Case report: A brief description of unseen facts in the comorbid COVID-19 patients

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Abstract

Data on two deceased individuals with COVID-19 and comorbidities such as hepatitis C, chronic kidney disease, diabetes mellitus type 2 and hypertension are discussed. Changes in laboratory signatures with impact on COVID-19 severity in both cases indicate the need for extensive monitoring of comorbid individuals to reduce morbidity and mortality.

1. INTRODUCTION

COVID-19 pandemic is caused by the SARS-CoV-2, infected human population of all ages, groups, ethnicities and genders. The clinical manifestation of COVID-19 ranged from common cold to severe illness including acute respiratory distress syndrome (ARDS), multisystem inflammatory syndrome (MIS-A), pneumonia, organ failure, and even death. COVID-19 progression and severity has significantly contributed by comorbidities of infected individuals. Currently, world health organization (WHO) confirmed 581.68 million positive cases along with 6.41 million deaths around the world (https://covid19.who.int/). Risks associated with COVID-19 are dependent mostly on age and pre-existing health history of patients. The chronic health conditions or comorbidities of aged patients are habitually encountered hypertension, chronic kidney disease (CKD), cardiovascular diseases (CVD), liver injury, diabetes mellitus (DM), and pulmonary diseases are predisposed to severe and fatal consequences. In line with the coinfections, studies shown 20–50% of the COVID-19 patients are exposing at least one comorbidity. The prevalent comorbidities are; DM (10-20%) and hypertension (10-15%), among other 7-40% diseases. Similarly, morbidity and mortality of chronic hepatitis C virus (HCV) individuals have been significantly accentuated along with the COVID-19 pandemic. Herein, we report data regarded with the two expired COVID-19 comorbid patients, as case I and II. In case I, the patient represents chronic HCV, whereas in case II, the evaluation of the data represented that the patient has previously suffered with CKD, hypertension and DMT-2, as explained.

2. CASE PRESENTATION

2.1. Case I

A 48 years old male was admitted to Northwest hospital Peshawar, Pakistan on 15 August, 2021 with historically reoccurred HCV. Patient has several sign and symptoms of fever (38 for 12 days), dry cough, chest congestion (9 days) and shortness of breath (SOB for 3 days). This individual was vaccinated with Moderna COVID-19 vaccine. On day first, oxygen saturation was 75%, thus the relevant patient sustained by continues positive air way pressure (CPAP) at maximum setting (PO_2 70.9 mmHg and PCO_2 30.6 mmHg). However,

oxygen saturation maintenance was up to 90 on CPAP. According to the nasopharyngeal swab analysis by RT-PCR, the patient was positive for COVID-19. Additionally, chest X-Ray was conducted that demonstrated COVID-19 pneumonia in left lung. In the later analysis, lymph adenopathy with the representation of left lung effusion was detected (for posterior-interior view, see **Figure 1**). Several medications such as Septran DS (Co-trimoxazole), Rifaximin (Rifagut 550mg) and diverse antibiotic injections administration were initiated since hospitalization. Patient was moved to intensive care unit (ICU) for ventilator support at day seventh. On day eight, patient's PCO_2 was increased to 76.1 mmHg against a reduced PO_2 of 54.1 mmHg. Later at day 10, because of the retained CO_2 (despite non-invasive ventilation) the patient was switched to a bi-level positive air way pressure (BIPAP). At a same day, BP and the O_2 level was constantly falling that caused coma, cardiopulmonary arrest, respiratory failure and finally death occurrence.

Table 1 displays laboratory findings from initial to the final death stage. The values of liver function test – e.g., alanine transaminase (ALT) was above normal range on first day. Blood parameters including hematocrit (HCT), total leucocyte count (TLC), lactic acid, neutrophils, lymphocytes, monocytes as well as eosinophils were determined. TLC (21266.66 x 10^9/L) and HCT (50.64%) were progressively increased along entire duration (day 1 to death). Similarly, the differential count was higher – e.g., persistent increase in neutrophils and decreased differential lymphocyte count was found, while monocyte and eosinophil count were remained normal. Platelets count (PLT) was realized decreasing (thrombocytopenia) from fourth to nineth days in clinical course. Levels of the inflammatory biomarkers indicate hyperinflammation due to increased serum ferritin, LDH, CRP, D-dimer, prothrombin time (PT), activated partial thromboplastin clotting time (APTT) and Trop-I (**Table 1**). Similarly, hyperlactatemia (higher lactate level in blood), was noticed on fourth, eighth and nineth day of the hospitalization.

