ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 13, Issue, 01, pp.15617-15624, January, 2021

DOI: https://doi.org/10.24941/ijcr.40508.01.2021

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

EXTRA- PULMONARY PRESENTATIONS OF COVID 19 PATIENTS ADMITTED UNDER INTERNAL MEDICINE TEAM IN RASHID HOSPITAL, DUBAI, UAE

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ARTICLE INFO

Article History:
Received 20th October, 2020
Received in revised form
18th November, 2020
Accepted 26th December, 2020
Published online 30th January, 2021

Key Words:
COVID.
COVID 19.
SARS COV-2.

ABSTRACT

Background: Covid-19 infection is primarily known as a pulmonary disease. We conducted a study to determine the various primary extra-pulmonary presentations of Covid-19 infection. **Objectives:** To identify the patients with Covid-19 infection presenting with extra-pulmonary manifestations, monitor the development and onset of clinical and/or radiological features of Pneumonia, determine the hospital course and outcome of these patients. **Methods:** We conducted a retrospective study by reviewing the charts of 111 patients admitted in Rashid Hospital, Internal Medicine department with COVID-19 infection who primarily had extra-pulmonary presentations with or without pneumonia from March,2020 - June,2020**.** We excluded the patients who presented with pneumonia. **Results:** Out of the 111 patients admitted with COVID 19 infection under medical team, 37 patients (33%) primarily had gastrointestinal presentation, 41(36.9%) had neurological presentation, 49(44%) had renal manifestations, 36(32.1%) presented with sepsis, 24(21.4%) were admitted with cardiovascular manifestations, 70(63%) had hematological features, 80(72%) had endocrine/metabolic features, 7(6.3%) had dermatological manifestations, 2 (1%) had arthritis, and 6(5.3%) were found to have psychiatric manifestations. Out of the 37 patients who had gastrointestinal presentation,16(43.2 %) had pneumonia at the time of admission, 6(16.2 %) developed pneumonia during admission and 15 (40.5 %) did not have pneumonia,9 patients (24.3 %) died whereas 28 (75.6 %) were discharged alive. Out of the 41 patients who had neurologic presentation,17(41.4%) had pneumonia at the time of admission, 13(31.7%) did not have pneumonia, whereas 11(26.8%) developed pneumonia during admission, 35 (85.3%) patients were discharged alive whereas 6 patients (14.6%) died in the hospital. Out of the 49 patients admitted with renal manifestations, 28(57%) had pneumonia on admission, 13 (26.5%) developed pneumonia during admission, whereas 8(16%) did not have pneumonia.35(71.4%) patients were discharged alive and 14(28.5%) died in the hospital. Out of 36 patients who presented with sepsis, 21(58.3%) had pneumonia on admission, 12 (33.3%) developed pneumonia during hospital stay, 24(66.7%) were discharged alive and 12 patients (33.3%) died. Out of the 24 patients (21.4%) who were admitted with cardiovascular manifestations, 21(87.5) had pneumonia on admission and 2(8.3%) developed pneumonia during hospital stay, 18(75%) were discharged alive and 6 patients (25%) died. Conclusion: Our study shows that a considerable number of COVID-19 patients presented with extra-pulmonary manifestations and in these patients pulmonary involvement was discovered radio logically, therefore it is important for the physicians to recognize these atypical presentations to avoid any potential hazard of exposure and any delay in the treatment of this infection.

Citation: ***Bina Nasim, Mohammad Saeed Yeddi, Essam Ahmad, Ayesha Zafar Gondal, Niaz Ahmed Shaikh and Jamila Mohammad Bin Adi.*** **2021.** "Extra- pulmonary presentations of COVID 19 patients admitted under Internal Medicine Team in Rashid Hospital, Dubai, UAE..", *International Journal of Current Research*, 13, (01), *15617-15624*.

