antivirals (remdesivir, favipiravir) and antibiotics, vitamins C supplements that have emerged as potential therapies [3]. In critical patients with respiratory failure, remdesvir and convalescent plasma may be considered; access to these therapies may, however, be limited [4]. In patients who have evidence of cytokine release syndrome, interleukin-6 (IL-6) antagonists may be used (CRS). Corticosteroids should be avoided unless there is evidence that they are used for refractory septic shock, acute respiratory distress syndrome (ARDS) or some other persuasive sign [5]. At this time, ACE inhibitors and ARBs should not be discontinued and ibuprofen for fever may be used. In the absence of well-established biomarker for the estimation of COVID-19 severity, the identification of a development stage to combat COVID-19 has been especially remarkable [6]. The aim of this case study is to add to the existing knowledge available on COVID-19 diagnostic parameters that helps health care professionals. Globally continuous efforts are being made by scientific research groups to identify suitable biomarker for predicting the COVID-19 severity as at early stages of the infection [7]. Furthermore, there were significant number of biomarkers spotted as key pathogenic drivers in the progression of COVID-19, such as hematological parameters (lymphocyte (L) count, neutrophil-lymphocyte ratio (NLR), neutrophil (N) count), C- reactive protein (CRP), procalcitonin (PCT), erythrocyte sedimentation rate (ESR), creatine kinase (CK), interleukin (IL)-6, D-dimer, aspartate aminotransferase (AST), and troponin respectively [8]. Among all, CRP has gained more attention in the general clinical diagnostic laboratories as a promising biomarker for assessing disease lethality, based on an assumption that the CRP levels continued to maintain high in significant number of patients who got infected and died due to corona virus disease 2019 (COVID-19) [9]. In addition, there is a positive correlation established lung lesions and CRP levels which directly point out the disease severity [10]. This has also been supported with a clinical observation that before computed tomographic (CT) findings, that the CRP levels in severe COVID-19 patients significantly increased at the initial stage. Notably, CRP has associated with disease severity development, predicted in an early severe COVID-19 patient's profile [11]. A study states CRP must be measured for the early detection of patients who need more respiratory support to avoid any complications arise from the poor prognosis [12]. The molecular mechanistic studies reporting that the over expression of cytokines which are human host defensive chemical mediators to fight against pathogenic virus, might be responsible for the damage of lung tissues since over stimulation may lead to self- destruction [13-15]. Consequently, CRP levels increases, induced by over expressed cytokines. In addition, there are several co morbidities also reported based on the degree of severity of the infection [16-18]. Although, CRP is a non-COVID-19 specific biomarker, there is a direct correlation well established between infection and inflammation due to tissue injury [19-20]. The average concentrations of CRP (30–50 mg/L) beyond this level indicates high severity of the disease, which is directly associated with the lung damage and also poor prognosis [21-22]. CRP levels can reflect disease changes, particularly for patients in critical condition who could not be referred to other services in emergency [23]. We have also noticed a similar observation in a case study which was used to understand the severity of the disease, follow-up on the therapeutic monitoring [24-25]. The case detailed in this article projects the significance of CRP biomarker to understand the patient healing progression and response to the pharmacotherapy.

Case

The patient case studied was a 29-year-old young man adult male with no history of tuberculosis. He was admitted to and hospitalized in the Aditya Multi Speciality Hospital on 12 December 2020, on the same day of the onset of common symptoms related to COVID-19 infection. Physical examination of cardiovascular, abdominal and neurological characteristics was that these were normal. The patient experienced symptoms such as fever, cough, sputum production, dizziness, weakness, chest tightness and dyspnoea

