Brief Communication

Assessment of COVID severity by measuring D-dimer and Serum Ferritin level in selected Tertiary Care Hospitals of Dhaka city

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Abstract

Aim: This study was aimed to evaluate the association between serum D-dimer, serum Ferritin with disease severity in patients having COVID-19. Methods: Total 80 confirmed COVID-19 patients were enrolled in this cross sectional study. Samples were assessed by positive SARS-CoV-2 by RT-PCR testing and were collected from two tertiary Hospitals (IbnSina Medical College Hospital and Ibrahim Cardiac Hospital and Research Institute). We also performed CT findings of COVID patients with or without pulmonary involvement. COVID positive patients were divided into two groups (Group 1 and Group 2) according to lungs involvement confirmed by CT-scan. In this analysis, several variables such as gender, age, D-dimer and serum ferritin were taken. Results: The mean of D-dimer in Group-1 subjects was 4.26±3.60mg/L and in Group-2, this was 0.59±1.08mg/L. So D-dimer level was significantly raised in COVID pneumonic patient (P value = <0.001). The mean of ferritin (554.65±515.841)ng/ml for pneumonic patient was also highly significant than the mean (133.70±109.22)ng/ml of COVID without pneumonia. Conclusion: D-dimer and S. ferritin were elevated in patients with COVID-19. These two reliable biomarkers are correlate with the disease severity and useful for better management of COVID positive patients.

Keywords: D-Dimer; Serum Ferritin; COVID-19 Patients; SARS-CoV 2

Introduction

For the last one and half year the entire World is experiencing the emergence and devastation caused by COVID-19. The clinical picture of patients with COVID-19 has a pattern of respiratory dominance and depends on the tropism of the virus towards the target organs of the body, because COVID-19 virus uses the ACE-2 receptor for its entry into the host cell. The virus binds ACE-2 with an affinity 10-20 times greater than SARS-CoV. This receptor is highly expressed in multiple body tissues, including lung, gastrointestinal, kidney and cardiac tissue, explaining the symptoms present in the prodrome of the disease. Usually in mild COVID, lung is not involved whereas in severe COVID patient develops ARDS. It is now universally acknowledged that severe COVID-19 cases have higher mortality than mild cases because severe cases are more likely to suffer ARDS, septic shock, or metabolic acidosis. So it is necessary to distinguish between severe and mild patients at an early stage. According to a report by Yong Gao, D-dimer can be measured to estimate the severity of COVID-19 and help to diagnose severe COVID-19 patients earlier.

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Patients were divided into two groups; in Group-1, the presence or absence of lung involvement. In Table II showed that in Group-1, with lung involvement and people without lung involvement. The mean age of group-1 and group-2 were 63.10±11.45 years and 53.78±14.15 years respectively. 60% patients were male and 40% female. In Group-1, 75% male and 25% female and in Group-2, 55% male and 45% female were affected by corona virus. The result was showed that majority of male persons were affected by corona virus. The result was showed that the majority of male persons were affected by corona virus. The result was showed that in Group-1, the mean of D-dimer was 4.26±3.60mg/L and in Group-2, COVID without lung involvement. In this analysis, several variables such as gender, age, D-dimer and serum ferritin were taken into account.

**Laboratory testing Determination of D- dimer and ferritin:** Both of D-dimer and ferritin level estimation were carried by ADVIA Centaur XPT/ VITROS Eci. Reference range are less than 0.5 mg/L for D-dimer and 22 -322ng/ml for ferritin.

**Exclusion criteria:** D-dimer has low specificity as there are many other conditions with ongoing activation of the hemostatic system in which D-dimer can be elevated such pregnancy, inflammation, malignancy, trauma, liver disease (decreased clearance), heart disease, sepsis or as a result of hemodialysis, CPR or recent surgery, so patient with these conditions were excluded from this study.

**Statistical Analysis:** Data were analyzed using SPSS statistical software, version 22.0 (SPSS). All continuous data are presented as means and standard deviations, while categorical data are presented as numbers and percentages. Their difference was compared by independent student’s t-test. A chi-square test was used to compare categorical variables. The relationship among biomarkers was assessed using Pearson correlation coefficient test and Multiple Logistic Regression test. Statistical tests were considered significant at the level of ≤5% and considered as test of significant when p <0.05.

**Ethical consideration:** Prior to commencement of the study, this research was approved by the Institutional Ethical Review Board(IERB) of Ibsnsina Medical College and Ibrahim Cardiac Hospital and Research Institute. Strict confidentiality was maintained regarding the information of the patients during and after the study.

**Result:** The study population included 40 COVID-19 patients with lung involvement and 40 COVID-19 patients without lung involvement. The mean age of group-1 and group-2 were 63.10±11.45 years and 53.78±14.15 years respectively. 60% patients were male and 40% were female. In Group-1, 75% male and 25% female and in Group-2, 55% male and 45% female was affected.

