ORIGINAL ARTICLE

Clinical Characteristics and Early Findings of Coronavirus Disease (Covid-19) at a Tertiary Care Teaching Hospital in Pakistan

WASEEM IQBAL^{1,2}, UROOSA IRAM³, MOIZ INAM KHAN⁴, NAZISH FAROOQ⁵, AMNA IRAM⁶, ZAHID REHMAN⁷, MATI ULLAH⁷, IHSAN ALI^{7*} ¹Department of Pathology, Marden Medical Complex, Mardan, KP, Pakistan.

- ²Department of Medical Laboratory Technology, Faculty of Basic & Applied Sciences, The University of Haripur, KP, Pakistan.
- ³Department of Microbiology, Abdul Wali Khan University, Mardan, KP, Pakistan.
- ⁴Medical Teaching Institution, District Head Quarter Hospital, Dera Ismail Khan, KP, Pakistan.
- ⁵Professor and Chairman, Pathology Department, Mardan Medical Complex, Mardan, Pakistan.
- ⁶Department of Physiology, Fatima Memorial Hospital Collage of Medicine and Dentistry, Lahore, Punjab, Pakistan.

⁷Institute of Paramedical Sciences, Khyber Medical University, Peshawar, KP, Pakistan.

Corresponding author: Dr. Ihsan Ali, Email: Ihsanmicro@gmail.com/ihsan.ipms@kmu.edu.pk

ABSTRACT

Background: Severe acute respiratory syndrome-2 (SARS-CoV-2) emerged as a novel coronavirus and associated with the pandemic. In our study we observed the clinical characteristics, early findings, and its association with comorbidity.

Methods: A single center retrospective study was carried out in Mardan Medical Complex (MMC), Khyber Pakhtunkhwa (KP), Pakistan from May 21st, 2020 to June 30th, 2020. Altogether three thousand, one hundred and fifteen (n=3115) COVID-19 suspected patients were included in the current study. Briefly nasopharyngeal swab, sputum and blood were collected. The viral amplification was carried out by qualitative RT-PCR using commercially available kit and routine laboratory tests of all the suspected patients were performed.

Results: Using RT-PCR total 19.8% (n=613/3115) confirmed cases of COVID-19 were observed. The majority were males' patients. The most common comorbidity was type-2 diabetes (T2DM); 24.8% followed by cardiovascular diseases; 6% and T2DM with cardiovascular disease 3.1%. Among the infected patient's leukocytosis was observed in 43% patients and 27.9% had abnormal findings on X-rays. The RNA detection efficacy from the sputum, nasopharyngeal swab, and blood specimens were 30%, 25.3% and 9.6% respectively. In total, 18.3% patients were critical, and 14.5% patients were on ventilator and the reported mortality rate were 5.2%.

Conclusion: Overall, the COVID-19 patients observed in our study was comorbid and asymptomatic or with mild symptoms like fever, cough, and shortness of breath. Higher, RNA detection efficacy was observed from sputum. **Keywords:** COVID-19, RT-PCR, T2DM, Clinical characteristics, comorbidity, Pakistan

INTRODUCTION

Sever acute respiratory syndrome-2 (SARS-CoV-2) emerged as a novel coronavirus and associated with severe respiratory diseases named as coronavirus diseases-2019 (COVID-19). On March 11, 2020 the World Health Organization (WHO) declared COVID-19 as a pandemic diseases and its cases has been reported in >200 regions and countries^{1,2,3}. Human to human transmission are mainly through respiratory droplets and close contact ^{4,5}. In mild infection the clinical manifestation is mainly fever, body aches and cough whereas in severe cases life threatening conditions such as shortness of breath, respiratory failure, and acute respiratory distress syndrome (ARDS) occurs 6,7,8. Currently, various studies have been reported on clinical characteristics of COVID-19 patients from different countries^{9,10,11}. There is scarcity of data from Pakistan regarding its clinical characteristics and early findings. Therefore, the current study is based on comparison of different specimens for the detection, clinical history, radiological findings, and its association with comorbidity.