respectively as shown in the Table 1. On the first day of admission, High-resolution computed tomography (HRCT) scans revealed that the imaging features of COVID-19 pneumonia are present (Figure 2), bilateral multifocal, multilobar peripheral ground glass opacities of rounded morphology which are signs of pneumonitis, with no evidence of pleural effusion, pleural thickening, abnormal air fluid levels, esophageal abnormalities, domes of diaphragm are normal and soft tissue and bony cage is normal. Laboratory results showed serious elevation of CRP levels (174 mg/L) on the first day of admission 12th December 2020 (Table 2, Figure 1). In addition, chest radiographs were abnormal with air-space shadowing such as ground-glass opacities, focal consolidation and patchy consolidation in both lungs. Chest X-ray figured out the traces of mono-lateral pneumonia (Figure 3). HRCT scan was used as a Diagnostic tool to identify the severity of infection for SARS-CoV-2 and treatment was initiated as per the pharmacotherapeutic protocol developed in the hospital. A combination of antiviral and antibiotic therapy was administered and further accompanied with vitamin supplements, the patient exhibited respiratory recovery. The patient recovery from the diseased symptoms and the changes in the levels of CRP has been clearly projected in the biochemical profile as shown in Figure 1. The patient clinical diagnostic reports showed improvement in CPR levels, bringing down to normal range from day by day; on the 8th day of admission 19th December 2020, the patient CRP levels has stabilized at 21.9 mg/L which is falling under normal reference range based on the studies reported. Successively, with continued medical supervision, on the 14th day of symptoms (25 December 2020) the Computed tomography (CT) of the chest report shows no features associated with pneumonia (Table 3); the trachea, carina, main bronchi appear patent and normal in caliber; the parenchyma of both lungs appears normal; no mass lesions; and no plural effusions. The patient does not experience any symptoms associated with COVID-19, based on the clinical reports the patient has been discharged in normal health.

Table 1. Baseline characteristics and supporting therapy for the patient infected with COVID-19 pneumonia.

Characteristic	**Patient**
Age (years)	29
Sex	Male
Date of illness onset	12 December 2020
Date of admission	12 December 2020
Signs and symptoms	Present
Fever	Yes
Body temperature	High
Cough	Yes
Sputum production	Yes
Dizzy	Yes
Weakness	Yes
Chest tightness	Yes
Lung involvement	Yes
Dyspnoea	Yes
Oxygen therapy	Mechanical ventilation
Antiviral therapy	Yes
Antibiotic therapy	Yes
Antioxidant therapy	Yes

Table 2. Biochemical profile of the in-patient infected with COVID-19 (SARS-CoV-2) pneumonia.

		Observed Values								
			12-Dec	**13-Dec**	**14-Dec**	**15-Dec**	**16-Dec**	**17-Dec**	**18 Dec**	**19-Dec**
	Reference Range	**Units**	**Test 1**	**Test 2**	**Test 3**	**Test 4**	**Test 5**	**Test 6**	**Test 7**	**Test 8**
CBP (Complete Blood Picture)										
Hemoglobin (Hb)	Male : 13.0 – 17.0 Female: 11 – 15.0	gms %	15.8	15.2	14.2	13.6	14.9	13.8	13.9	14.3
Total Red Blood Cell (RBC) Count	3.5 - 5.5	Millions / cu.	6.6	6.1	5.6	5.6	6.2	5.8	5.7	6
Total Leucocyte or White Blood Cell (WBC) Count	4,000 - 10,000	cells/cu.mm	8700	3200	10,700	8500	7,700	7,400	10,400	11,700
Differential Count										

Neutrophils (N)	40 - 70	%	80	71	81	85	87	85	83	81
Lymphocytes (L)	20 - 45	%	15	26	14	10	9	9	08	12
Eosinophils (E)	1 - 6	%	4	2	4	4	3	4	07	5
Monocytes (M)	2 - 10	%	1	1	1	1	1	2	02	2
Basophils (B)	0 - 1	%	0	0	0	0	0	0	0	0
Platelet Count (PC)	1.5 - 4.5	Lakhs/cumm	276000	259000	420000	376000	387000	378000	349000	2,91,000
Packed Cell Volume (PCV)	37 - 54	%	52	48	43	45	48	47	45	46
Mean Cell Volume (MCV)	78 - 94	fL	78	78	78	80	77	81	79	78
M. C. H (Mean Corpuscular Hemoglobin)	27 - 32	Pg	23	23	23	23	23	23	24	23
M.C.H.C (Mean Corpuscular Hemoglobin Concentration)	30 - 36	gms %	30	30	30	29	30	29	30	30
C-Reactive Protein (CRP)	0 - 5	mg/L	174	215	>211.9	150.1	85.8	51.8	34.1	21.9
D-DIMER (DD)	< 0.5	mg/L	0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1

Figure 1. Biochemical profile of the in-patient infected with COVID-19 (SARS-CoV-2): (a) C- Reactive Protein (CRP); (b) Hemoglobin (Hb); (c) Total Red Blood Cell (RBC); (d) Neutrophils (N); (e) Lymphocytes (L); (f) Monocytes (M); (g) Platelet Count (PC); (h) Mean Cell Volume (MCV); (i) Mean Corpuscular Hemoglobin (MCH); (j) Mean Corpuscular Hemoglobin Concentration (MCHC); (k) Packed Cell Volume (PCV); (l) Eosinophils (E); (m) Total Leucocyte or White Blood Cell (WBC).

