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Case Report

Briefly highlighting some unseen evidence of two comorbid COVID-19 patients

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Abstract: In recent years, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused substantial morbidity and mortality worldwide. Comorbidities have negatively impacted the pandemic of coronavirus disease 2019 (COVID-19). This case report discusses the data of two deceased individuals with COVID-19 and pre-history of chronic infections in Pakistan. COVID-19 positivity of the patients was based on RT-PCR at early hospitalization. Similarly, the patients were undergone through the chest X-ray, which exposed COVID-19 pneumonia with left lung effusion. All laboratory parameters including hematologic (e.g., total leucocyte count and hematocrit) and inflammatory biomarkers (e.g., C-reactive protein, prothrombin time, activated partial thromboplastin clotting time, D-dimer and serum ferritin) of the deceased candidates were highly abnormal on day one onward. Septic shock, neutrophilia, lymphopenia, thrombocytopenia and leukocytosis were evident in both cases. Despite giving full-fledged treatments, patients conditions deteriorated rapidly, retaining CO_2 with low oxygen saturation. Blood pressure and oxygen saturation markedly dropped and turned to cardiopulmonary arrest at the final stages in each case. These findings confirm the impact of comorbidities on COVID-19 severity, based on remarkable changes in laboratory parameters. Current report suggests extensive monitoring of COVID-19 comorbid individuals to reduce morbidity and mortality.

Keywords: SARS-CoV-2; COVID-19; Comorbidities; Laboratory findings; Clinical course; Mortality.

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1. Introduction

COVID-19 pandemic was caused by the SARS-CoV-2, infecting human populations 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 are significantly contributed by comorbidities of infected individuals [1]. Currently, the World Health Organization (WHO) confirmed 775.55 million positive cases along with 7.05 million deaths around the world [2].

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, including hypertension, chronic kidney disease (CKD), cardiovascular diseases (CVD),

liver injury, diabetes mellitus (DM), and pulmonary diseases, usually predispose to severe and fatal consequences [3]. In line with the coinfections, studies shown that 20–50% of the COVID-19 patients are exposed to at least one comorbidity. The most prevalent comorbidities are DM (10-20%) and hypertension (10-15%) among the population, comprising approximately 7-40% of all reported diseases [4–7]. Similarly, morbidity and mortality of chronic hepatitis C virus (HCV) individuals have been significantly accentuated along with the COVID-19 pandemic [8, 9].

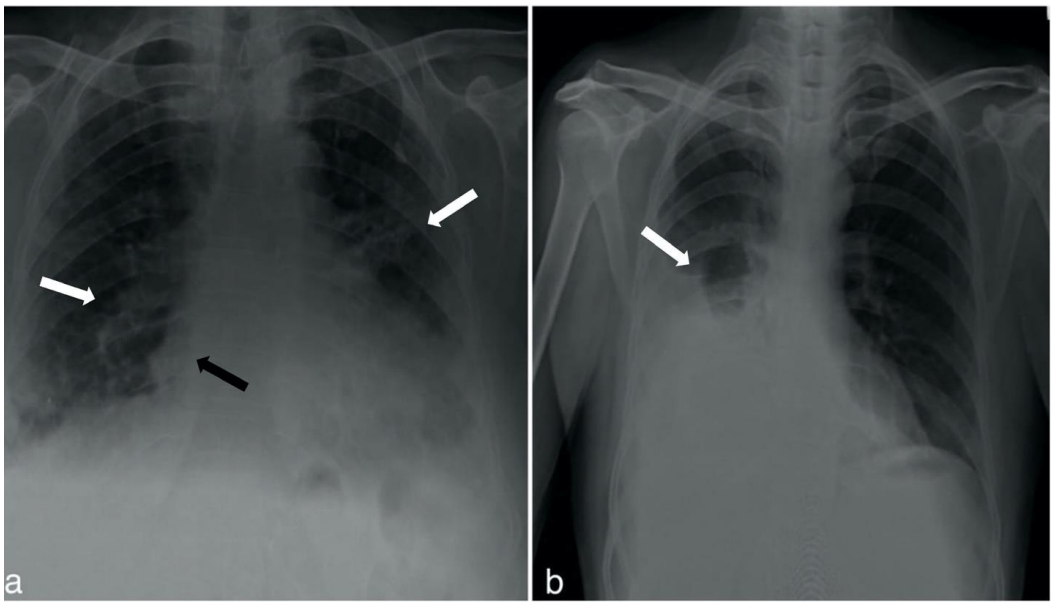
Herein, we report data regarding two deceased COVID-19 comorbid patients, as case I and II. These two cases are the critical follow-up studies among 11 patients in severe diseases level, as reported in our previous research [10]. In case I, the patient presented chronic HCV, whereas in case II, the evaluation of the data indicated that the patient has previously suffered with CKD, hypertension, and DM type 2 (DMT-2).

