ISSN : 2309-3234

TMSS Medical College Journal (TMCJ)

Volume 16, No. 01, January 2021

COVID-19 Special Issue

Contents

An Official Publication of TMSS Medical College

TMSS Medical College Journal (TMCJ)

January 2021

An Offical Publication
of
TMSS Medical College, Bogura, Bangladesh

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Printed by

TMSS Printing Press
Bogura, Bangladesh
e-mail: tmssprintingpress@gmail.com

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Original Article

Hematological, Biochemical and Infection Related Biomarkers among survivor and non-survivor patients infected with SARS-CoV-2 in Bogura, Bangladesh

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Abstract

Background: Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) infection showed different laboratory abnormalities among patients. We aim to investigate laboratory findings of patients infected with SARS-COV-2. **Materials and Methods:**: Hospital admitted patients' laboratory data which includes hematological, biochemical and inflammatory biomarkers were extracted and analyzed. **Results:** Of 253 COVID-19 patients (218 survivor and 35 non survivor) laboratory findings showed Neutrophilia, lymphocytopenia, raised serum ferritin, C-reactive protein, ESR were observed among large number of the patients. Significantly higher levels of Neutrophil count, decrease lymphocyte count, raised serum ferritin, C-reactive protein, ESR were associated with non-survivor patients compared to survivor patients (all $p < 0.05$). **Conclusion**: Laboratory investigations of 253 hospitalized COVID-19 cases suggests abnormalities of infection related biomarkers could results fatal outcomes.

Key words: SARS-CoV-2, coronavirus, COVID-19, Laboratory findings, mortality.

Introduction

Coronavirus disease 2019 (COVID-19), a form of respiratory and systemic zoonosis caused by virus belonging to the Coronaviridae family, originated from town of Wuhan in China, is still spreading around the world thus assuming the dramatic features of a pandemic emergency[1]. According to the recent statistics of the World Health Organization (WHO), the disease has already involved all continents, with 93.21 million confirmed cases and 2.02 million deaths have been reported until January 19, 2021[2]. In Bangladesh, from the first case identified in early March 2020, 527,632 individuals tested positive for covid-19, and 7,906 died with case fatality rate 1.5% up to 18th January 2021[3]. A recent report suggests that the number of COVID-19 related Although the clinical characteristic of COVID-19 have been broadly defined[3], an outline of the most representative laboratory abnormalities found in patients with COVID-2019 infection is still lacking to the best of our knowledge. It was previously highlighted that laboratory medicine plays an essential role in the early detection, diagnosis and management of many diseases[4]. COVID-2019 makes no exception to this rule, whereby real-time reverse transcription polymerase chain reaction (RT-PCR) enables direct virus identification, whilst detection of anti-COVID-19 antibodies by means of fully- automated immunoassays is the mainstay of serological surveillance[5]. Nevertheless, the role of laboratory diagnostics extends far beyond etiological diagnosis and epidemiologic surveillance, whereby in vitro diagnostic tests are commonly used for assessing disease severity, for

defining the prognosis, for following-up patients, for guiding treatment and for their therapeutic monitoring[6].

Materials and Methods

Study design and participants

A total of 253 inpatients from TMSS Medical College and Rafatullah Community hospital between 5th August 2020 to 15th November 2020 who were COVID 19 RT-PCR positive enrolled in this retrospective study. The study was approved by the Research Ethics committee of TMSS Hospital.

Data collection

Data were extracted from electronic medical records and laboratory information system using a standardized form. Laboratory data were collected within one day of patient admission.

Laboratory procedures

Complete blood count and coagulation testing were assessed at sysmex i-800 (Jappan), assessments liver and renal function were performed at Homostar-600 (Germany); C-reactive protein was assessed at Getein 1100 (China); Serum ferritin was performed on Backmancolter-acces 2 (USA). Specimens, including nasal swab and throat swabs were used for testing the N gene and ORF gene of SARS-CoV-2 by qRT-PCR .

Statistical Analysis

Continuous variables were expressed as medians and inter-quartile ranges (IQR); categorical variables were summarized as counts and percentages. The frequencies of categorical variables were compared using Chi-square test and fisher's exact test as appropriate. A two sided alpha of <0.05 was considered statistically significant. All analysis were performed with SPSS software (version 22.0).