Figure 2. Chest X-ray findings of the patient with COVID-19 pneumonia. (A) On admission (day 1 of Hospitalization, symptom's onset). (B) On discharge (day 14 of hospitalization, symptom's end).

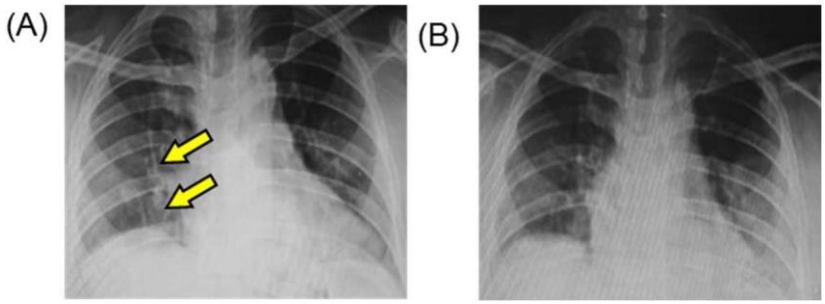

Figure 3. Radiological findings on chest high-resolution computed tomography (HRCT) of the patient with COVID-19 pneumonia. (A) On admission (day 1 of Hospitalization, symptom's onset). (B) On discharge (day 14 of hospitalization, symptom's end).

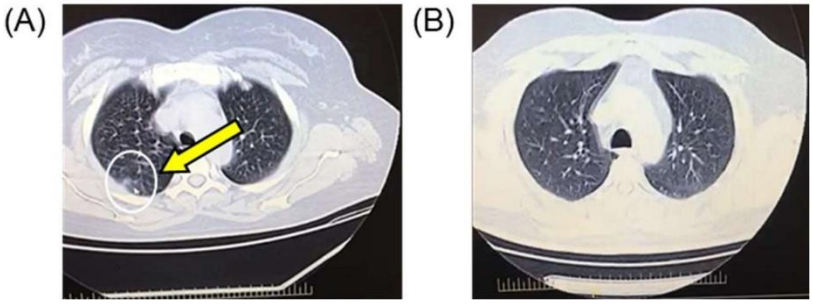

Table 3. Radiological findings on chest high-resolution computed tomography (HRCT) of the patient with COVID-19 pneumonia. (A) On admission (day 1 of Hospitalization, symptom's onset). (B) On discharge (day 14 of hospitalization, symptom's end).

Classification	Suspicion	Chest HRCT Findings for the Interpretation	Patient report (Day 1)	Patient report (Day 14)
CO-RADS 1	No	Normal or Non-infectious abnormalities	-	Indicator
CO-RADS 2	Low	Abnormalities consistent with infections other than COVI-19	-	-
CO-RADS 3	Indeterminate	Unclear whether COVID-19 is present	-	-
CO-RADS 4	High	Abnormalities suspicious for COVID-19	-	-
CO-RADS 5	Very High	Typical COVID-19	Indicator	-
CO-RADS 6	PCR+	If accessible	-	-

In summary, this case report could support the existing information associated with the role of CRP as a prognostic indicator in disease progression and severity of COVID-19.

References

1. Guo YR, Cao QD, Hong ZS, Tan YY, Chen SD, Jin HJ, Tan KS, Wang DY, Yan Y. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak–an update on the status. Military Medical Research. 2020 Dec;7(1):1-0.
2. Hou C, Chen J, Zhou Y, Hua L, Yuan J, He S, Guo Y, Zhang S, Jia Q, Zhao C, Zhang J. The effectiveness of quarantine of Wuhan city against the Corona Virus Disease 2019 (COVID-19): A well-mixed SEIR model analysis. Journal of medical virology. 2020 Jul;92(7):841-8.
3. Nitulescu GM, Paunescu H, Moschos SA, Petrakis D, Nitulescu G, Ion GN, Spandidos DA, Nikolouzakis TK, Drakoulis N, Tsatsakis A. Comprehensive analysis of drugs to treat SARS-CoV-2 infection: Mechanistic insights into current COVID-19 therapies. International journal of molecular medicine. 2020 Aug 1;46(2):467-88.
4. Phua J, Weng L, Ling L, Egi M, Lim CM, Divatia JV, Shrestha BR, Arabi YM, Ng J, Gomersall CD, Nishimura M. Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations. The Lancet