2. Case Report

2.1 Case I

A 48-year-old male was admitted to Northwest hospital Peshawar, Pakistan, on 15th August 2021 with historically chronic HCV. The 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 previously vaccinated with Moderna COVID-19 vaccine and, on the day first of admittance, his oxygen saturation was 75%. Thus, the patient was immediately sustained by continuous 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. Nasopharyngeal swab analysis by RT-PCR tested positive for COVID-19. Additionally, chest X-Ray demonstrated COVID-19 pneumonia in left lung and lymph adenopathy, as shown in Figure 1a.

Figure 1. X-Ray representation of A. Case I with COVID-19 pneumonia in left and right lungs (white arrows), and heart size is within normal limit. Para hilar soft tissue is dense, showing lymph adenopathy (black arrow). 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 (white arrow) and normal heart size.



A persistent increase in neutrophils and decreased differential lymphocyte counts were also observed, while monocyte and eosinophil counts remained normal. Platelets count (PLT) decreased indicating thrombocytopenia from day 4 to 9 of the clinical course.

The levels of inflammatory biomarkers indicated hyperinflammation, with increased serum ferritin (Fer), lactate dehydrogenase (LDH), C-reactive protein (CRP), D-dimer, prothrombin time (PT), activated partial thromboplastin clotting time (APTT) and troponin-I. Similarly, hyperlactatemia (higher lactate level in blood), was noticed on the fourth, eighth and nineth day of hospitalization.

Table 1. Hematological and ventilatory data for case I.

Day	HCT (%)	PLT (x 109/L)	N (%)	L (%)	M (%)	E (%)	TLC (x 10^9/L)	PCO_2 (mmHg)	PO_2 (mmHg)
1	50.8	227	88	4	7	1	18,200	30.6	70.0
2	49.5	210	90	5	4	1	19,400	40.8	88.0
3	50.4	168	87	4	8	1	20,400	41.8	76.0
4	50.1	120	90	6	4	1	20,500	50.9	72.0
5	50.0	107	91	4	5	1	18,200	66.8	67.0
6	42.0	107	94	1	3	2	19,400	78.9	56.0
7	50.0	100	93	2	3	3	20,400	76.1	54.7
8	54.0	70	93	2	2	2	22,500	87.5	59.1
9	59.0	65	93	2	3	3	32400	91.1	42.0
Mean	50.64	130.4	91	3.33	4.33	1.66	21,266	-	-

Day	Fer (ng/mL)	Dd (ng/mL)	ALT (mg/dL)	ALP (mg/dL)	Lac (mg/dL)	LDH (IU/L)	CRP (mg/dL)	Cre (mg/dL)	Trop-I (ng/mL)	PT	APTT	Urea (mg/dL)
1	1,120	4,250	170	80	-	567	58	0.5	36.0	14.1/10	31.4/30	45
2	-	-	200	110	-	636	66	0.8	-	-	-	58
3	-		188	120		640	70	0.7	-	-	-	51
4	1,350	4,569	176	122	44.8	650	103	1.0	-	-	-	69
5	-	-	166	132	-	777	116	1.1	-	14.4/10	-	47
6	-	-	188	135	-	679	100	1.2	88.9	14.7		46
7	-	-	125	141	-	688	96	1.2	-	22.5/11	32/30	44
8	-	-	198	156	49.6	767	107	1.0	60.9	24.7/11	34.6/30	43
9	2,300	5,600	200	167	52.3	780	125	0.9	-	23/11	35/30	41
Mean	1,590	4,806	180.1	129.2	48.9	687.1	93.48	0.99	61.93	18.4	33.25	49.33

HCT, hematocrit; PLT, platelets; 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.