INTRODUCTION

COVID-19 exhibits a diverse range of clinical presentations. Patients can present with either classical symptoms of fever, cough, difficulty in breathing, loss of taste, or with atypical symptoms such as gastrointestinal symptoms (diarrhea, vomiting, abdominal pain) as the index presentation, even occurring in the absence of other features (1). In a study of 67 COVID-19 patients with diarrhea, 13 cases had no other manifestations (2). Ocular manifestations, primarily conjunctivitis, have also been reported in case series, and the possibility of tear transmission has been suggested (3). Signs of renal dysfunction at presentation exhibited by high urea, creatinine, proteinuria and hematuria were reported in earlier studies done in China (4). Hematological manifestation like autoimmune hemolytic anemia, thrombocytopenia have also been reported as the initial presentations in COVID infected patients (5).

In critically ill patients with COVID 19 infection, evidence of raised inflammatory markers suggests Cytokine storm that may lead to certain atypical presentations. In this context, infected COVID patients have been reported to present solely with cardiac symptoms such as palpitations and chest pain, often due to underlying virus-induced myocardial injury (6). Cytokines have also been attributed to certain neurologic symptoms: a patient presenting with fever, cough and altered mental status eventually developed acute necrotizing hemorrhagic encephalopathy (7). Other atypical neurologic presentations include acute cerebrovascular disease and muscle injuries (8). Notably, the elderly and those with multiple comorbidities are severely affected by COVID-19, and atypical symptoms in these susceptible groups warrant further investigation.

Many dermatologic manifestations have been described in COVID-19 patients in studies done in China (9-11). Recalcati S, has analyzed dermatologic manifestations in 88 COVID-19 confirmed cases and he found that 20.4% of these patients were having cutaneous manifestations, almost half of the patients were found to have cutaneous manifestations at the initial presentation. He reported different dermatologic manifestations like erythematous rash, widespread urticaria, chicken pox like vesicles (9). Both venous and arterial thromboembolism have been reported in patients with COVID 19.

It has been proposed that the underlying mechanism could be due to the interaction between several factors like excessive inflammation, hypoxia, immobilisation and diffuse intravascular coagulation (DIC). Thromboembolic manifestations, including Deep vein thrombosis, Pulmonary embolism and acute large vessel stroke have been reported as the initial presentation in young patients without risk factors (12-16). A case series of 22 patients was published recently in June 2020, presenting with acute ischemic stroke and COVID 19. According to this study stroke was present on presentation in 18 (81.8%) of the patients (17). Our study aims to identify these extra pulmonary manifestations of COVID infection as a presenting featureto help guide the clinicians in early recognition of the infection and in initiating treatment. This will avoid any potential hazard of exposure of the clinicians and delay in treatment of the infection.

MATERIALS AND METHODS

This is a retrospective study in which the charts were reviewed of the patients admitted under INTERNAL MEDICINE service in Rashid Hospital with COVID-19 infection from March, 2020 - June, 2020, and the following components were determined: Baseline characteristics (nationality, age, gender), duration of stay in hospital, symptoms at presentation, admission diagnosis and preexisting comorbid conditions.

Study participants: Adults between- 16-90 years of age.

No of participants: 111. Male: 93, Female- 18.

Inclusion criteria

All Patients admitted under RH medical department with confirmed COVID-19 infection with atypical presentation with or without pneumonia.

Exclusion criteria

Patient primarily admitted with pneumonia

RESULTS AND DISCUSSION

Current century has witnessed pandemics with three lethal corona viruses, namely Severe Acute Respiratory Syndrome-SARS COV-1in 2002, Middle Eastern Respiratory Syndrome Corona virus- MERS COV in 2012and the recently ongoing COVID 19 pandemic with Severe Acute Respiratory Syndrome- SAR COV-2 that has affected over 77 million of the world population with a mortality of over 1.7 million.
All of these three lethal zoonotic viruses , have homologous structure therefore their pathogenic mechanisms are also similar causing direct viral cytotoxic endothelial damage, dysregulation of immune system and the renin angiotensin system(18).Inflammation leading to high levels of cytokines has been attributed to the cardiologic (6,7)and neurologic presentations (19). Studies done on patients infected with SARS COV 1 reported involvement of multiple organ systems otherthan the respiratory tract, namely gastrointestinal, renal, hematological and neurological system involvement.