Results

Table-I: Hematological parameters of COVID-19 patients on admission

Hematological parameters	All patients (n=253)	Survivor patients (n=218)	Non-survivor patients (n=35)	*P-Value*
Complete blood count				
Leukocytes ($\times 10^9$/L; normal range 3.5-11) Increased-No./total No. (%) Decreased-No./ total No. (%)	7.04 (4-11) :n=253 55/253 (21.73) 03/253 (1.2)	8.11 (3.2-23.5) :n=218 44/218 (20) 1/218 (0.7)	9.91 (4.9-20.0) :n=35 11/35 (31) 2/35 (5.71)	0.953
Lymphocytes($\times 10^9$ /L; normal range 1.1-3.2) Increased-No. /total No. (%) Decreased-No./ total No. (%)	1.55 (0.64-6.50): n=253 3/253 (1.2) 65/253 (25.7)	1.53 (0.64-3.56) :n =218 02/218 (0.1) 40/218 (18.3)	1.60 (0.63-6.50) :n=35 1/35 (2.8) 25/35 (71.4)	**0.027**
Neutrophils ($\times 10^9$/L; normal range (2.16-6.04) Increased-No. /total No.(%) Decreased-No./ total No. (%)	6.39 (1.17-19.98) : n=253 73/253 (28) 6/167 (3.5)	6.02 (1.17-19.9) :n=218 52/218 (23.9) 6/218 (4.5)	7.83 (2.43-16.83) :n=35 21/35 (60) 0/35	**0.04**
Platelets ($\times 10^9$ /L; normal range 150-400) Decreased-No./ total No. (%)	228.29 (40-523) :n=253 16/167 (9.6)	235 (60-523) :n=218 7/218 (3.2)	203 (40-394) :n=35 9/35 (26)	0.568

On admission majority of the patient showed normal Leukocyte (76.64%), lymphocytes (73.1%), neutrophil (72%) and platelet count (90.4%).

Compared to survivor patient, non-survivor patient were more likely to have increased leukocyte count (31%vs20%), decrease lymphocyte count (71% vs18.3%), increased neutrophil count (60% vs 23.9%) and decreased platelet count (26% vs 3.2%).

Table-II: Blood biochemistry findings COVID-19 patients on admission

Laboratory parameters: Blood biochemistry	All patients (n=253)	Survivor patients (n=218)	Non-survivor patients (n=35)	*P-Value*
Alanine aminotransferase (U/L); normal range (15.0-40.0) Increased-No./total No. (%)	60.32 (2-270) :n=219 80/219 (37)	46 (2-270) :n=184 62/184 (33.7)	46 (2-151) :n=35 18/35 (51.4)	0.243
Serum Creatinine (mg/dl); normal range 0.7 to 1.4 mg/dl) Increased- No./total No. (%)	1.61 (0.01-13.70) :n=191 52/191 (27)	1.48 (0.59-13.70) :n=156 31/156 (20)	2.17 (0.01-7.60) :n=35 21/35 (60)	0.932

Most of the admitted patient showed normal alanine aminotransferase level (63%) and serum creatinine level (73%). Compared to survivor patient Non-survivor patients were more likely to have increased Alanine transferase level (51.4% vs 33.7%) and increased serum creatinine level (60% vs 20%)

Table-III: Infection related biomarker of patients with COVID-19 on admission

Laboratory parameters: Infection - related biomarker	All patients (n=253)	Survivor patients (n=218)	Non-survivor patients(n=35)	*P-Value*
D-Dimer (µg/ml); normal range (0-.5) Increased- No./total No. (%)	1.61 (0.1-16.80): n=214 43/214 (20)	46 (2-270): n=183 22/177 (12)	46 (2-151) 21/37 (56.8)	.914
Serum ferritin (ng/ml:normal range 18-270 for male and 18-160 ng/ml for female) Increased- No./total No. (%)	449.92 (19-2920): n=188 96/188 (51)	408 (19-2920) 62/151 (41)	621 (1.2-2588) 34/37 (92)	**.032**
CRP; normal range 3.9-6.1) Increased- No./total No. (%)	49.22 (2-250): n=163 128/163 (78.5)	46.52 (2-250) 112/148 (75.7)	81.20 (8-198) 24/25 (96)	**.003**
ESR(mm/h; normal range 0-15) Increased- No./total No. (%)	46 (2-109): n=167 139/167 (83)	44 (2-109) 105/132 (79)	54 (12-95) 34/35 (97)	**.006**

Most of the admitted patient had normal D-Dimer level (80%) on admission. However Majority of the patient showed increased CRP level (78.5%) and increased ESR (83%) after admission. Elevated serum ferritin was found among 51% admitted covid-19 positive patients.

