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Original Article

Radiologic Severity Index (RSI) Score in COVID-19 Patients After Administration of Remdesivir: A Study on High CRP and D-dimer Levels in a Group of Patients

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Abstract

Background : The COVID-19 pandemic has high mortality and morbidity. The lungs are the main target organ with a variety of symptoms ranging from asymptomatic to respiratory failure. Chest X-ray plays an important role in diagnosis, management, and prognosis. One of the chest X-ray assessment systems used is the Radiology Severity Index (RSI). Serum CRP and D-dimer levels can also be used to determine the severity of COVID-19. The aimsof this study was to examine changes in RSI scores after remdesivir therapy in COVID-19 patients with high CRP and D-dimer values.
Methods : A prospective cohort study of 64 COVID-19 patients at Dr. Kariadi Hospital Semarang from July 2020 to July 2021. Each consisted of 32 patients with high CRP (>5 mg/L) and D-dimer (>500 ng/mL) levels. Patients were given Remdesivir 200 mg therapy on day 1, followed by 100 mg/day until day 9. Chest X-rays were performed before and on day 7 after initial therapy. Patients with CHF, malignancy, autoimmune, pulmonary TB, interstitial lung disease and receiving azythromycin therapy were excluded from the study. Correlation analysis between variables was performed using the Spearman rho test and comparison test between groups. Significant results if p <0.05.
Results : There was a significant decrease in the RSI score of COVID-19 patients with high CRP and D-dimer levels after therapy, from 21.97±16.88 and 21.22±19.92 to 15.69±14.12 and 15.78±15.69, respectively (p<0.001). There was a weak significant relationship between high CRP levels and pre-therapy RSI scores (r=0.473, p=0.006) and high D-dimer levels and post-therapy RSI scores (r=0.362, p=0.041).
Conclusion : Remdesivir provides a significant correlation in the form of a decrease in RSI scores in COVID-19 patients with high CRP or D-dimer levels.

Keywords : COVID-19, CRP, D-Dimer, RSI Score, Remdesivir

INTRODUCTION

Coronavirus Disease 2019 (COVID-19) was declared a pandemic by the World Health Organization (WHO) on March 11, 2020 due to the rapidity and scale of the disease's transmission. As of April 6, 2021, WHO has recorded 131,309,792 confirmed cases of COVID-19, with a death toll of 2,854,276.2 cases. The clinical manifestations of COVID-19 primarily attack the lungs, and have a wide impact on other organs of the body, such as the cardiovascular, gastrointestinal system, liver, kidneys, eyes, and skin. The most common clinical manifestations are cough, shortness of breath, fever, and sore throat. In severe cases, acute respiratory distress syndrome (ARDS), respiratory failure, and death are found. Imaging modalities play an important role in the diagnosis and management of COVID-19. Chest X-ray (CXR) is considered the first-line imaging modality for the initial triage of suspected COVID-19 cases. Although CXR is considered insensitive (CXR sensitivity is only 56%) in the early stages, CXR can be used to monitor clinical response and disease severity.[1–3]

A systematic review by Vidali *et al*., stated that most COVID-19 patients showed consolidation (68%) and ground glass opacity (GGO) (48%) with bilateral lung involvement and mostly distributed in the lower and peripheral lungs.[4] There are many CXR scoring systems to determine the severity of COVID-19, one of which is the Radiologic Severity Index (RSI). This scoring system interprets CXR changes more complexly with higher scores correlating with more severe clinical course and higher mortality.[5,6]

Characteristics of severe COVID-19 is the presence of a systemic inflammatory response, such as increased C-reactive protein (CRP) (58.3–60.7%) and increased D-dimer (46.6%). CRP levels can increase in patients with positive chest X-rays and those with severe disease, lung damage, and poor prognosis.[7] Its concentration is not affected by age, gender, or physical condition.[8] Kadek *et al*., found that confirmed COVID-19 patients with severe and critical degrees had the highest mean CRP values (133 mg/L, p <0.001) with an AUC value of 0.88 (p <0.001, 95% CI: 0.8290.948) to determine mortality.[9] In evaluating and diagnosing severe pulmonary infection, CRP levels >5 mg/L can be found.[8]