Various studies done on the extrapulmonary organ dysfunction seen in MERS COV infected patients(20) reported increased mortality in this group of patients. The extrapulmonary system involvement seen in these patientswere hepatic dysfunction as manifested by the elevated liver enzymes, hemodynamic instability leading to septic shock, gastrointestinal involvement with patients presenting with acute abdomen and diarrhea, acute kidney injury, hematologic and neurological complications. Similarly studies done on SAR COV-2 infected patients demonstrated various extra pulmonary features due to the multiple organ involvement seen in patients who presented with respiratory tract infection (21,22). Our study highlights on the extra pulmonary presentations of COVID infection other than the typical pulmonary presentation. We admitted 111patients under the medical team between March-September 2020, who were found to have COVID-19infection and had extra-pulmonary presentation. 93 patients were male and 18 were female.

Baseline characteristics

Variables		Number of patients
Age	12-40	37
	41-65	57
	More than 65	17
Gender	Male	93
	Female	18
Ethnicity	South Asian	90
	Middle east	18
	Others	04
Co-morbidities	Hypertension	44
	Diabetes mellitus	56
	Neurological (Old CVA, Alzheimer, Epilepsy)	7
	Cardiac (IHD, Atrial fib, Cardiomyopathy, CHF, Prosthetic valve)	15
	Renal (CKD)	9
	Gastrointestinal (Hepatitis C)	2
	Rheumatology (Gout)	1
	Pulmonology (Asthma, ILD, COPD)	1
	Endocrine (Thyroid disorders)	4
	Malignancy	1
	None	38

Extra-pulmonary features

System involved		Number of patient	Relation to pneumonia		
			On admission	During admission	No pneumonia
Neurology		41	17	11	13
Neurological manifestation	TIA/Stroke	30	13	8	9
	Meningoencephalitis	1	0	0	1
	Neuropathy	5	2	2	1
	Exacerbation of underlying neurological disease	1	1	0	0
	Seizures	4	1	1	2
Cardiovascular		24	21	1	2
manifestation	Acute Coronary Syndrome	3	3	0	0
	Cardiac arrhythmia	4	4	0	0
	Acute heart failure	2	2	0	0
	Hypertension emergency/urgency	15	12	1	2
	Endocarditis	0	0	0	0
	Myocarditis	0	0	0	0
Gastrointestinal		37	16	6	15
manifestation	Acute hepatitis	25	12	6	7
	Hepatic encephalopathy	1	1	0	0
	Gastroenteritis	5	2	0	3
	Inflammatory bowel disease	2	0	0	2
	Acute gastrointestinal hemorrhage	4	1	0	3
Renal		49	28	13	8
manifestation	Acute Pyelonephritis	4	0	3	1
	Acute kidney injury	32	17	9	6
	Acute on chronic Kidney disease	13	11	1	1
	Acute Glomerulonephritis	0	0	0	0
Endocrine/ Metabolic		80	35	12	33
manifestation	Diabetic Ketoacidosis	11	7	0	4
	Diabetic hyperosmolar state	5	3	0	2
	Electrolyte imbalance	79	33	12	34
	Thyroid disease	0	0	0	0
	Alcohol withdrawal	5	1	0	4
Hematological		70	37	19	14
	Thrombotic Event DVT, PE, Systemic/ Visceral Thrombosis	7	3	0	4
	Clotting / Bleeding disorder	17	9	5	3
	Leukemia	1	1	0	0
	ANEMIA	44	17	6	11
	Thrombocytopenia	18	7	6	5
	Leucopenia/Leukocytosis	24	12	8	4
Dermatological		7	2	4	1
	Digital gangrene	1	0	1	0
	Other (herpes zoster and skin abscess)	2	1	1	0
Psychiatric		6	3	2	1
	Acute Psychosis	0	0	0	0
	Anxiety	0	0	0	0
	Depression	6	3	2	1
Rheumatology					
	Arthritis	2	0	1	1
Multi-systemic features		17	10	4	3
Sepsis		36	21	12	3