**Materials and Methods**

This cross sectional study started in May 2020 and continued until December 2020. Within this period samples were assessed by positive SARS-CoV-2 by real-time reverse transcription polymerase chain reaction (RT-PCR) assay and were collected from two tertiary Hospitals(IbnSina Medical College Hospital and Ibrahim Cardiac Hospital and Research Institute). All patients underwent HR-CT scan of chest. Depending on CT Scan report, the COVID-19 patients were divided into two groups regarding the presence or absence of lung involvement. Patients were divided into two groups; in Group-1, COVID patient with lung involvement and in Group-2, COVID without lung involvement. This cross sectional study started in May 2020 and continued until December 2020. Within this period samples were assessed by positive SARS-CoV-2 by real-time reverse transcription polymerase chain reaction (RT-PCR) assay and were collected from two tertiary Hospitals(IbnSina Medical College Hospital and Ibrahim Cardiac Hospital and Research Institute). All patients underwent HR-CT scan of chest. Depending on CT Scan report, the COVID-19 patients were divided into two groups regarding the presence or absence of lung involvement. Patients were divided into two groups; in Group-1, COVID patient with lung involvement and in Group-2, COVID without lung involvement. In this analysis, several variables such as gender, age, D-dimer and serum ferritin were taken into account.
Table I: Comparison of Age and Gender between two Groups

| Variables         | Group: 1 Covid with Lung involvement | Group : 2 Covid without Lung involvement |
|-------------------|------------------------------------|------------------------------------------|
| Age (in Years)    | 63.10±11.45                        | 53.78±14.15                              |
| Male Gender       | 30(75%)                            | 18(45%)                                  |
| Female            | 10(25%)                            | 22(55%)                                  |

Statistical analysis was done by independent sample t-test and Frequency distribution. Results are expressed as (mean±SD) and number (n) and percentage (%).

Our results showed that majority of male persons were affected by corona virus. The result was shown the comparison of D-dimer levels between people with lung involvement and people without lung involvement. In Table II showed that in Group-1, the Mean of D-dimer was 4.26±3.60mg/L and in Group-2, this was 0.59±1.08mg/L. So D-dimer level was significantly raised in COVID pneumonic patient (P value = <0.001).

Table II: Comparison of D-dimer with both groups

| Variables   | Group: 1 Covid with Lung involvement Mean ±SD | Group: 2 Covid without Lung involvement Mean ±SD | P-value  |
|-------------|-----------------------------------------------|-----------------------------------------------|----------|
| D-dimer mg/L| 4.26±3.60                                      | .59±1.08                                      | <0.001***|

Statistical analysis was done by independent sample t-test. Results are expressed as (mean±SD), ***p<0.001, **p<0.01, *p<0.05 was taken as the level of significance.

According to table III, the mean of S. Ferritin (554.65±515.841)ng/ml for pneumonic patient was highly significant than the mean(133.70±109.22)ng/ml of COVID without pneumonia.

Table III: Comparison of S. Ferritin with both groups

| Variables   | Group: 1 Covid with Lung involvement Mean ±SD | Group: 2 Covid without Lung involvement Mean ±SD | P-value  |
|-------------|-----------------------------------------------|-----------------------------------------------|----------|
| S. Ferritin Ng/ml | 554.65±515.841                               | 133.70±109.22                                | <0.001***|

Statistical analysis was done by independent sample t-test. Results are expressed as (mean±SD), ***p<0.001, **p<0.01, *p<0.05 was taken as the level of significance.

Table IV showed significant positive association of COVID with lung involvement with D-dimer (<0.001) and S.Feritin (<0.05). So D-dimer and S.Feritin can be said independently associated with COVID with lung involvement.

Table: IV Association of COVID with lung involvement with different variables

| Variables   | Beta | p-value | 95.0% Confidence Interval |
|-------------|------|---------|---------------------------|
| D-dimer (mg/L) | 1.172 | 0.000*** | (1.774, 5.875)             |
| S.Feritin (ng/ml) | .006  | 0.017*  | (1.001, 1.010)             |

Analysis was done by multiple logistic regression. Beta for standardized regression coefficient *=significant, *p<0.05, **p<0.01 , ***p<0.001.