Abnormal coagulation function is one of the factors thought to be associated with the development of disease due to SARS-CoV-2 infection, which is characterized by increased D-dimer levels >500 ng/mL. D-dimer levels tend to be higher in patients with severe and critical cases than in patients with mild or moderate cases.[10] A study by Marco Francone *et al*., using CT scores to assess the level of lung involvement in patients with COVID-19 found that there was a statistically significant relationship between CT scores and D-dimer levels.[3]

One of the drugs under investigation for the treatment of COVID-19 is Remdesivir. Remdesivir is a direct-acting nucleotide-analog prodrug that inhibits ribonucleic acid (RNA) by incorporating triphosphate and interfering with the activity of viral RNA polymerase.[11] Kate *et al*., identified 55 patients treated with remdesivir for COVID-19 showed a significant decrease in CRP levels after administration of remdesivir in patients who remained non-intubated during the study period.[12]

To date, there has been little research on radiological images and biomarkers that can be used to predict the severity and death of COVID-19 patients using D-dimer and CRP levels. Reliance on CT scans places a large burden on the radiology department and this makes CXR the modality of choice. Therefore, researchers used CXR modality to describe changes in RSI scores after administration of remdesvir in COVID-19 patients with high CRP and D-dimer values.

METHODS

A prospective cohort study conducted at the Radiology Department of Dr. Kariadi Hospital Semarang, from July 2020 to July 2021 using data collected through electronic medical records. A total of 64 different patients were declared positive for COVID-19 based on clinical and laboratory (positive PCR) with age >18 years. There were 32 different patients with high CRP levels (> 5 mg/L) and 32 patients with high D-dimer levels (> 500 ng/mL). All patients received remdesivir therapy of 200 mg on the first day followed by 100 mg/day until day 9 based on disease severity and clinical response to therapy. CXR examination was performed before starting therapy and day 6 or 7 after initial Remdesivir therapy and the RSI score was calculated. Patients who received azythromycin therapy, and comorbid CHF, CKD, history of malignancy, autoimmune, pulmonary TB, or interstitial lung disease were excluded from the study.

The RSI scoring system was conducted by researchers by assessing 2 main variables from chest X-ray, namely lesion pattern and lesion area volumetrically where the right and left lung fields were each divided into 3 parts; upper zone (up to the carina), middle zone (below the carina to the upper limit of the inferior pulmonary vein), and lower zone (below the inferior pulmonary vein). The lesion pattern was divided into 3 value categories; 1 for normal lungs, 2 for GGO images, and 3 for consolidation images. The volumetric area was divided into 5 area categories; 0%, 1 for area 124%, 2 for area 2549%, 3 for area 5074%, 4 for area 75100%. RSI was obtained by multiplying the lesion pattern value and its volumetric area in each zone, with a total value between 172.[13]

Correlation analysis between variables was performed using the non-parameter Spearman rho test and the difference test between the high CRP group and

the high D-dimer group using the chi square test if the data distribution was normal or Wilcoxon if the data distribution was not normal. Data were declared significant if they obtained a p value <0.05.

RESULTS

In this study, the average age of patients was 52.95 ± 15.10 years with an age range of 21 to 87 years. The average levels of CRP and D-dimer were 11.95 ± 8.79 mg/L and 2389.69 ± 3709.76 ng/mL, respectively. There was a decrease in the average overall RSI score post-remdesivir therapy compared to pre-remdesivir therapy (15.73 ± 14.12 vs. 21.59 ± 18.32) for 24 patients in the high CRP group and 27 patients in the high D-dimer group, respectively. Further patient characteristics are described in Table 1.

Based on the results of the Spearman Rho correlation analysis in the high CRP group (Table 2), a significant weak correlation was found between high CRP levels and pre-therapy RSI score (r = 0.473, p = 0.006) and a non-significant weak correlation between high CRP levels and post-therapy RSI score and delta RSI score (high CRP with post-therapy RSI score r = 0.416, p = 0.18 and high CRP with Delta RSI score r = 0.273, p = 0.130). There was no correlation between age and high CRP