Outcome and hospital course

Extra-pulmonary manifestation	Hospital course				Outcome	
	Duration of hospital stay			Intensive care unit admission	Alive	Died
	Less than 7 days	8-14 days	More than 14 days			
Neurology	10	11	20	12	35/41	6/41- 14.6%
Cardiovascular	4	10	10	9	18/24	6/24- 25%
Gastrointestinal	8	14	15	13	28/37	9/37- 24.3%
Renal	16	15	18	19	35/49	14/49- 28.5%
Endocrine/ Metabolic	25	28	27	23	67/80	13/80- 16%
Hematological	23	21	26	23	58/70	12/70- 17%
Dermatological	1	2	4	0	7/7	0/7- 0%
Psychiatric	2	2	2	1	6/6	0/6- 0%
Rheumatology	0	1	1	0	2/2	0/2- 0%
Multi-systemic features	5	5	7	10	11/17	6/17- 35%
Sepsis	6	12	18	22	24/36	12/36- 33%

73 patients (65.7%) had multiple comorbidities with Diabetes present in 56 patients (50%), Hypertension in 44 (39.6%) and Cardiac comorbidities were present in 15 patients (13.5%), whereas 38 patients (34.2%) did not have any comorbidities.

Gastrointestinal presentation: In our study, 37 of the patients (33%) admitted with COVID 19 infectionprimarilyhad gastrointestinal presentation. The gastrointestinal manifestations of COVID 19 infected patients in our study were acute hepatitis/ jaundice (25 patients), gastroenteritis (5 patients), hepatic encephalopathy (one patient), and acute gastrointestinal hemorrhage (4 patients), in two of these it occurred due to ulcerative colitis. As per Table 2 in our study, out of the 37 COVID-19 patients who presented with gastrointestinal manifestations, 16 patients (43.2 %) had pneumonia at the time of admission, whereas 6 patients (16.2 %) developed pneumonia during admission and 15 (40.5 %) did not have any respiratory involvement. As per table 3 of our study, out of these 37 patients, 9 patients (24.3 %) died and 28 patients (75.6 %) were discharged alive. SAR COV-2 virus targets the gastrointestinal cells by attaching on the angiotensin converting enzyme-2 receptor which is expressed in a high concentration in the gastrointestinal tract. Studies done in China, have indicated an oro-fecal mode of transmission, as they have shown that the viral RNA was detected in the feces in about one half of the patients infected with this virus (23) and in about a quarter of the cases the stool sample tested positive even when the respiratory samples were negative (24). Other studies also done in China have reported few cases in which patients infected with COVID 19 presented with only gastrointestinal symptoms and did not have any respiratory involvement (25). Deranged liver enzymes and jaundice in COVID 19 infected patients could be due to direct infection by SAR COV 2 virus itself or drug induced liver damage.

