CASE SERIES

Contagion of coronavirus disease—the first family cluster of Pakistan: a case series

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Abstract

Coronavirus Disease has resulted in public health crisis all over the world. We describe the case series of a family, who travelled together to a mass gathering in Iraq, toured Syria, Lebanon, and Doha and returned to Karachi. The data describes the demographic and clinical features of these six members. There were three males and three females. One developed severe disease and died. Incubation period was between 8-14 days. Four patients were symptomatic, had diabetes mellitus and hypertension; and presented with fever. They also had bilateral airspace opacifications on chest X-ray. Our study describes familial clustering of SARS-CoV-2 and its person-to-person transmission.

Keywords: Covid-19, Family cluster, Mass gathering, Epidemiological features.

DOI: 10.47391/JPMA.5128

Submission completion date: 09-11-2021
Acceptance date: 21-07-2022

Introduction

The World Health Organisation (WHO) on March 11, 2020, declared the Covid-19 outbreak a global pandemic.[1] Till June 2021, 955,657 cases were reported in Pakistan.[2] The SARS CoV2 virus mainly spreads through respiratory secretions from an infected person, indirect contact through fomites and aerosol transmission in enclosed spaces with poor ventilation. Its transmission has been rapid in household/healthcare settings and in large gatherings, e.g. places of worship, and workplace. Therefore, contact tracing of cases is essential to control the spread of the virus. Here, we report the epidemiological, clinical, radiological, and laboratory findings of the first family cluster identified in Karachi, Pakistan.

Case Series

The first case of Covid-19 in Pakistan was confirmed by the Ministry of Health (Government of Pakistan) on February 26, 2020, in Karachi, Sindh. On March 8, 2020, the index case of the first family cluster of Pakistan presented to the Aga Khan University Hospital, Karachi. The indexed case was a 54-year-old gentleman, who presented to the AKUH emergency department, with the complaints of fever, shortness of breath, myalgia's and generalised weakness for the past one week. The family cluster had a history of travel from a region where Covid-19 outbreak was ongoing. Here, we describe the characteristics of the first familial cluster of Covid-19 in Pakistan. Subsequently, five other members of the family, who had travelled along, also presented to our hospital after being identified through contact tracing by the Health Department of Sindh, Pakistan.

The family had travelled from February19, 2020 to March 1, 2020. Their visit coincided with the time frame when the first case of SARS CoV2 was reported in Iraq, Lebanon, and Qatar in February 2020; as well as the first case of Covid-19 in Pakistan. The ages of our patients ranged between 50 and 70 years, whilst the time since onset of symptoms was between 8 and 15 days. Patients 1, 2, 3, and 5 were symptomatic (Table 1). Patients 1, 2, 3 had fever during travel, while patient 5 developed fever after his return and had taken antibiotic for five days before presenting to the hospital on March 10, 2020.

Oral and Nasopharyngeal swabs of these six patients were taken for qualitative SARS CoV-2 coronavirus RT-PCR test. Blood samples for other laboratory investigations were also obtained. Patient 1 developed shortness of breath on the third day of illness and required mechanical ventilation on day 9. Patient 3 started becoming hypoxic on day 3, was kept on up to four litres/minute of oxygen supplementation and was weaned off oxygen support by day 9. Patients 1 and 3 developed shortness of breath. patient 3 and 4 also developed diarrhoea on day 4 to 9 of their hospital admission. A normal complete blood count was found amongst most (n=5) of our patients. However, Patient 1 had neutrophilia and lymphopenia. Initially, he was treated with tablet Oseltamivir 75mg (every 12 hours) for 11 days and tablet Chloroquine 500mg (every 12 hours) for 10 days. He had prolonged intensive care stay complicated by secondary bacterial infections, for which

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Table-1: Summary of clinical features and laboratory results, at presentation