[**Table1** near here]

2.2. Case II

Similar to the previous case, herein a 49 years old male who has DMT-2, chronic kidney disease (CKD), left renal nephrectomy and hypertension was admitted to the same hospital on 11 August, 2021. This patient has fever (7 days) dry cough since last one week and SOB from last four days. According to nasopharyngeal swab, the patient was tested positive for COVID-19, yet the patient was fully vaccinated with SINOVAC COVID-19 vaccine. Then, the chest X-Rays examination revealed COVID allied left lung pneumonia having lower and middle lobe effusion (see **Figure 1**). However, steroid(s), anticoagulant, antibiotic, proton-pumped inhibitor (PPIs) and Lantus® (insulin glargine, 100 U/mL) were prescribed to the patient. Due to lower O_2 saturation (60%), the patient was switched to O_2 therapy (CPAP). Despite a full-fledged treatment, patient's condition was worsening (septic shock and respiratory arrest), oxygen requirement was increasing, and retaining CO_2 on daily basis. Similarly, BP and O_2 saturation (10%) were dropped, switching to full inotropic support but unfortunately occurred cardiopulmonary arrest. The patient spent one day on high dependency unit (HDU) and 11 days in ICU with ventilator.

Additional routine-base blood profile showed TLC (1483.33 x 10^9/L) progression (acquiring leukocytosis) and a declined hemoglobin (12.3 mg/dl). Instead, a differential calculation depicted polymorphs progression and decreased differential lymphocyte count, yet monocyte along with eosinophil count remained normal throughout hospitalization. PLT was realized continuously lessening on day first onward to death. An average value of the PLT was 124.41 x 10^9/L. Renal function tests were severely amplified (urea 213.5 mg/dl and creatinine 3.41 mg/dl). Accordingly, the patient experienced hyperinflammation, and hypercoagulation within entire clinical course. Nevertheless, patient was spotted with an elevated CRP, LDH, serum ferritin, D-dimer, lactate, Trop-I, PT and APTT (see**Table 2**). Additional findings of the glucose levels indicated that the patient was hyperglycemic (689.66 mg/dl and HbA1C, 11.4%).

[**Table 2** near here]

[**Figure 1** near here]

3. DISCUSSION

A highly contiguous SARS-CoV-2 has been major cause of global COVID-19, morbidity and mortality cases. Disease severity ranges from mild to moderate or severe to higher fatality. The mortality can be encouraged, mostly by the health history of patients. Herein, we show the reports of two died individuals with pre-existed comorbidities, exemplified case I and II.

3.1. Case I

In line, the related case (patient I) was co-infected with chronic HCV and COVID-19, and also an elevated liver biochemistry (ALT). The findings of liver parameters conformed earlier data, showing highest mortality (13%) of patients with increased levels of liver chemistries. In contrast, it has revealed an elevated ALT in non-hepatic COVID-19 candidates. Severity occurrence in hepatic comorbidities indicate SARS-CoV-2 antagonistically impacted viral hepatitis reactivation or liver cells. This case report confirms fluctuation in certain coagulation parameters involving thrombocytes (thrombocytopenia), lymphocytes (lymphopenia), D-dimer, APTT and PT. Abnormalities in blood coagulation markers have a huge impact with the COVID-19 severity. Such parameters contribute to serious health complications in COVID-19 patients such as pulmonary embolism, venous thromboembolism, deep vein thrombosis, arterial thromboembolism, and sepsis-induced coagulopathy. According to evaluation, case I proven TLC, LDH, CRP, troponin-I, PT, APTT, serum ferratin and D-dimer in chronic HCV state, with significantly altered parameters. These findings are logically consistent with the reported data, where substantial changes in hematological parameters associated to liver damage were observed in HCV patients. We found that cardiac arrest in case I can be attributed to increased ferratin, troponin, leukocytosis, lymphopenia, thrombocytopenia, sepsis and vasopressors, whereas this is in harmony with other data. As per our understanding, higher troponin contributes to heart failure, fairly in HCV individuals, and it is claimed that HCV infection significantly contributes in cardiac disorder. We additionally observed higher lactate in deceased condition. Accordingly, raised lactate in blood can cause organs sepsis that expressively produced hypoperfusion, tissue hypoxia, necrosis in infected tissue, and often leading to higher mortality.