Neurologic manifestation: We had 41 patients (36.9%) with COVID 19 infection who had neurological presentation. Out of these30 patients (73.1%)had TIA/ Stroke, critical illness neuropathy was present in 5 (12.1%) of the patients and 5 (12.1%) presented with exacerbation of the underlying neurological problem mainly seizures leading to status epilepticus. We had one patient who was admitted with meningitis who had COVID 19 infection also, but later it was confirmed to be TB meningitis. As per Table 2 in our study, out of the 41 COVID patients who presented with neurological manifestations, 17 (41.4%) had pneumonia at the time of admission, 13 (31.7%) did not have pneumonia, whereas 11 (26.8%) developed pneumonia during admission. As per Table 3 in our study, 20 out of the 41 patients (48.7%) had average duration of stay of more than 2 weeks with 12 (29.2%) patients needing Intensive care and 35 (85.3%) patients were discharged alive whereas 6 patients (14.6%) died in the hospital. Angiotensin-2 plays an important role in the cerebral autoregulation and the blood flow.A study on intracerebral hemorrhage in SARS COV 2 infected patients has shown that abnormal rise in the cerebral blood pressure that leads to intracerebral hemorrhage in these patients could be due to the dysfunction in the renin angiotensin system caused by this virus (26). In a study done by Desforges M., COVID 19 infected patients presenting with meningoencephalitis had fever, abnormal behavior, abnormal movements, seizures and focal neurologic deficits and CSF analysis in these patients also showed the presence of SARS COV 2 virus (27). The virus can also enter through the cribriform plate leading to hyposmia and anosmia (28).

Renal manifestation: In our study 49 patients (44%) had renal manifestation. Out of these Acute kidney injury was present in 32 patients (65%), acute on chronic kidney disease was present in 13 (26.5%) and acute pyelonephritis was present in 4 patients (8%). As per Table 2 in our study, 28 of these patients (57%) had pneumonia on admission, 13 (26.5%) developed pneumonia during admission, whereas 8 (16%) did not have pneumonia. As per Table 3 in our study, 16 of these patients (32.6%) had hospital stay for upto one week, 15 (30.6%) had hospital stay between 1-2 weeks and 18 of these patients (28%) had hospital stay of more than two weeks. 19 of these patients (38.7%) needed Intensive care. 35 (71.4%) patients were discharged alive and 14 patients (28.5%) died in the hospital. In a study done in China by Cheng et al, it was found that Acute kidney injury was associated with increased mortality (29). Direct cytotoxic damage leading to renal failure has been seen as the second fatal complication after respiratory failure in SARS COV-2 infection (30) and dysfunction of the renin angiotensin system are the potential pathogenic mechanisms by which the SARS COV 2 virus causes renal damage.

Sepsis: We had 36 patients (32.1%) who presented with sepsis and out of which 21 patients (58.3%) had pneumonia on admission and 12 patients (33.3%) had developed pneumonia during hospital stay, whereas 3 patients did not have pneumonia. As described further in table (3), 18 patients (50%) had hospital stay more than 2 weeks and 12 patients (33.3%) had hospital stay of 2 weeks and the rest

had hospital stay of 1 week. More than half of the patients (61.1%) required ICU admission, 24 patients (66.7%) were discharged alive and 12 patients (33.3%) had died. Many patients with severe COVID-19 infection worldwide, were found to common features that were typical for Sepsis. Most deaths in critically ill COVID-19 patients are precipitated by sepsis (31). Interestingly, about 80% of specimen cultures in septic patients from a COVID-19 cohort, had no bacterial or fungal infection which makes viral infection the most likely reason for sepsis. Common features of viral sepsis are intense cytokine release, prolonged inflammation, which results in immunosuppression, T cell exhaustion, with subsequent development of multiple organ damage, and increased susceptibility to secondary bacterial infections. SARS-CoV-2 can induce the cytokine storm in a subgroup of patients producing high levels of inflammatory mediators in COVID-19 patients, which was associated with severity and death. It is crucial to define these patients with sepsis by close monitoring and early detection (patients with high inflammatory markers, c-reactive protein, ferritin, lymphopenia, high IL-6, etc) for early intervention and introduction of medications which has proven of great efficacy in such cases, for example with dexamethasone, tocilizumab (32).