Respiratory Medicine. 2020 May 1;8(5):506-17.
5. Song Y, Zhang M, Yin L, Wang K, Zhou Y, Zhou M, Lu Y. COVID-19 treatment: close to a cure?–a rapid review of pharmacotherapies for the novel coronavirus. International journal of antimicrobial agents. 2020 Jul 4:106080.
6. Böhm M, Frey N, Giannitsis E, Sliwa K, Zeiher AM. Coronavirus Disease 2019 (COVID-19) and its implications for cardiovascular care: expert document from the German Cardiac Society and the World Heart Federation. Clinical Research in Cardiology. 2020 Jan 1:1-4.
7. Holmes EA, O'Connor RC, Perry VH, Tracey I, Wessely S, Arseneault L, Ballard C, Christensen H, Silver RC, Everall I, Ford T. Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science. The Lancet Psychiatry. 2020 Apr 15.
8. Ponti G, Maccaferri M, Ruini C, Tomasi A, Ozben T. Biomarkers associated with COVID-19 disease progression. Critical reviews in clinical laboratory sciences. 2020 Aug 17;57(6):389- 99.
9. Sahu BR, Kampa RK, Padhi A, Panda AK. C-reactive protein: a promising biomarker for poor prognosis in COVID-19 infection. Clinica chimica acta. 2020 Oct 1;509:91-4.
10. Wang L. C-reactive protein levels in the early stage of COVID-19. Medecine et maladies infectieuses. 2020 Jun 1;50(4):332-4.
11. Tan C, Huang Y, Shi F, Tan K, Ma Q, Chen Y, Jiang X, Li X. C-reactive protein correlates with computed tomographic findings and predicts severe COVID-19 early. Journal of medical virology. 2020 Jul;92(7):856-62.
12. Poggiali E, Zaino D, Immovilli P, Rovero L, Losi G, Dacrema A, Nuccetelli M, Vadacca GB, Guidetti D, Vercelli A, Magnacavallo A. Lactate dehydrogenase and C-reactive protein as predictors of respiratory failure in CoVID-19 patients. Clinica chimica acta. 2020 Oct 1;509:135-8.
13. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, Yu T. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The lancet. 2020 Feb 15;395(10223):507- 13.
14. Mo P, Xing Y, Xiao Y, Deng L, Zhao Q, Wang H, Xiong Y, Cheng Z, Gao S, Liang K, Luo M. Clinical characteristics of refractory COVID-19 pneumonia in Wuhan, China. Clinical Infectious Diseases. 2020 Mar 16.
15. Gao Y, Li T, Han M, Li X, Wu D, Xu Y, Zhu Y, Liu Y, Wang X, Wang L. Diagnostic utility of clinical laboratory data determinations for patients with the severe COVID-19 [published online March 17, 2020]. J Med Virol. doi.;10.
16. Wark PA, Lau R, Norat T, Kampman E. Magnesium intake and colorectal tumor risk: a case- control study and meta-analysis. The American Journal of Clinical Nutrition. 2012 Sep 1;96(3):622-31.
17. Yan D, Wei L, Kui L, Yuan-Yuan F, Jin S. zhou Ling, Wang Ke, Leng Fan, Wei Shuang, Chen Lei, Liu Hui-Guo. Clinical characteristics of fatal and recovered cases of coronavirus disease 2019 (COVID-19) in Wuhan, China: a retrospective study. Chin Med J. 2020;1.
18. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. New England journal of medicine. 1999 Feb 11;340(6):448-54.
19. Vasileva D, Badawi A. C-reactive protein as a biomarker of severe H1N1 influenza. Inflammation Research. 2019 Jan;68(1):39-46.
20. Huang KJ, Su IJ, Theron M, Wu YC, Lai SK, Liu CC, Lei HY. An interferon-γ-related cytokine storm in SARS patients. Journal of medical virology. 2005 Feb;75(2):185-94.
21. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The lancet. 2020 Mar 28;395(10229):1054-62.
22. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. New England journal of medicine. 1999 Feb 11;340(6):448-54.
23. Shine B, De Beer FC, Pepys MB. Solid phase radioimmunoassays for human C-reactive protein. Clinica chimica acta. 1981 Nov 25;117(1):13-23.
24. Pepys MB, Hirschfield GM. C-reactive protein: a critical update. The Journal of clinical investigation. 2003 Jun 15;111(12):1805-12.
25. Vigushin DM, Pepys MB, Hawkins PN. Metabolic and scintigraphic studies of radioiodinated human C-reactive protein in health and disease. The Journal of clinical investigation. 1993 Apr 1;91(4):1351-7.