TABLE 1
Characteristics of research subjects

Variable	Mean ± SD	Median (min – max)	Amount (%)
Age (year)	52.97 ± 15.10	57 (21 87)	
Male			36 (56%)
Female			28 (44%)
CRP level (mg/L)	11.95 ± 8.79	8.63 (5.16 – 38.75)	
D-dimer level (ng/mL)	2389.69 ± 3709.76	1045 (520 – 20000)	
RSI score			
Pre- therapy	21.59 ± 18.32	20.5 (0 – 66)	
Post- therapy	15.73 ± 14.12	14.00 (0 – 54)	
Delta RSI score	5.85 ± 8.93	4.5 (-24 – 34)	
High CRP group			
Age (year)	52.97 ± 15.10	57 (21 – 87)	
Gender			
Male			17 (53.1%)
Female			15 (46.9%)
Pre therapy RSI *score*	21.97 ± 16.88	24.5 (0 – 52)	
Post therapy RSI *score*	15.69 ± 14.12	14 (0 – 47)	
Delta RSI *score*	6.28 ± 8.39	4.5 (-9 – 37)	
High D-dimer level			
Age (year)	53.34 ± 14.22	54 (18 – 73)	
Gender			
Male			19 (59.4%)
Age (year)			13 (40.6%)
Pre therapy RSI *score*	21.22 ± 19.92	15 (0 – 66)	
Post therapy RSI *score*	15.78 ± 15.69	12 (0 – 54)	
Delta RSI *score*	5.44 ± 9.56	4,5 (-24 – 34)	

*Delta = the difference between pre- and post-therapy RSI scores

TABLE 2
Spearman Rho correlation test results for the high CRP group

Variable	CRP	Pre RSI	Post RSI	Delta RSI
Age				
Correlation coefficient	0.119	0.186	0.160	0.163
P value	0.515	0.308	0.382	0.373
CRP				
Correlation coefficient		0.416	0.416	0.273
P value		0.006*	0.018	0.130
Pre RSI				
Correlation coefficient			0.906	0.578
P value			<0.001*	0.001*
Post RSI				
Correlation coefficient				0.271
P value				0.134

Note: *Significant (p <0.05)

TABLE 3
Spearman Rho correlation test results for the high D-dimer group

Variable	D-dimer	Pre RSI	Post RSI	Delta RSI
Age				
Correlation coefficient	-0.227	-0.085	-0.223	0.122
P value	0.212	0.643	0.219	0.607
CRP				
Correlation coefficient		0.331	0.362	0.200
P value		0.064	0.041*	0.273
Pre RSI				
Correlation coefficient			0.887	0.747
P value			<0.001*	<0.001*
Post RSI				
Correlation coefficient				0.439
P value				0.012*

Note: *Significant (p <0.05)

levels in COVID-19 patients, pre- and post-therapy RSI scores, and differences in RSI scores. The Wilcoxon test found a significant decrease in RSI score after remdesivir therapy in the high CRP group (21.97 ± 16.88 vs. 15.69 ± 14.12, p <0.001).

Based on the Spearman Rho correlation test in the high D-dimer group (Table 3), a low, insignificant correlation was obtained between high D-dimer levels and the RSI score pre-remdesivir therapy (r = 0.331, p = 0.064). There was no correlation between high D-dimer levels and the delta RSI score (r = 0.200, p = 0.273). The age variable was inversely correlated with pre- and post-therapy RSI values, delta RSI scores, and D-dimer levels. There was a significant decrease in the

RSI score after remdesivir administration in the high D-dimer group (21.22 ± 19.92 vs. 15.78 ± 15.69, p <0.001). Furthermore, the Fisher Exact test was performed for the difference in delta RSI scores in the high CRP and high D-dimer groups. There was no significant difference (p = 0.536) in the delta RSI score between the two groups. This shows that the therapeutic effect of remdesivir is similar in COVID-19 patients in both groups with high CRP and high D-dimer.