Hematological manifestation: In our study we had 70 patients (63%) who had hematological manifestations with COVID-19 infection. Blood dyscrasias namely anemia was seen in 44 patients (62.8 %) with one patient having autoimmune hemolytic anemia. Leucopenia or leucocytosis was seen in 24 patients (34.2 %), and thrombocytopenia was seen in 18 patients (25.7 %). Around 30 of these patients had bicytopenia or pancytopenia. 17 patients (24.2 %) had deranged coagulation with elevated Prothrombin time (PT) and International Normalized ratio (INR). Seven patients (10.0 %) presented with Acute thromboembolism out of which deep vein thrombosis was found in 3 (4.2 %), Pulmonary Embolism in 2 patients (2.8 %), cerebral venous sinus and jugular vein thrombus was found in one patient, and one patient presented with carotid arterial thrombus leading to large vessel ischemic stroke.

One patient who was admitted with COVID 19 infection was later found to have Chronic Lymphocytic Leukemia on further investigations. As per Table 2 of our study, out of these 70 patients, pneumonia was present in 37 (52.8 %) at the time of admission, 19 patients (27.1 %) developed pneumonia during admission, while 14 patients (20.0 %) did not have pneumonia. As per Table 3 of our study, duration of hospital admission was noticed to be as follow: 23 patients (32.8 %) stayed less than one week, 21 patients (30.0 %) were admitted from one to two weeks and 26 patients (37.1 %) stayed in the hospital for more than two weeks. While most of patients 47 (67%) were managed in general ward, 23 patients (32.8 %) needed intensive care unit admission, half of them (12) died. 58 patients (82.8 %) presented with hematological manifestations were safely discharged. It has been proposed that the underlying mechanism for venous and arterial thromboembolism in COVID 19 infected patients could be due to several factors like excessive inflammation, hypoxia, immobilization and diffuse intravascular coagulation (DIC) (33).

Cardiac manifestation: In our study we had 24 patients (21.4%) who were admitted with cardiovascular manifestations of Acute Coronary Syndrome, arrhythmias, acute heart failure, hypertensive urgency and emergency, and were found to be having COVID 19 infection. As described in Table 2, out of these 21 patients (87.5) had pneumonia on admission and 2 patients (8.3%) developed pneumonia during hospital stay. With further analysis of the above mentioned patients, 3 patients were admitted with ACS, all (100%) had pneumonia on admission, 4 patients had cardiac arrythmias, all of them were found to have pneumonia on admission, 2 patients were admitted with acute heart failure and all of them had pneumonia on admission and 15 patients were admitted with hypertensive urgency/emergency, out of them 12 patients (80%) had pneumonia on admission and one patient (6.6%) developed pneumonia during hospital stay.

As described in table (3), 10 patients (41.6%) stayed for 2 weeks , 10 (41.6%) stayed in the hospital for more than 2 weeks and the rest 4 patients stayed less than 1 week. Out of these patients, 9 patients (37.5%) required ICU admission, 18 patients (75%) were discharged alive and 6 patient (25%) died. Cardiac injury is common among hospitalized COVID-19 patients, and is associated with a higher risk of morbidity and mortality. In a study Shi S et al found cardiac injury in 19.7% of COVID-19 patients and first demonstrated that cardiac injury was independently associated with an increased risk of mortality in patients with COVID-19. Compared with patients without cardiac injury, patients with cardiac injury presented with more severe acute illness, manifested by abnormal laboratory and radiographic findings, such as higher levels of C-reactive protein, NT-proBNP, and creatinine levels, more extensive multiple mottling and ground-glass opacity, and a greater proportion requiring noninvasive or invasive ventilation(34). That was similar to our finding, 21.4% of COVID-19 patients were found to have cardiovascular complications. Most of these patients were having pneumonia on admission and had a complicated hospital course, including ICU admissions and higher mortality rate when compared to patients who did not develop cardiovascular complications. The mortality rate in these COVID 19 patients with cardiovascular involvement is high due to the development of the complications of Acute ST Elevation Myocardial infarction (STEMI) and Non STEMI and acute heart failure, myocarditis and arrhythmias.