3.2. Case II

In case II, the individual (patient II) represented comorbidities of CKD and DMT-2 as well as hypertension. In context, maximum comorbidity can double mortality risk of COVID-19 patients. Since highly severe frequency of mortality in such candidates revealed manifold comorbidities, involving hypertension, DMT-2 and CKD. In this case, the deceased individual was observed with higher levels of creatinine, urea and D-dimer, yet these results were in strong agreement with the previous data. The involvement of diseased kidney and pre-infected cells have huge impact on COVID-19 progression. Reasonably, angiotensin converting enzyme 2 (ACE2) receptor tightly binds these pre-infected cells (comorbid patients) which have higher expression rate than lung cells, forming shed soluble ACE2 (sACE2). Higher extent sACE2 on transmembrane surface of the host easily allows entering SARS-CoV-2. Besides, we assessed random blood sugar (¿800 mg/dL, RBS) and HbA1C (11.4 %) in case II. These findings conformed the reported data that showed hospitalized patients were at the peak of RBS and HbA1C.

Meta-analysis of the comorbid patients (11,755) from Iran demonstrated a highest prevalence and death ratio comparatively attributed to the diabetic patients. However, in the present report, the deceased individuals came across hypercoagulation disorder. Major coagulation markers such as PT, APTT and D-dimer were detected highly increased. Our findings are consistent with the previous reports, where at different tests levels, the coagulation indicators were raised in deceased subjects. Hypercoagulation is an alarming signature for both COVID-19 and DMT-2. It results vascular thrombosis, including cardiac arrest. Laboratory and biochemical parameters including CRP, LDH, ferritin, troponins, etc. have been significantly higher in the critical patients as compared to mild/moderate. Elevated CRP level could contribute in ADRS, increased serum ferritin in cytokine storm, LDH and troponin protein (I and T) in tissue hypoperfusion and could also play a role in heart failure.

Our clinical case reports claimed that the deceased subjects may also acquire multi-system inflammatory syndrome in adult (MIS-A), because all the inflammatory biomarkers were highly augmented. The reason

of patient's mortality can also be MIS-A. These patients fulfilled the criteria of MIS-A: a) critically ill with hospitalization (¿20-year age); b) COVID-19 positive; c) severe organs dysfunction (septic shock, liver injury, cardiac arrest, etc.); d) elevated inflammatory biomarkers e.g., CRP, LDH, D-dimer, serum ferratin and others.

4. CONCLUSION

Here, we reported comorbid COVID-19 patients with HCV (case I), CKD, DMT-2, and hypertension. The patients were died due to cardiac arrest, the case reports highlight complications of the patients having comorbidities (e.g., HCV, CKD, diabetes, and hypertension) and COVID-19. Additionally, by this study we conclude that comorbidities with COVID-19 can bring dramatic adverse effects. We recommend extensive monitoring of comorbid patients to reduce morbidity and mortality.

AUTHOR CONTRIBUTIONS

All authors have equally contributed in writing, editing and revising this manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data supporting the findings in this study are available, and can be obtained with a reasonable request from the corresponding author.

CONSENT

A written informed consent was obtained from the patients to publish this report in accordance with the journal's patient consent policy.

REFERENCES

FIGURE CAPTIONS

Figure 1. X-Ray representation of: a) Case I with COVID-19 pneumonia in left lung and heart size is within normal limit. Para hilar soft tissue is dense that is seen lymph adenopathy. Airspace and interstitial opacity can be seen throughout the left lung and effusion (posterior-interior view). b) Case II demonstrating COVID-19 pneumonia in left lung and normal heart size. Left lung shows middle and lower lobe effusion (posterior-interior view).

Table1 . Laboratory and ventilator data for case I.