DISCUSSION

COVID-19 is a disease with high mortality and morbidity, especially in the elderly population and patients with comorbidities. Host factors can also affect susceptibility to infection and disease progression. The elderly and people with comorbidities are susceptible to SARS-CoV-2 and tend to develop into critical conditions. Comorbidities that increase susceptibility include hypertension, chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), and cardiovascular disease. This was shown in this study, with a mean total patient age of 52.95 ± 15.10 years and age 21–87 years. Both groups of high CRP and high D-dimer indicated more severe disease conditions in COVID-19 patients and in older adult patients due to poorer immune system conditions compared to younger patients.[14–16] The gender characteristics of patients were similar, with 36 (56%) male patients and 28 (44%) female patients. COVID-19 disease can attack all genders, but women in East Asian populations are known to express higher ACE2 receptors and are therefore more susceptible to SARS-CoV-2 infection.[17]

C-reactive protein (CRP) is a protein produced by adipocytes and liver, which is associated with IL-1, IL-6, and TNF.[9] Its increase can occur in cases of hypertension, diabetes mellitus, and severe disease, so these confounding factors have been excluded from the study. The mean CRP level of patients after diagnosis was 11.95 ± 8.79 mg/L with a range of 5.16 to 38.75 mg/L. This result is lower than the results of the study by Sunil *et al*., in COVID-19 patients who had a mild CTSS picture of 21.4 (6.6 –35.4) mg / L, but there was an increase in CRP levels proportional to the increase in the degree of CTSS.[7] In the study by Geetika *et al*., CRP levels of 10.70 ± 11.08 mg / L were found to be significantly correlated with the severity as measured by the RSI score.[18] A significant decrease in the pre-therapy RSI score value was found from 21.97 ± 16.88 mg / L to 15.69 ± 14.12 mg / L post-therapy (p <0.001). Remdesivir has the effect of reducing the severity of patients in the form of a decrease in the RSI score in the high CRP group. Unfortunately, this study did not calculate the post-therapy CRP levels, so it is recommended to calculate the post-therapy CRP levels in further studies.

D-dimer is one of the markers of active coagulation and thrombin formation that can be used to assess the progression of SARS-CoV-2 disease. The average D-dimer level was 2389.69 ± 3709.76 ng/mL with a range of 1045 (520–20000) ng/mL. This result is much higher than the study by Herdiman *et al*., which had 58.4% of moderate clinical COVID-19 cases, obtained a range of D-dimer levels of 300-1600 ng/mL.[17] In this study, administration of remdesivir decreased the RSI score in the high D-dimer group as evidenced by a significant decrease in the pre-therapy RSI score of 21.22 ± 19.92 compared to post-therapy 15.78 ± 15.69 (p<0.001). In the study by Herdiman *et al*., it was found that increased D-dimer levels also increased the severity of radiological images (p<0.001). The presence of coagulopathy is associated with the severity of lung parenchymal involvement in COVID-19 which is caused by coagulation dysregulation due to excess inflammatory mediators. In the study by Amela *et al*., which used the CXR assessment system with the Brixia score, a significant positive correlation was found between D-dimer levels and the Brixia score (r = 0.45, p <0.001).[19]

There was no significant difference in RSI score between the high CRP and D-dimer groups (p=0.536). This may be due to increased CRP levels also in the high D-dimer group, and vice versa, considering that both of these markers increase in moderate to severe COVID-19 cases. It is known that D-dimer levels will exceed the upper limit >500 ng/mL and are significantly associated with increasingly severe disease (RR = 1.58; 95% CI = 1.25 2.00; p <0.001). In the study by Yao *et al*., D-dimer levels increased approximately 7-folds in moderate to critical COVID-19 (4.76 [2.02 – 13.3] mg/L vs. 0.6 [0.33 – 1.49] mg/L; p <0.001).17 Although no significant results were obtained, these results also indicate that remdesivir therapy has an effect on COVID-19 patients with both high CRP and high D-dimer levels. However, careful interpretation of the results is still needed considering the exclusion of groups with high CRP and D-dimer markers.

CONCLUSION

There was a significant decrease in RSI score in COVID-19 patients with high CRP levels and high D-dimer after administration of remdesivir. There was a weak significant relationship between high CRP levels and RSI score pre-remdesivir therapy, indicating that the higher the CRP levels, the higher the RSI score. There was no significant difference between the RSI score difference in the high CRP and high D-dimer groups, so remdesivir provided a similar therapeutic effect in both patients with high CRP or high D-Dimer levels.