Dermatologic manifestation: In our study7 patients were found to have dermatological manifestations with COVID 19 infection. Out of these 4 patients (57.1%) presented with widespread cutaneous small vessel vasculitis and were found to have COVID 19 infection subsequently,and 1 (14.2%) patient was admitted with digital gangrene. As per Table 2 of our study, out of these 7 patients, only 2 patients (28.5%) were found to have pneumonia at the time of presentation, whereas 4 patients (57.1%) developed pneumonia during hospitalization and 1 patient (14.2%) did not develop pneumonia. As per Table 3 in our study, 4 of these 7 patients (57.1%) had hospital stay of more than two weeks, 2 (28.5%) had hospital stay of more than one week and only one (14.2%) had hospital stay of less than a week. None of the COVID patients admitted with dermatological manifestations needed intensive care admission and all of them were discharged alive from the hospital with 0% mortality. The pathogenesis for the dermatological manifestations appears to be SARS COV-2 induced direct vascular injury leading to inflammation. Other potential mechanisms behind the pathogenesis of these dermatological manifestations have

been found to be the presence of microthrombi due to hypoxic injury to the vascular endothelial cells in the skin leading to vasculitis, and immune hypersensitivity response leading to cytokine storm (35).

Rheumatologic land Immunological manifestations: In our study we had one patient who presented with Septic Arthritis and had COVID-19 infection. Another patient was admitted with autoimmune hemolytic anemia and was diagnosedto have Systemic Lupus Erythematosus and Antiphospholipid Syndrome and Autoimmune thyroiditis. The first patient did not develop pneumonia while the later developed pneumonia after admission, none of them needed intensive unit care and both were discharged home. It has been proposed that as SARS COV-2 causes dysfunction of the immune system therefore it can precipitate autoimmune diseases (36).

Psychiatric manifestation: In our study there were 6 patients (5.3%) who were found to have psychiatric manifestation, all of these were found to have features of depression with or without suicidal ideation. As shown in Table 2 of our study, 3 patients (50%) had pneumonia on admission and 2 patients (33.3%) developed pneumonia during hospital admission. As shown in Table 3 of our study, out of these only one patient (16.6%) required ICU admission, and all patients were discharged alive. The pathogenesis of psychiatric symptoms which occur during (COVID-19) pandemic may include biologic and psychosocial factors. COVID-19 can indirectly affect the central nervous system through, probably, the associated inflammatory immune response as well as the medical interventions used. COVID-19 appears to be frequently associated with a neuropsychiatric syndrome in the acute phase of the illness. Deng J et al, assessed the prevalence of depression, anxiety and sleeping disorder in COVID-19 patients and concluded that 45% of COVID -19 patients had experienced depression, 47% of the patient had anxiety and 34% of the patient had sleeping disorders (37). Psychiatric manifestations should be sought thoroughly in COVID 19 infected patients, as they need active management by psychiatry team for better outcome and helps in reducing the morbidity and hospital stay. In our research the number of patients admitted with psychiatric manifestations appears less when compared to other studies because in our studies we focused on the patient who were admitted under medical team because of their active medical problem but we believe that many patients were admitted under infectious/psychiatry team who had COVID 19 infection with underlying psychiatry illness.

Endocrine manifestation: In our study, we had 80 patients (72%) with COVID 19 infection who had endocrine/metabolic presentation. Out of these 11 patients (13.7%) presented with diabetic ketoacidosis, 5 patients (6.25%) were found to have Hyperosmolar Non ketotic state, and 5 patients (6.25%) presented primarily with alcohol withdrawal. Two patients in our study were found to have hypothyroidism and one of these patients had autoimmune thyroiditis with very high levels of thyroid peroxidase antibodies. 79 patients (98.7%) had electrolyte imbalances including hyponatremia, hypokalemia, metabolic acidosis, hypomagnesemia etc. Many of these patients had electrolyte imbalances in addition to diabetes. As described in table 2, with further analysis of these patients, it was found that of the 11 patients who presented with DKA, 7 patients (63.6%) were found to have pneumonia on admission, while 3 of the 5 patients who presented with HONK, had pneumonia on admission. The rest of the above mentioned patient (admitted with DKA and HONK) did not havepneumonia.