Several medications such as Septran DS (Co-trimoxazole), Rifaximin (Rifagut 550 mg) and diverse antibiotic administration were initiated since hospitalization. Patient was moved to intensive care unit for ventilator support on the 7th day. On the day 8, patient's PCO2 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 this same day, BP and O2 level continued to drop leading to coma, cardiopulmonary arrest, respiratory failure and finally death.

2.2 Case II

Like the previous case, herein a 49-year-old male who has DMT-2, chronic kidney disease (CKD), left renal nephrectomy and hypertension was admitted to the same hospital on 11th August 2021. This patient had fevered dry cough for one week and SOB for four days prior to admittance. Nasopharyngeal swab tested positive for COVID-19, despite being previously vaccinated with SINOVAC COVID-19 vaccine. The chest X-Rays examination revealed COVID associated left lung pneumonia having lower and middle lobe effusion (see Figure 1B). 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 worsened (septic shock and respiratory arrest), with increased oxygen requirement, and retained CO_2 on daily basis. At the same time, BP and O_2 saturation (10%) dropped substantially, switching to full inotropic support. However, this patient unfortunately had cardiopulmonary arrest, thus spending one day on high dependency unit (HDU) and 11 days in ICU with ventilator.

Additional routine-base blood profile showed TLC (1,483 x 10^9/L) progression (acquiring leukocytosis) and a declined hemoglobin (12.3 mg/dL), as shown in Table 2. A polymorphs progression with decreased differential lymphocyte count were observed, while monocyte and eosinophil counts remained normal throughout hospitalization. Like case I, the deceased individual in case II came across hypercoagulation disorder, with higher values of major coagulation markers such as PT, APTT and D-dimer.

Table 2. Hematological and ventilatory data for case II.

Day	HB	PLT (x10^9/L)	N (%)	L (%)	M (%)	E (%)	TLC (x10^9/L)	CRP (mg/L)	ALT (mg/dL)	LDH (IU/L)	Urea (mg/dL)	Cre (mg/dL)	PCO_2 (mmHg)	PO_2 (mmHg)
1	14.4	180	85	10	4.0	1,0	13,600	40	32	760	151	2.6	25.0	67.8
2	13.9	165	88	7	5.0	0	13,800	45	38	790	185	2.9	26.0	65.3
3	13.1	163	90	5	4.0	1.0	13,900	55	41	820	196	3.0	29.0	61.2
4	13.0	158	92	5	5.0	1.0	13,600	57	44	860	202	3.2	66.7	60.0
5	12.9	145	90	6	2.0	0	14,100	59	49	890	215	3.3	70.9	59.6
6	12.6	141	87	5	4.0	0.2	12,900	61	57	902	216	3.4	66.8	58.0
7	11.9	138	91	4	1.0	0.6	13,800	63	62	922	222	3.4	78.9	59.0
8	11.8	100	89	5	0.6	0	14,100	67	63	955	225	3.7	82.0	57.0
9	11.5	90	93	3	0.4	1.0	15,600	69	65	1,002	229	3.7	86.5	55.0
10	11.2	85	94	4	0.1	0.1	15,900	72	69	1,225	235	3.9	88.9	50.5
11	11.0	78	95	3	0.6	0.2	16,000	73	75	1,305	240	3.9	88.9	49.2
12	10.9	50	95	2	0	0	16,500	75	76	1,400	246	4.0	90.8	46.0
Mean	12.32	124.4	90.75	4.91	2.22	0.42	14,833	61.33	55.91	985.9	213.5	3.41	-	-

Day	PT	APPT	RBS (mg/dL)	HbA1C	Fer (ng/mL)	Lac.	Dd (ng/mL)	Trop-I (ng/mL)
1	12.8/10	30/30	833	11.4	637	43.8	1,992	645.5
2	13/10	32/30	-	-	-	-	-	-
3	15/10	35/30	-	-	-	-	-	-
4	16/10	36/30	670	-	1,250	-	2,236	-
5	18/10	36/30	-	-		49.8	-	-

6	18/10	37/30	566	-		-	-	-
7	20/10	38/30	-	-	988	56.8	4,370	777.9
Mean	16.11	34.85	689.6	.	958.3		2,866	711.7

HB, hemoglobin; PLT, platelets; N, neutrophils; L, lymphocytes; TLC, total leucocyte count; CRP, C-reactive protein; ALT, alanine transaminase; LDH, lactate dehydrogenase; Cre, creatinine; PCO2, partial pressure of carbon dioxide; PO2, 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.