Laboratory Investigations	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Relationship	Brother	Brother	Brother	Wife	Sister	Helper
Age(years)	54	51	67	61	70	49
Gender	Male	Male	Male	Female	Female	Female
Comorbidities	Diabetes, Hypertension	Hypertension	Diabetes, Hypertension	None	Diabetes, Hypertension	None
Time from illness onset to first hospital admission	15 days	15 days	7 days	15 days	15 days	NA
Oral and Nasopharyngeal swab	8th march	10th march	10th march	10th march	10th march	10th march
Clinical Symptoms	Fever, SOB, Myalgia	Fever	Fever, Cough	NA	Fever	NA
CBC						
Hb (12.3-16.6)/(11-4.5) g/dl	12.2	13	13.3	12.3	12.3	12.6
MCV (78.1-95.3) fl	80.8	71	86.2	87.3	83	81.6
WBC (4.6-10.8) x10E9/L	11.7	6.4	5.4	5.1	6.4	5
Neutrophils (34.9-76.2) %	84.7	59	56.8	56.6	46.3	55.8
Lymphocytes (17.5-45.0) %	9.6	29.8	37.5	31	37.1	36.5
Eosinophils (0.3-7.4) %	0.8	0.3	0	2.2	5.8	0.2
Monocytes (3.9-10) %	4.8	10.7	5.5	9.6	10.2	7.3
Basophils (0-1) %	0.1	0.2	0.2	0.6	0.6	0.2
Platelets (154-433) x10E9/L	394	247	254	304	239	283
Peripheral film	normocytic, normochromic, neutrophilia	hypochromic, microcytic	normocytic, normochromic	normocytic, normochromic	normocytic, normochromic	normocytic, normochromic
Neutrophil to Lymphocyte ratio	9	2	2	2	1	2
Kidney function						
BUN (6-20) mg/dl	11	9	11	14	9	5
Cr (0.6-1.1) mg/dl	0.9	0.8	1.2	0.6	0.7	0.6
Electrolytes						
Na (136-145) mmol/L	147	142	136	140	143	142
K (3.5-5.1) mmol/L	4.4	4	5.4	4.3	4.5	4.1
Cl (98-107) mmol/L	111	105	99	107	108	105
BIC (20-31) mmol/L	22.2	24.9	24.8	23.8	25.2	28.3
Liver Profile						
TB (0.1-1.2) mg/dl	1.4	0.3	0.3	0.3	0.4	0.6
DB (0-0.2) mg/dl	0.4	0.1	0.1	0.1	0.1	0.2
IB (0.1-0.8) mg/dl	0.9	0.2	0.2	0.2	0.3	0.4
GGT (Male : <55 / Female : <38) IU/L	96	52	61	77	22	14
SGPT (Male : <45 / Female : <35) IU/L	27	37	35	22	21	29
AP (45-129) IU/L	67	92	74	96	77	129

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SGOT IU/L	(Male : <35 / Female : <31)	25	34	59	24	20	30
Coagulation profile							
PT	(9.3-12.8) seconds	10.3	10.2	10.7	10.1	NA	10.5
INR	(0.9-1.2) ratio	1	1	1	0.9	NA	1
APTT	(22.9-34.5) seconds	26.2	25.3	24.6	NA	NA	23.2
HbA1C %		6.8	NA	9.1	5.7	6.2	NA
Abnormal Chest X-ray		Bilateral vascular congestion with airspace shadowing predominantly in bilateral lower lung zones	Bilaterally areas of pneumonic consolidation in upper lung field.	Bilateral patchy airspace densities representing diffuse infection.	Unremarkable	Patchy areas of airspace opacification seen in left perihilar region and both lower lobes.	No evidence of infiltrates, consolidation or pleural effusion. Left mild basal atelectatic changes.