REFERENCES

1. ACR Recommendations for the use of Chest Radiography and Computed Tomography (CT) for Suspected COVID-19

Infection [Internet]. American College of Radiology. 2020 [cited 2023 Mar 20]. Available from: https://www.acr.org/Advocacy-and-Economics/ACR-Position-Statements/Recommendations-for-Chest-Radiography-and-CT-for-Suspected-COVID19-Infection
2. Hosseiny M, Kooraki S, Gholamrezanezhad A, Reddy S, Myers L. Radiology Perspective of Coronavirus Disease 2019 (COVID-19): Lessons From Severe Acute Respiratory Syndrome and Middle East Respiratory Syndrome. Cardiopulm Imaging. 2020;215:1–5.
3. Coronavirus disease 2019 [Internet]. World Health Organization. 2019 [cited 2023 Mar 20]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019
4. Kazerooni EA. High-Resolution CT of the Lungs. AJR. 2001;177:501–19.
5. Susilo A, Rumende CM, Pitoyo CW, Santoso WD, Yulianti M, Sinto R, *et al*. Coronavirus Disease 2019: Tinjauan Literatur Terkini. J Penyakit Dalam Indones. 2020;7(1):45–67.
6. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, *et al*. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet [Internet]. 2020;395(10229):1054–62. Available from: http://dx.doi.org/10.1016/S0140-6736(20)30566-3
7. Patel SK, Adhikari S, Gauli B, Bhattarai MD, Paudel B, Adhikari D, *et al*. Association of CRP and D-dimer with CT Severity Scoring in COVID-19 Patients. J Chitwan Med Coll. 2021;11(38):120–5.
8. Chen Y, Liu Q, Guo D. Emerging coronaviruses: Genome structure, replication, and pathogenesis. J Med Virol. 2020;92:418–23.
9. Fachri M, Hatta M, Widowati E, Akaputra R, Dwiyanti R, Syukri A, *et al*. Correlations between comorbidities, chest x-ray findings, and C-Reactive protein level in patients with COVID-19. Ann Med Surg [Internet]. 2022;77(103553):1–5. Available from: https://doi.org/10.1016/j.amsu.2022.103553
10. Sun J, He W, Wang L, Lai A, Ji X, Zhai X, *et al*. COVID-19: Epidemiology, Evolution, and Cross-Disciplinary Perspectives. Trends Mol Med [Internet]. 2020;26(5): 483–95. Available from: https://doi.org/10.1016/j.molmed.2020.02.008
11. Tanni SE, Silvinato A, Floriano I, Pneumologia D De. Use of remdesivir in patients with COVID-19: a systematic review and meta-analysis. J Bras Pneumol. 2022;48(1):1–13.
12. Udugama B, Kadhiresan P, Kozlowski HN, Malekjahani A, Osborne M, Li VYC, *et al*. Diagnosing COVID-19: The Disease and Tools for Detection. ACS Nano. 2020;14:3822–35.
13. Sari EF, Rumende CM. Factors related to Pneumonia Diagnosis in Elderly [Faktor – Faktor yang Berhubungan dengan Diagnosis Pneumonia pada Pasien Usia Lanjut]. J Penyakit Dalam Indones. 2016;3(4):183–92.
14. Laffan M MR. Investigation of thrombotic tendency. In: Lewis SM, Bain BJ BI, editor. Dacie and Lewis Practical Haematology. 10th ed. Philadephia: Churcill Livingstone; 2006. p. 441–64.
15. AC H. D-dimer testing and acute venous thromboembolism. Inst Transfus Med Updat. 2000;
16. Pan F, Ye T, Sun P, Gui S, Liang B, Li L. Time Course of Lung Changes On Chest CT During Recovery From 2019 Novel Coronavirus (COVID-19) Pneumonia. Radiology. 2020;
17. Herdiman H, Basyar M, Khairsyaf O. Association Between D-Dimer Level with Clinical Severity and Radiological Imaging of Confirmed COVID-19 Patients at RSUP Dr. M. Djamil Padang. J Respir Indo. 2022;42(4):328–34.
18. Geetika P, J MV, Suresh A, Sudhanva N. Correlation Of Chest X-Rays With Lab Parameters In Covid-19. Eur J Mol Clin Med. 2022;09(04):1911–20.
19. Sofic A, Cizmic M, Beslagic E, Becirevic M, Mujakovic A. Brixia Chest X-ray Severity Scoring System is in Relation with C-reactive Protein and D-dimer Values in Patients with COVID-19. Mater Sociomed. 2022;34(2):95–9.