Compared with survivor patient non-survivor patients were more likely to have increased D-Dimer (56.8% vs 12%), increased serum ferritin level (92% vs 41%), increased CRP level (96% vs 75.7%), increased ESR level (97 % vs 79%).

Discussion

In this study including 253 covid-19 RT-PCR positive patient (218 survivor and 35 non-survivor) Hematological analysis showed Leukocytosis, lymphopenia, neutrophillia and thrombocytopenia in 21.73%, 25.7%, 28% and 9.6% patient respectively. Non survivor patient showed higher rate of these

hematological abnormalities in comparison to survivor patient. In the study published by Huang et al involving 140 COVID-19 patients (13 with severe disease) showed leukocytosis, neutophillia, lymphocytopenia, thrombocytopenia among hospital admitted patients and higher frequency of these findings had found among severe disease [7].

Similar findings emerged from the article published by liu et al who found that disease severity could be predicted by lymphopenia, neutrophillia and thrombocytopenia [8].

However Leukocytopenia was observed among COVID-19 positive patient among few studies which reflected the dominance of lymphocytopenia rather than neutrophilia[9-10].

Decreased lymphocyte count is considered as bad prognostic marker and occurs due to novel corona virus act on lymphocytes, especially T lymphocytes. Some studies suggest that a substantial decrease in total number of lymphocyte indicates coronavirus consumes many immune cells and inhibits the body' cellular immune immune function. Damage to T lymphocytes might be an important factor leading to exacerbations of patients. The low absolute value of lymphocyte could be used as a reference index in the diagnosis of new coronavirus infection[8].

In agreement with this study findings Wan et al reported that ICU patients had more neutrophil count than non-ICU and the reason is due to secondary infection[11].

Thrombocytopenia was associated with an increased risk of severe disease and mortality. Thrombocytopenic COVID-19 patients will experience disease with higher risk of adverse outcomes during hospitalization[12].

Elevated Alanine aminotransferase was observed among 37% (80/219) admitted covid positive patients with higher frequency of 50% (18/36) found among non-survivor in comparison to 34%(62/183) of survivor cases. In relation to this finding 31% (59/189) covid positive patient had elevated ALT with 48% (26/54) non-survivor and 24% (33/135) survivor patient showed raised ALT in a study conducted among admitted hospitalized patients of china [10].There are many potential contributing etiologies to elevated liver enzymes in patients with SARS-COV2 including direct liver injury, associated inflammatory responses, congestive hepatopathy, hepatic ischemia, drug induced liver injury and muscle breakdown[13].

Serum creatinine was found higher among 27% (56/196) cases in the current study. A study on analysis of creatinine in 149 cases demonstrated 28.8% of covid-19 patients had increased levels, representing SARS-COV-2's ability to induce kidney injury[14].

Study population showed elevated D-Dimer among 60% of non-survivor cases in comparison to 20 % of survivor cases. Tang et al followed up 183 patients with confirmed COVID-19 infection during their hospital stay and found that coagulation parameters were more frequently deranged in those who died than in those who survived and increased D-dimer value may indicate worse prognosis[15].

Higher rate of serum ferritin was found among non-survivor case compare to survivor cases (92% vs 41%). Study population also showed higher rate of CRP level in non-survivor patient compare to survivor patient (96 % vs 75%). In a study investigating the clinical predictor of COVID-19 mortality reported that increased levels of serum ferritin (70% in fatal case vs 38% in discharged case) and increased levels of CRP (93% fatal case vs 55% in discharged case) was found among Covid-19 patients[16]. Notably it has been reported that hyperferritinemia can activate macrophages, which increases the pro-inflammatory cytokines, and the subsequent inflammation is mainly responsible for organ damage. Although ferritin is a positive acute phase reactant and serum level of this intracellular protein increases during inflammation, dying cells may also release ferritin. Thus, it is reasonable to assume that higher serum ferritin levels in severely affected COVID-19 patients might indicate a greater extent of organ damage[17]. Raised CRP

suggesting systemic inflammation which considered as one of the major cause of disease severity in SARS-CoV-2 infection[8].

Elevated ESR was found among 83% admitted patient with higher rate of elevated ESR observed among non-survior group. Cao et al reported that 86.8% elevated ESR was observed among admitted patient where critical patient had higher rate of elevation compared to noncritical (100%vs 85.5%). COVID–19 could trigger the change of the form of erythrocyte or plasma characteristics including the immune system by an unknown mechanism to increase the ESR. The sustained high level of ESR possibly brings the negative effect on COVID–19 patient's prognosis[9].