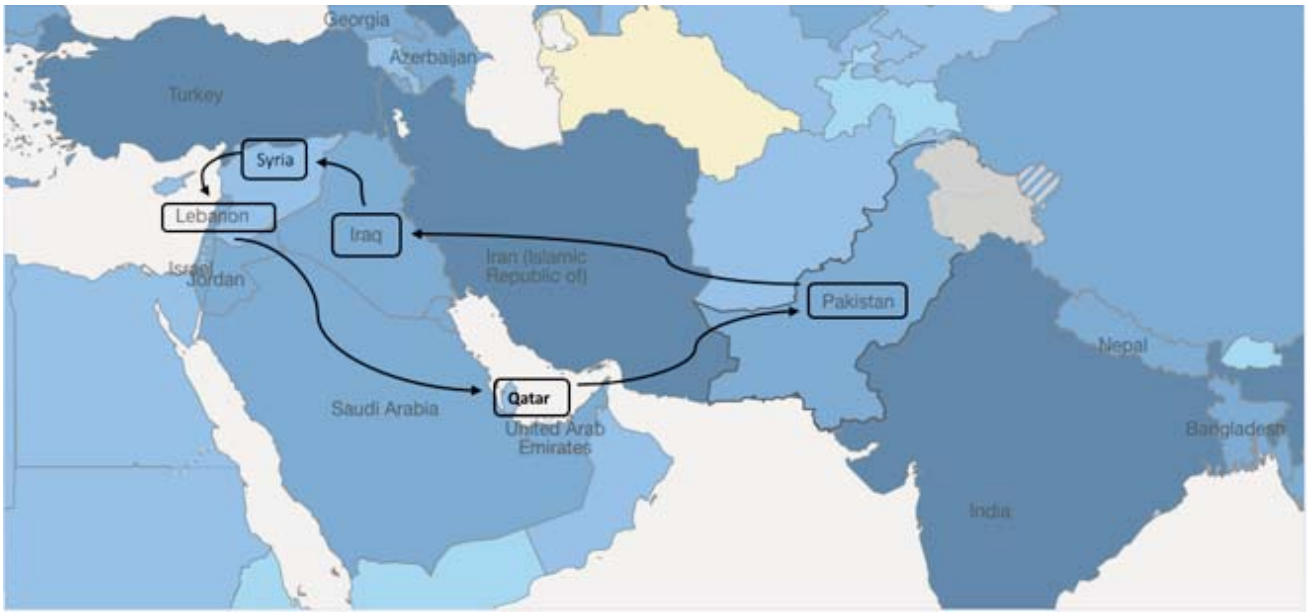

Figure: MAP showing the route taken by family cluster, mass gathering sites. SARS CoV2: Severe acute respiratory syndrome coronavirus 2 , RT-PCR: Reverse Transcription-Polymerase Chain Reaction AKUH: Aga Khan University Hospital

he was treated with intravenous antibiotics. Patient 2 was given tablet Fexofenadine 120 mg (once a day) for 7 days. Patient 3 was treated with tablet Oseltamivir 75 mg (every 12 hours) for 7 days and tablet chloroquine 500mg (every 12 hours) for seven days. Patient 5 was given probiotics Dioctahedral Smectite (every 12 hourly) for five days and tablet Surbex-Z (once a day) for six days. Patient 4 and 6 did not require any treatment. Patient 1 expired, whilst the remaining patients did not require follow-up; as all of them were discharged upon having two consecutive negative SARS CoV-2 PCR tests done 24 hours apart (after 14 days of in-hospital isolation). Informed consent was taken from the patients prior to writing the manuscript.

Discussion

Familial clustering has been integral in the development of Covid-19 pandemic. Our case series describes the clinical course of the first familial cluster of Covid-19 from Pakistan where majority had a mild course of illness, with only one mortality. Minimal data regarding epidemiological and clinical correlation of Covid-19 in

siblings is reported to date. Bacharaki D et al reports a case of two elderly diabetic siblings who were infected simultaneously with Covid-19 but had opposite outcomes. The brother with normal renal function died, whereas the sibling on haemodialysis followed a benign course.[3] Yousefzadegan et al hypothesised genetic predisposition in Covid-19, reporting death of three middle-aged brothers, within two weeks of contracting the virus from the indexed case brother.[4] In our family cluster, four amongst six were siblings and had similar moderate pulmonary involvement as evidenced by their chest X-rays.