MATERIALS AND METHODS

A single center retrospective study was carried out in Mardan Medical Complex (MMC), Khyber Pakhtunkhwa (KP), Pakistan from May 21st, 2020 to June 30th, 2020. The MMC is the largest referral tertiary care teaching hospital of the province with the capacity of 520 beds. The hospital has emergency, intensive care unit, supportive services and all the minor and major facilities with state of the art diagnostics. The study population included all the patients who were initially presented with fever, respiratory symptoms and pulmonary infiltrates on chest radiographs and had been diagnosed as SARS-CoV-2 pneumonia as per WHO interim guidelines ¹². The patients related information such as history, physical findings, radiological, microbiological, biochemical, and hematological investigations were recorded.

The patients detailed data were collected including age, gender, history of exposure, initial sign and symptoms (cough, fever, chest pain, headache and vomiting etc), vital signs (blood pressure, heart rate, respiratory rate), laboratory investigations and co-infections.

A total three thousand one hundred and fifteen (n=3115) individuals suspected of coronavirus infection were included. Briefly, nasopharyngeal swab, sputum and blood were collected. The nasopharyngeal swabs were placed in viral transport medium (VTM). Plasma and serum were separated from EDTA and clotted blood, respectively. The study was approved by Ethical committee Department of Medical Laboratory Technology, Th University of Haripur, and Mardan Medical Complex, Mardan.

On the basis of observed symptoms routine laboratory tests of all suspected patients including inflammatory biomarkers, D-Dimer, Lactate dehydrogenase, C reactive protein (Architect C 4000, Abbott, USA), Ferritin and Troponin I (Architect I 1000, Abbott, USA), complete blood count (CELL DYN ruby system, Abbott, USA), Alanine transaminase (ALT), bilirubin, urea and creatinine (Architect C 4000, Abbott, USA) were performed.

The viral RNA was extracted by MagMax *mirVana* Total RNA isolation Kit (Thermo Fisher Scientific) and amplification was carried out by qualitative RT-PCR using commercially available kit (Sansure Biotech Inc) in Rotor Gene Plate (QIAGEN, Germany).

SPSS software, version 21.0 was used for statistical analysis and for comparison of variables Chi square test was performed. The percentages of patients in each group were calculated for categorical variables.

RESULTS

During study period a total of three thousand one hundred and fifteen (n=3115) samples were processed for corona virus detection by RT-PCR and 613 (19.8%) confirmed cases of CoVID-19 were observed. Among positive cases 421 (66.7%) were male and 210 (33.3%) were female. The confirmed patients were categorized into 4 age groups and the highest numbers of cases were in the age group of 21-40 years (Table 1).

Overall, 112 (18.3%) patients were critical, and 89 (14.5%) patients were on ventilator and the reported mortality were 32/613 (5.2%). The most common symptoms observed during infection were headache 595 (97.1%), fever 586 (95.6%), sore throat 511 (83.4%) and cough 444 (72.4%) etc (Table 1). The common comorbidity observed were type-2 diabetes (DM2) 152 (24.8%)

followed by cardiovascular diseases 37 (6.03%), DM2 with cardiovascular disease 19 (3.09%) and other diseases (liver, lungs, and kidney diseases etc) were 26 (4.24%). Remarkably, 379 (61.8%) had no underlying comorbidities and no cases of immunodeficiency was observed. Among the infected patient's leukocytosis and lymphocytosis were observed in 176/409 (43.03%) and 58/409 (14.18%) patients whereas lymphocytopenia, thrombocytopenia and leukopenia were 170/409 (41.56%), 167/409 (40.83%) and 14/409 (3.43%) respectively as shown in table 2.