Days	HCT (%)	HCT (%)	PLT x $10^{9/L}$	PLT x $10^{9/L}$	N (%)	N (%)	L (%)
	50.8	50.8	227	227	88	88	04
2	49.5	49.5	210	210	90	90	05
3	50.4	50.4	168	168	87	87	04
4	50.1	50.1	120	120	90	90	06
5	50.0	50.0	107	107	91	91	04
6	42.0	42.0	107	107	94	94	01
7	50.0	50.0	100	100	93	93	02
8	54.0	54.0	70	70	93	93	02
9	59.0	59.0	65	65	93	93	02
Mean	50.64	50.64	130.44	130.44	91	91	3.33

Days	HCT (%)	HCT (%)	PLT x $10^{9/L}$	PLT x $10^{9/L}$	N (%)	N (%)	L (%)
	Fer. (ng/ml)	Dd (ng/ml)	Dd (ng/ml)	ALT (mg/dl)	ALT (mg/dl)	ALP (mg/dl)	ALP (mg/
1	1120	4250	4250	170	170	80	80
2	-	-	-	200	200	110	110
3	-			188	188	120	120
4	1350	4569	4569	176	176	122	122
5	-	-	-	166	166	132	132
6	-	-	-	188	188	135	135
7	-	-	-	125	125	141	141
8	-	-	-	198	198	156	156
9	2300	5600	5600	200	200	167	167
Mean	1590	4806.33	4806.33	180.12	180.12	129.22	129.22

HCT, hematocrit; PLT, platelets count; N, neutrophils; L, lymphocytes; M, monocytes; E, eosinophils; TLC, total leucocyte count; PCO_2, partial pressure of carbon dioxide; PO_2, partial pressure of oxygen; Fer., ferritin; Dd, D-dimer; ALT, alanine transaminase; ALP, alkaline phosphatase; Lac., lactate; LDH, lactate dehydrogenase; CRP, C-reactive protein; Cre., creatinine; Trop-I, troponin-I; PT, prothrombin time; APTT, activated partial thromboplastin clotting time.

Table 2 . Laboratory and ventilator data of case II.

Day	HB	PLT x10^9/L	N (%)	N (%)	L (%)	Monocytes (%)	Monocytes (%)	Eosinophils (%
1	14.4	180	85	85	10	04	04	1
2	13.9	165	88	88	07	5	5	0.001
3	13.1	163	90	90	05	4	4	1.00
4	13.0	158	92	92	05	5	5	1
5	12.9	145	90	90	06	2	2	00
6	12.6	141	87	87	05	4	4	0.2
7	11.9	138	91	91	04	1	1	0.6
8	11.8	100	89	89	05	0.6	0.6	00
9	11.5	90	93	93	03	0.4	0.4	1
10	11.2	85	94	94	04	0.06	0.06	0.08
11	11.0	78	95	95	03	0.6	0.6	0.23
12	10.9	50	95	95	02	0.01	0.01	00
Mean	12.32	124.41	90.75	90.75	4.91	2.22	2.22	0.42
	PT	PT	PT	APPT	APPT	APPT	RBS (mg/dl)	RBS (mg/dl)
1	12.8/10	12.8/10	12.8/10	30/30	30/30	30/30	833	833
2	13/10	13/10	13/10	32/30	32/30	32/30	-	-
3	15/10	15/10	15/10	35/30	35/30	35/30	-	-
4	16/10	16/10	16/10	36/30	36/30	36/30	670	670
5	18/10	18/10	18/10	36/30	36/30	36/30	-	-
6	18/10	18/10	18/10	37/30	37/30	37/30	566	566
7	20/10	20/10	20/10	38/30	38/30	38/30	-	-
Mean	16.11	16.11	16.11	34.85	34.85	34.85	689.66	689.66

HB, hemoglobin; PLT, platelets count; N, neutrophils; L, lymphocytes; TLC, total leucocyte count; CRP, C-reactive protein; ALT, alanine transaminase; LDH, lactate dehydrogenase; Cre., creatinine; PCO_2, partial pressure of carbon dioxide; PO_2, partial pressure of oxygen; PT, prothrombin time; APTT, activated partial thromboplastin clotting time; RBS, random blood sugar; HbA1C, glycated hemoglobin; Fer., ferritin; Lac.,

lactate; Dd, D-dimer; Trop-I: troponin-I.