Our patients primarily reported with upper and lower respiratory tract infection symptoms and later developed gastrointestinal symptoms. Four out of six had fever, one of 6 had cough, and 2 of 6 had shortness of breath and diarrhoea. Huang et al reports similar findings in their study.[5]

Male gender has been identified as an independent risk factor for higher severity and mortality in patients with Covid-19, independent of the age in a study.[6] The male members in our family cluster had characteristic Covid-19 chest radiographic findings at initial presentation, contracted more severe disease (as compared to the female family members) with requirement of supplemental oxygen, mechanical ventilation, and there was one mortality as well. However, no correlation of death with age of the patients was observed in our cohort, as the younger member of the family had a greater severity of illness and fatal outcome.

Chest x-rays are 69% sensitive in detecting changes due to Covid-19.[7] Portable chest X-ray was done in the isolation ward as a baseline investigation and to minimise the risk of cross infection.[8] Chest x-ray of four patients showed abnormal findings. Three of the four patients showed bilateral airspace opacifications. The most frequent findings in CXR were airspace opacities described as lung consolidation/ground glass opacities.[8] These were bilateral (in 3 of 6), peripheral and at the lower ones (in 1 of 6).

Lymphopenia is a predictor for disease progression and severity.[9] Amongst our family cohort, five out of six members had a normal lymphocyte count. Only one patient had a decreased lymphocyte count, and his disease was severe as compared to other patients. Another study comparing three family clusters showed lymphocyte counts of sporadic cases to be lower than family cluster cases.[10] Higher neutrophil to lymphocyte ratio (NLR) is an independent risk factor of the in-hospital mortality for Covid-19 patients especially males,[11] which was a finding in our patient No. 1.

Fifty percent of the patients in our cluster suffered from diabetes. A high HbA1C did not correlate to a worse prognosis in our study (see Table-1); patient 1, recently diagnosed, recently diagnosed with diabetes (on in-hospital admission HbA1C), had poor outcome. Those already diagnosed and on oral hypoglycaemic agents fared well. Huiqing et al observed that newly diagnosed diabetes had highest percentage of ICU admission,[12] as seen in patient one. Four out of 6 of our patients had hypertension.

Chloroquine has historically been used for malaria prophylaxis. Studies have shown its potential as an anti-viral agent, by interfering with the glycosylation of cellular receptors of SARS-CoV. It has shown efficacy and acceptable safety against Covid-19 pneumonia in multicentre clinical trials conducted in China in February 2020.[13] Similarly, the use of Oseltamivir and Lopinivar/Rotinivar as an anti-viral therapy was observed in a large case series of 99 patients reported in China in January 2020.[14] The duration of antiviral treatment for Chen N. et al[14] was between three and 14 days, whereas in our patients the duration varied from 7 to11 days, depending on the clinical condition. The above mentioned drugs are no longer used and recent data has failed to show any clinical benefit for Covid-19.

Our study had some notable limitations. Firstly, Chest Computed Tomography of our patients was not done. Secondly, other inflammatory biomarkers, e.g. serum ferritin, serum lactate dehydrogenase, albumin, and D-Dimer were not done due to the limited information on the pathophysiology of the disease and relevance of these biomarkers in the initial phase. These markers could have helped in characterising the severity of the disease and predicting mortality of hospitalised Covid-19 pneumonia patients.[15]

Conclusion

The findings are consistent with family clustering of the novel coronavirus and its person-to-person transmission. We report that among siblings, the male member who had early worsening of chest X-ray findings, decreased lymphocyte count along with newly diagnosed diabetes, had poor outcome. Further research is needed in recognising the disease pattern of Covid-19 in people with similar genetic background, i.e. families. It is also important to recognise the epidemiology of Covid-19 as the family cluster had history of travel to mass gathering from Covid-19 outbreak regions to Pakistan. This would help the government and public health authorities devise mitigation measures for communal spread of the disease.

Acknowledgement: We are grateful to Dr Taymmia Ejaz and Dr Henna Fatima for their support and guidance and contribution of Dr Syed Faisal Mahmood, Associate Professor, Aga Khan University in drafting in final manuscript.

Disclaimer: None to declare..

Conflict of Interest: None to declare.

Funding Disclosure: None to declare.

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