Table 1. Study population and characteristics of COVID-19 patients

Demographic and cinical readies of the patients					
Age group					
Variables %(n)		1-20yrs	21-40yrs	41-60yrs	>60yrs
Overall		9.3 (57)	43.4(266)	37.2(228)	10.1(62)
Male 53	3.8(330)	9.7(32)	44.5 (147)	35.2 (116)	10.6 (35)
Female 46	6.2(283)	8.8 (25)	42 (119)	39.6 (112)	9.5 (27)
Onset Symptoms					
Headache	97(595)	5.9 (35)	33.8 (201)	39.1 (233)	21.2 (126)
Fever	95.6(586)	5.1 (30)	33.8 (198)	24.7(145)	36.4 (213)
Cough	83.4(511)	9.4 (48)	26.4 (135)	24.8(127)	39.4 (201)
Chest pain	72.4(444)	12.2 (54)	19.4 (86)	26.6 (118)	41.8 (186)
Loss of taste	64(393)	3.8 (15)	18.8 (74)	43 (169)	34.4 (135)
Loss of smell	39.3(241)	10.4 (25)	34.8 (84)	30.3 (73)	24.5 (59)
Shortness of breath		1.4 (3)	23.8 (51)	35 (75)	39.8 (85)
	35(214)				
Diarrhea	22.5(138)	5 (7)	27.5 (38)	28.3 (39)	39.2 (54)
Abdominal pain 17.4(107)		5.6 (6)	26.2 (28)	38.3 (41)	29.9 (32)
Runny nose/Flu 14.5(89)		13.5 (12)	16.8 (15)	24.8 (22)	44.9 (40)
Comorbidity					
Diabetes	24.8 (152)	0	12.5 (19)	38.8 (59)	48.7 (74)
Cardiac Disease 6.2 (38)		2.70 (1)	13.51 (5)	32.43 (12)	54.0 (20)
Diabetes+ Cardiac		0	0	57.89 (11)	42.1 (8)
	3.3(20)				
Others	4.2(26)	7.7 (2)	23.1 (6)	26.9 (7)	42.3 (11)

Table 2. Laboratory findings of COVID-19 patients

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Variables	Positive mean ±	Negative mean	Units	Reference
	SD value	± SD value		range
TLC	9.24±4.75	6.65±2.23	(10e3/uL)	3.70-10.1
Neutrophils	64.52±18.19	57.43±10.20	(%)	39.3-73.7
Lymphocytes	26.66±16.98	34.52±9.81	(%)	18.0-48.3
Monocytes	7.08±2.35	6.93±1.45	(%)	4.40-12.7
Platelets	221.56±91.60	293.58±53.74	(10e3/uL)	155-366
D Dimer	1917±2110.497	156.05±15.93	(ng/mL)	140-198
LDH	340.63±138.79	211±13.2	(U/L)	125-220
Ferritin	560.82±749.94	188.01±53.72	(ng/mL)	4.63-
				274.66
CRP	3.73±2.89	0.32±0.19	(mg/dL)	0.00-0.50
ALT	39.45±43.39	34.29±13.11	(U/L)	0-55
Bilirubin	0.74±0.47	0.8±0.2	(mg/dL)	0.2-1.2
Urea	31.75±14.49	35.44±9.2	(mg/dL)	10-50
Creatinine	0.85±0.35	0.91±0.25	(mg/dL)	0.57-1.25
Tron I	158 94+1234 93	18 81+4 06	(na/ml)	0.0-29.7

LIC; Total leucocytes count, LDH; lactate dehydrogenase, CRP: C Reactive protein, ALT: Alanine Transaminase

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X rays Findings	No of Patients 25.1%(n=154)		
Normal x ray	72.1 (111)		
Abnormal x ray	27.9(43)		
Lung disease			
Unilateral	46.5(27)		
Bilateral	53.5(16)		
Shadows in Zones	100%(n=43)		
Upper part of lungs	9.3(4)		
Mid part of lungs	18.6(8)		
Lower part of lungs	25.6(11)		
Mid + Lower part of lungs	30(13)		
Consolidation	20.8%(n=32)		
Upper part of lungs	9.4(3)		
Mid part of lungs	15.6(5)		
Lower part of lungs	21.8(7)		
Lower + Mid part of lungs	37.5(12)		

n: numbers, %: Percentages

Chest X-rays were performed in which 43(27.9%) had abnormal findings. The 27 (62.8%) patients had unilateral and 16(37.2%) patients had bilateral lungs involvement (Table 3). The

RNA amplification from the sputum, nasopharyngeal swab, and blood were 25 (30.12%), 21 (25.3%) and 8 (9.6%) respectively.