3. Discussion

The highly contagious SARS-CoV-2 has been the major cause of global morbidity and mortality cases. The severity of COVID-19 ranges from mild to moderate or severe to higher fatality, and the mortality rates may increase depending on the health history of patients [11]. Herein, we reported the cases of two deceased individuals with COVID-19 and pre-existing comorbidities. In case I, the patient was co-infected with chronic HCV and had high ALT levels, which is agreement with previous data indicating that high liver biochemical parameters are associated with highest mortality (13%) of patients by COVID-19 [12]. Although elevated ALT concentrations have been reported in non-hepatic COVID-19 patients [13,14], the severity of elevated liver biochemical parameters such as ALT observed in case I correlated with the outcome of COVID-19, as demonstrated elsewhere [12].

The hematological data for case I also indicated fluctuation in certain coagulation parameters involving thrombocytes (thrombocytopenia), lymphocytes (lymphopenia), D-dimer, APTT and PT. Abnormalities in blood coagulation markers have a huge impact on the COVID-19 severity, indicating serious health complications in patients such as pulmonary embolism, venous thromboembolism, deep vein thrombosis, arterial thromboembolism, and sepsis-induced coagulopathy [15]. In addition, case I had altered values of TLC, LDH, CRP, troponin-I and serum ferritin, which are logically consistent with changes in hematological parameters associated to liver damage in HCV patients [16]. Based on these findings, we hypothesized that cardiac arrest in case I can be attributed to increased ferritin, troponin-I, leukocytosis, lymphopenia, thrombocytopenia, sepsis and vasopressors, as our findings in this context are in agreement with previous data [17]. This is also supported by the fact that higher troponin contributes to heart failure in HCV individuals, and that HCV infection significantly contributes to cardiac disorder [18,19].

Patient II presented comorbidities of CKD and DMT-2, as well as hypertension, which according to previous reports can duplicate the mortality risk of COVID-19 patients [20,21]. In this case, the deceased individual had higher levels of creatinine, urea and D-dimer, similarly to data reported previously in COVID-19 comorbid patients [22]. The involvement of affected kidneys and pre-infected cells has huge impact on COVID-19 progression. The angiotensin converting enzyme 2 (ACE2) receptor tightly binds these pre-infected cells in comorbid patients, which have higher expression rate than lung cells, forming shed soluble ACE2 (sACE2). The increase of sACE2 on transmembrane surface of the host easily allows entering SARS-CoV-2 [23], which may have favored the rapid outcome of COVID-19 in case II. Besides, case II also had elevated random blood sugar (RBS, >800 mg/dL) and glycated hemoglobin (HbA1C, 11.4 %), thus corroborating previous reports on higher levels of these parameters in hospitalized COVID-19 patients [24]. A meta-analysis of comorbid patients (n = 11,755) from Iran demonstrated a highest prevalence and death ratio comparatively attributed to diabetic patients [20], which is consistent with data reported here regarding case II.

The higher values of major coagulation markers such as PT, APTT and D-dimer in cases I and II are consistent with previous reports indicating that, at different tests levels, the coagulation indicators also raised in deceased subjects [25]. Hypercoagulation is an alarming signature for both COVID-19 and DMT-2, resulting in vascular thrombosis,

including cardiac arrest [26]. In our observations, we additionally noted higher lactate levels in the two deceased individuals. Sepsis, which causes poor tissue perfusion, leads to elevated lactate levels in the blood. This, in turn, can result in hypoperfusion, tissue hypoxia, and necrosis in infected tissue, ultimately contributing to higher mortality rates [27].

4. Conclusion

Here, we reported comorbid COVID-19 patients with HCV (case I), CKD, DMT-2, and hypertension (case II) that came to death due to cardiac arrest. These case reports highlight the severe complications of patients having comorbidities (e.g., HCV, CKD, diabetes, and hypertension) and COVID-19. The case reports described in this study also suggest that the deceased subjects may have acquired a multi-system inflammatory syndrome in adult (MIS-A), because they had severe organs dysfunction (septic shock, liver injury, cardiac arrest, etc.) and elevated inflammatory biomarkers (e.g., CRP, LDH, D-dimer, serum ferritin, among others). Thus, comorbidities associated with COVID-19 can bring dramatic adverse effects, stressing the need for extensive monitoring of comorbid patients to reduce morbidity and mortality.

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Supplementary Materials: None.

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