Of the 79 patients who had electrolyte imbalance, 33 patients (41.7%) had pneumonia on admission and 12 patients (15.1%) had developed pneumonia after admission. Out of the 5 patients who were admitted with alcohol withdrawal, 1 patient (20%) had pneumonia on admission. As described in table 3, 23 patients (28.7%) with endocrine/metabolic presentation, required ICU admission and 63 patients (83.7%) were discharged alive and 13 patients (16.3%) died. Recent published studies have reported that patients with diabetes exhibithigher mortality and had a worse prognosis when comparedto patients without diabetes (38). Acute hyperglycemic crises, including; diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS), are the serious acute metabolic complications of diabetes, and might be precipitated by COVID-19 infection (39). Thus, intensive monitoring and aggressive supportive care are mandatory for the poorly controlled diabetic patients with COVID-19 infection. Studies on electrolytes abnormalities in COVID-19 patients, showed higher prevalence of hyponatremia, hypokalemia and hypocalcemia. A pooled analysis included five studies, with a total sample size of 1415 COVID-19 patients,was performed to estimate the weighted mean difference (WMD) with 95% confidence interval for each electrolyte (sodium, potassium, chloride and calcium) in laboratory-confirmed COVID-19 patients with or without (i.e. versus) severe disease.

It has been found that COVID-19 severity is associated with lower serum concentrations of sodium, potassium and calcium (40). This was similar to our study as hyponatremia was the most common electrolyte imbalance seen followed by hypokalemia. So we recommend to monitor the electrolytes on admission and during hospital stay to prevent any further complications. In our study, 5 patients (6.25%) presented primarily with alcohol withdrawal. During the COVID-19 pandemic in order to control the spread of the disease with subsequent lockdown, alcohol consumption was greatly affected. A population survey of 1555 active drinkers in the UK identified that 21% increased alcohol consumption during the lockdown, while 35% reduced their alcohol intake. Lockdown poses a major risk of increasing alcohol intake in people with alcohol use disorders and chance of relapse for those who were previously abstinent. Support from alcohol liaison services might prevent relapse during lockdown.

Conclusion

Our study shows that a considerable number of COVID patients presented with extra-pulmonary manifestations like stroke(ischemic and hemorrhagic), diarrhea, thromboembolism, Acute coronary syndrome, acute heart failure, hypertensive emergency and urgency, sepsis with acute kidney injury, hemolytic anemia secondary to precipitation of autoimmune diseases, widespread cutaneous rash, electrolyte imbalance (hyponatremia, hypokalemia) and in these patients pulmonary involvement was discovered radiologically, therefore in the light of the widespread COVID 19 pandemic it is important for the physicians to

recognize these atypical presentations in order to avoid any potential hazard of exposure of the clinicians and avoid any delay in the treatment of this infection.

Conflict of Interest statement: None.

Funding statement: No funding was done for the study.

Abbreviations

Severe Acute Respiratory Syndrome- SARS COV-1
Middle Eastern Respiratory Syndrome Corona virus- MERS COV
Severe Acute Respiratory Syndrome- SAR COV-2
Diffuse intravascular coagulation- DIC.
Intensive care unit- ICU.
Prothrombin time and International Normalized ratio- PT & INR.
Acute Coronary Syndrom- ACS.
Acute ST Elevation Myocardial infarction (STEMI)
Diabetic ketoacidosis- DKA.
Hyperosmolar Non ketotic state- HONK.
Hyperglycemic Hyperosmolar State- HHS.

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