DISCUSSION

CoVID-19 is an aggressive infectious disease that has infected a large population¹³. The patient have variable clinical manifestation and the outcome of the diseases are also very different¹⁴. The MMC hospital was assigned by the government to treat CoVID-19 patients in Khyber Pakhtunkhwa (KP) province, so our data partially represent SARS-CoV-2 infection in KP. In our study we observed high infections rate of CoVID-19 in aged population (>41 years) with comorbidity, which is comparatively lower than the previous reports^{15, 16,17}. The most common co-morbid infections were diabetes ,cardiac diseases, or both which are in consistence with other study¹⁸. Interestingly, during the first week of observation no bacterial super infection was observed.

At the initial phase of CoVID-19 outbreak, the clinical sign and symptoms , imaging findings and laboratory investigations were not clear. In our study we reported fever and cough in 95.6% and 83.4% patients, respectively. Previously the same findings were observed in SARS-CoV infected patients^{21,22,23}. Fever and cough were more common in the infected patients of SARS- CoV - 2 as compared to gastrointestinal symptoms observed in SARS-CoV and MERS-CoV^{24,25}. Critical illness occurred in 18.3% (n=112) patients after admission in hospital. Overall , 41.6% patient have lymphocytopenia which are in consistence with the other studies^{21,23}. Regarding increased values of lactate dehydrogenase, C Reactive protein, ,D-dimer, Alanine transaminase, bilirubin, urea, creatinine, and ferritin the same findings have been reported elsewhere^{26,27}.

We observed the fatality rate of 5.2% which is comparatively higher from the previous study and lower from another report ^{21,28}. The difference in fatality rate may be due to variation in sample size and inclusion criteria. Since all those patients who have mild illness and did not seek medical attention were excluded from our study. Early detection, diagnosis and management might have collectively contributed to the reduction of fatality rate in Pakistan. In our study the detection and amplification of RNA were higher from sputum samples which are in accordance with the previous findings²⁹.

The current study has some limitations such as duration of the study, incomplete information of the exposure history, information on incubation period, missed patient who had mild infection and treated at home, due to overwhelmed medical resources patient didn't undergo sputum bacteriological or fungal assessment on admission and data generated were clinical driven and not systematic.

CONCLUSION

COVID-19 is a pandemic disease that has unprecedently changed the world, rapidly spreading worldwide including Pakistan. The patients mostly presented were asymptomatic or with fever, cough, and shortness of breath. Further, we suggest testing from both nasopharyngeal and sputum to reduce false negative rate.

REFERENCES

- World Health Organization (WHO). WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. Geneva: WHO. 11 Mar 2020. Available from: https://www. who.int/dg/speeches/detail/who-director-general-s-openingremarksat-the-media-briefing-on-covid-19---11-march-2020
- Cowling BJ, Leung GM. Epidemiological research priorities for public health control of the ongoing global novel coronavirus (2019nCoV) outbreak. Euro Surveill. 2020;25 10.2807/1560-7917.ES.2020.25.6.2000110 [CrossRef] [Google Scholar]
- Deng CX. The global battle against SARS-CoV-2 and COVID-19. Int J Biol Sci. 2020;16(10):1676-1677. [PMC free article] [PubMed] [Google Scholar]
- Chan JFW, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-toperson transmission: a study of a family cluster. Lancet 2020.