The results had indicate that measuring the hematological, biochemical as well as infection related parameters not only retains specific diagnostic significance in this infection but their abnormalities may also correlate with unfavorable outcomes.

Our study has some limitations. First, due to the retrospective study design, not all laboratory tests were done all patients. Secondly, interpretation of our findings might be limited by sample size.

Conclusion

Although in vitro diagnostics efficiently contribute to the early identification Novel coronavirus infection, there is evidence that laboratory medicine may also provide essential assistance to discriminate between severe and non-severe COVID-19. The large variation in the clinical features of the disease, spanning from asymptomatic to fatal, necessitates the identification and application of novel laboratory biomarkers to rapidly and economically predict COVID-19 prognosis.

References

1. Perlman S. Another decade, another coronavirus. N Engl J Med 2020; 382:760–2.
2. World Health Organization. Novel Coronavirus (2019-nCoV) situation reports. https://www.who.int/ emergencies/ diseases/ novel coronavirus- 2019/ situation-reports. Accessed: January 2021.
3. World Health Organization. Novel Coronavirus (2019-nCoV) situation reports. https://www.who.int/ bangladesh/ emergencies/ coronavirus- disease- (covid-19) update/ coronavirus- disease- (covid-2019)- bangladesh-situation-reports Accessed: January 2021
4. Mattiuzzi C, Lippi G. Which lessons shall we learn from the 2019 novel coronavirus outbreak?. Annals of translational medicine. 2020 Feb;8(3).
5. Plebani M, Laposata M, Lippi G. A manifesto for the future of laboratory medicine professionals.
6. Lippi G, Plebani M. The novel coronavirus (2019-nCoV) outbreak: think the unthinkable and be prepared to face the challenge. Diagnosis. 2020 May 26;7(2):79-81.
7. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The lancet. 2020 Feb 15;395(10223):497-506.
8. Liu Y, Yang Y, Zhang C, Huang F, Wang F, Yuan J, Wang Z, Li J, Li J, Feng C, Zhang Z. Clinical and biochemical indexes from 2019-n CoV infected patients linked to viral loads and lung injury. Science China Life Sciences. 2020 Mar;63(3):364-74.
9. Cao M, Zhang D, Wang Y, Lu Y, Zhu X, Li Y, Xue H, Lin Y, Zhang M, Sun Y, Yang Z. Clinical features of patients infected with the 2019 novel coronavirus (COVID-19) in Shanghai, China. MedRxiv. 2020 Jan 1.
10. 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.
11. Wan S, Xiang YI, Fang W, Zheng Y, Li B, Hu Y,

Lang C, Huang D, Sun Q, Xiong Y, Huang X. Clinical features and treatment of COVID-19 patients in northeast Chongqing. Journal of medical virology. 2020 Jul;92(7):797-806.

12. Lippi G, Plebani M, Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: a meta- analysis. Clinica chimica acta. 2020 Jul 1; 506:145-8.
13. Guan, W.J., Ni, Z.Y., Hu, Y., Liang, W.H., Ou, C.Q., He, J.X., Liu, L., Shan, H., Lei, C.L., Hui, D.S. and Du, B., 2020. Clinical characteristics of coronavirus disease 2019 in China. New England journal of medicine, 382(18), pp.1708-1720.
14. Yang W, Cao Q, Qin LE, Wang X, Cheng Z, Pan A, Dai J, Sun Q, Zhao F, Qu J, Yan F. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): a multi-center study in Wenzhou city, Zhejiang, China. Journal of Infection. 2020 Apr 1; 80(4):388-93.
15. Tang YW, Schmitz JE, Persing DH, Stratton CW. Laboratory diagnosis of COVID-19: current issues and challenges. Journal of clinical microbiology. 2020 May 26;58(6).
16. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive care medicine. 2020 May;46(5):846-8.
17. Piero R, Onorina B, Paolo C, Annamaria I, Yehuda S. Severe hyper- inflammatory COVID-19, another piece in the puzzle of the" htperferritinemic syndrome. Rheumatol Point View. 2020.
18. Coomes EA, Haghbayan H. Interleukin-6 in COVID-19: a systematic review and meta-analysis. Reviews in medical virology. 2020 Nov; 30(6):1-9.

(TMSS Medical College Journal 2021;16(1):47-52)