Discussion:

This study was done on Mild and severely ill patients with COVID-19 infection. Results showed a significant relation with D-dimer and S.Ferritin levels with Pneumonia in COVID positive patients. D-dimer levels were significantly higher in the group with Pneumonia as compared to the group without Pneumonia. Several studies showed strong association between COVID Pneumonia and D-dimer level. We found that an elevated D-dimer was associated with an increased composite poor outcome, especially mortality and severe COVID-19. This finding supports the hypothesis that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection...
could induce the dysfunction of the hemostatic system, leading to a hypercoagulable state, a condition which we commonly encounter in sepsis. Recent evidence of lung pathology dissection has shown occlusion and micro-thrombosis formation in pulmonary small vessels of patients critically ill with COVID-19. However, the etiology of elevated serum D-dimer level is multifactorial and the optimal cutoff value of elevated D-dimer in patients with COVID-19 remains to be established. It is clear that COVID-19-associated coagulopathy warrants distinct emphasis and special treatment. According to the International Society of Thrombosis and Hemostasis (ISTH) guideline, a markedly elevated serum D-dimer level (which is still poorly defined as a three- to four-fold increase) implies an increased thrombin production. Patients with COVID-19 with markedly elevated D-dimer levels may require hospitalization, despite the severity of clinical presentation. Another study also support my research, D-dimer is a fibrin degradation product used to exclude the diagnosis of thrombosis. Increased D-dimer levels have been observed in severe Covid-19 cases accompanied by microangiopathy and a hypercoagulable state. The present study was evaluated that S. ferritin is one of important biomarker for COVID positive patients. It also detects severity of corona infection. Our study revealed that S. ferritin was raised significantly in severe infection and several similar studies described this association. A study was involving 20 patients with Covid-19 evaluated ferritin, and reported increased serum ferritin levels in patients with severe and very severe Covid-19, with the levels being significantly higher in the very severe group. Another study involving 69 patients with severe Covid-19 reported significantly higher ferritin levels in patients with severe disease than in those with non-severe disease.

**Limitation:** This study has some limitations. First, for severity analysis, only 80 patients with SARS-CoV-2 were included which were not sufficient number to elicit the research goal. This was due to detailed patient information, particularly regarding clinical outcomes, was unavailable in the hospital data set. Second, other important biomarkers were not assessed to evaluate the severity. Thirdly, previous similar type of study could affect the analysis and any possible biased results. Another limitation, this study was done in only tertiary hospital, not grass root level, so real scenario is not visualized. However, this is the first preliminary analysis investigating the relation of D-dimer and S. ferritin severity in patients with SARS-CoV-2.

**Conclusion:** Our Study revealed that D-dimer and ferritin levels are associated with severe pulmonary involvement as detected by CT scan. These two biomarkers are good indicator to assess the severity in patients with SARS-CoV-2. Abnormal level of D-dimer and S. ferritin suggest that early anticoagulant and antiviral therapy might be needed and useful for reduction of morbidity and mortality in COVID positive patients.

**Recommendations:** For better clinical services and patient care all important biomarkers should be studied in view of their prognostic value in the treatment of COVID-19 and COVID associated symptoms.

**Conflict of interest:** None declared

**Author’s contribution:**

**Data gathering and idea owner of this study:** Afrin SF, Salma N

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Reference

1. Thomas J. A Short Note on COVID-19. *ARCHIVOS DE MEDICINA* 2020;16(5):4

2. Kenneson A, Cannon MJ. Review and meta-analysis of the epidemiology of congenital cytomegalovirus (CMV) infection. *Rev Med Virol* 2007; 17:253–76.

3. 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. 10.1002/jmv.2577.

4. LifestyleDesk. 2021. What is the D-Dimer test recommended for coronavirus patients? Available at: https://indianexpress.com/article/lifestyle/health/d-dimer-covid-19-patient-test-lungs-oxygen-blood-clots-7309125/ Accessed July 30, 2021.

5. Mehta, P., McAuley, D. F., & Brown, M., et al. HLH AcrossSpeciality Collaboration, UK. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020; 395(10229), 1033–1034.

6. Alunno, A., Carubbi, F. & Rodriguez-Carrio, J. Storm, typhoon, cyclone or hurricane in patients with COVID-19? Beware of the same storm that has a different origin. *RMD Open*. 2020; 6(1), e001295.

7. Peckham H, Grujter NM, et al. Male sex identified by global COVID-19 meta-analysis as a risk factor for death and ITU admission. *Nature Communications* 2020; 11

8. Levi M, van der Poll T. Coagulation and sepsis. *Thromb Res* 2017; 149: 38–44.

9. Lin L, Lu L, Cao W, et al. Hypothesis for potential pathogenesis of SARS-CoV-2 infection – a review of immune changes in patients with viral pneumonia. *Emerg Microbes Infect* 2020; 1–14.

10. Lue W, Yu H, Gou J, et al. Clinical pathology of critical patient with novel coronavirus pneumonia (COVID-19). *Preprints* 2020; 1–18.

11. Thachil J, Tang N, Gando S, et al. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. *J Thromb Haemost* 2020; 1023–1026.

12. Yao Y, Cao J, Wang Q, Shi Q, Liu K, Luo Z et al. D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study. *J Intensive Care* 2020; 8:49.

13. Zhou B, She J, Wang Y, Ma X. Utility of Ferritin, Procalcitonin, and C-reactive Protein in Severe Patients with 2019 Novel Coronavirus Disease. In: 10.21203/rs.3.rs-18079/v1 [22 May 2020]

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 Mol Med* 2020;12:e12421.