2020;395:514-523. [CrossRef] [Google Scholar] 10.1016/S0140-6736(20)30154-9

- Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506. [PMC free article] [PubMed] [Google Scholar]
- Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323:1061-1069. 10.1001/jama.2020.1585 [CrossRef] [Google Scholar]
- 6. Chen ŽM, Fu JF, Shu Q, et al. Diagnosis and treatment recommendations for pediatric respiratory infection caused by the 2019 novel coronavirus. World J Pediatr. 2020;16:240-246. 10.1007/s12519-020-00345-5 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- 7. DeBiasi RL, Song X, Delaney M, et al. Severe COVID-19 in children and young adults in the Washington, DC Metropolitan Region. J Pediatr. 2020. 10.1016/j.jpeds.2020.05.007 [CrossRef] [Google Scholar]
- Xu X-W, Wu X-X, Jiang X-G, Xu K-J, Ying L-J, Ma C-L, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. BMJ. 2020;368:m606. https://doi. org/10.1136/bmj.m606 PMID: 32075786
- Wu J, Liu J, Zhao X, Liu C, Wang W, Wang D, et al. Clinical Characteristics of Imported Cases of COVID-19 in Jiangsu Province: A Multicenter Descriptive Study. Clin Infect Dis. 2020. PMID: 32109279
- Colaneri Marta , Sacchi Paolo , Zuccaro Valentina , Biscarini Simona , Sachs Michele , Roda Silvia , Pieri Teresa Chiara , Valsecchi Pietro , Piralla Antonio , Seminari Elena , Di Matteo Angela , Novati Stefano , Maiocchi Laura , Pagnucco Layla , Tirani Marcello , Baldanti Fausto , Mojoli Francesco , Perlini Stefano , Bruno Raffaele , the COVID19 IRCCS San Matteo Pavia Task Force . Clinical characteristics of coronavirus disease (COVID-19) early findings from a teaching hospital in Pavia, North Italy, 21 to 28 February 2020. Euro Surveill. 2020;25(16):pii=2000460. https://doi.org/10.2807/1560-7917.ES.2020.25.16.2000460.
- WHO. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected. Jan 11, 2020. https://www.who.int/publications-detail/clinical-management-of severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)infection-is-suspected.
- Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. Lancet. 2020; 31:S0140-6736(20)30260-9. pmid:32014114.
- 14. Paules CI, Marston HD, Fauci AS. Coronavirus Infections-More Than Just the Common Cold. JAMA. 2020; 23: pmid:31971553
- Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395(10223):507-13. https:// doi.org/10.1016/S0140-6736(20)30211-7 PMID: 32007143

- Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. [The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China]. Zhonghua Liu Xing Bing Xue Za Zhi. 2020;41(2):145-51. PMID: 32064853.
- Marta Colaneri¹, Paolo Sacchi¹, Valentina Zuccaro¹, Simona Biscarini¹, Michele Sachs¹, Silvia Roda¹, et al. Clinical characteristics of coronavirus disease (COVID-19) early findings from a teaching hospital in Pavia, North Italy, 21 to 28 February 2020.
 Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical
- Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020;323(11):1061. https://doi.org/10.1001/jama.2020.1585 PMID: 32031570
- Huang, R., Zhu, L., Xue, L., Liu, L., Yan, X., Wang, J., Zhang, B., Xu, T., Ji, F., Zhao, Y. and Cheng, J., 2020. Clinical findings of patients with coronavirus disease 2019 in Jiangsu province, China: A retrospective, multi-center study. PLOS Neglected Tropical Diseases, 14(5), p.e0008280.
- Pan F, Ye T, Sun P, Gui S, Liang B, Li L, et al. Time course of lung changes on chest CT during recovery from 2019 novel coronavirus (COVID-19) pneumonia. Radiology 2020 Feb 13:200370. doi: 10.1148/radiol.2020200370. [Epub ahead of print].
- Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497-506
- Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. N Engl J Med. DOI: 10.1056/NEJMoa2001316
- Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507-13.
- 24. Leung WK, To KF, Chan PK, et al. Enteric involvement of severe acute respiratory syndrome-associated coronavirus infection. Gastroenterology 2003;125:1011-7. 23.
- Assiri A, McGeer A, Perl TM, et al. Hospital outbreak of Middle East respiratory syndrome coronavirus. N Engl J Med 2013;369:407-16.
- N. Zhu, D. Zhang, W. Wang, X. Li, B. Yang, J. Song, X. Zhao, B. Hua ng, W. Shi, R. Lu, P. Niu, F. Zhan, X. Ma, D. Wang, W. Xu, G. Wu, G. F. Gao, W. TanA novel coronavirus from patients with Pneumonia in China, 2019 N. Engl. J. Med., 382 (8) (2020), pp. 727-733 CrossRefView Record in ScopusGoogle Scholar.
- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395(10223):497–506. pmid:31986264
- W. Guan, Z. Ni, Yu Hu, W. Liang, C. Ou, J. He, L. Liu, H. Shan, C. Lei, D.S.C. Hui, B. Du, L. Li, G. Zeng, K.-Y. Clinical Characteristics of Coronavirus Disease 2019 in China. The new england journal of medicine
- Liu Y, Yang Y, Zhang C, Huang F, Wang F, Yuan J, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. Sci China Life Sci 2020 Feb 9. doi: 10.1007/s11427-020-1643-8.