Original Research Article

Clinical Course of Asymptomatic and Mildly Symptomatic COVID-19 Patients Who had A Positive PCR Test in Multicenter in Khartoum

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Abstract: ***Background***: While most people follow social distancing and are avoiding contact with anyone displaying flu-like symptoms, still asymptomatic patients are having positive SAR COV 2 test can transfer disease to others, as well as the outcome of their disease sill not well understood. ***Objective***: To assess the clinical course of asymptomatic COVID-19 patients who had a positive PCR test in multicenter. ***Methods***: This was a prospective cohort multicenter study conducted in the study was conducted in Khartoum State COVID-19 Centres. Namely Alia Hospital, Fedail, and Ministry of Health Laboratories during the period from December 2020 to April 2021. Data was collected using a questionnaire from 98 patients who fulfilled the inclusion criteria. The questionnaire was filled with patients after taking informed consent. ***Results***: The mean age was 49±7.3 years. Males were 58(59.2%) and females were 40(40.8%). The male to female ratio was 1.5:1. The frequency of symptomatic patients' COVID-19 positive test results experience symptoms was 80(81.6%), while the frequency of asymptomatic patients was 18(18.4%). The time and period of appearance of manifestations among COVID 19 patients, the study indicated that among symptomatic patients after PCR test, the moment of appearance of symptoms was 1 – 7 days in 76(95%) and 8 – 14 days after test in 4(5%). After 28 days follow up the outcome of the patients was recovery 76(76.6%), remain Asymptomatic 18(18.4%), and remain symptomatic 4(4.0%). ***Conclusion***: The study demonstrated that the appearance of symptoms before and after the PCR test was significantly affected by chronic diseases as well as chronic medications in use ($P.\ value < 0.05$).
Keywords: Clinical Course, Asymptomatic, Covid-19, Mildly Symptomatic, PCR, Khartoum, Sudan.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a potentially serious condition caused by a novel coronavirus termed "severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)". COVID-19 is clinically characterized by respiratory system involvement. COVID-19 disease was first seen in Wuhan, China, in December 2019, when a series of patients presented with pneumonia of unknown etiology. COVID-19 has very rapidly spread worldwide and on March 11, 2020, the World Health Organization officially announced COVID-19 as a pandemic [1].

The novel coronavirus SARS-CoV-2 was first isolated from the lower respiratory tract, in patients having unexplained pneumonia. Coronaviruses are a group of RNA viruses that dominantly affect vertebrates. There have been two novel coronavirus outbreaks in the past. In 2002–2003, an outbreak of severe acute respiratory syndrome (SARS) took place that was caused by SARS-CoV. Another outbreak of SARS took place in 2012 that was termed the Middle East respiratory syndrome (MERS). MERS was caused by MERS-CoV. The current SARS, which is termed COVID-19, is caused by SARS-CoV-2 [2].

As per the latest World Health Organization report, globally there were 4534731 confirmed COVID-19 cases along with 307537 deaths. COVID-19 has now been reported in 216 countries. India, so far, reported 0.

According to the latest meta-analysis (published on April 14, 2020) that analyzed data of 47,344 patients, the noted sex ratio (male to a female) of 1.06, and an average age of an affected person was more than 40 years. Diabetes, hypertension, cardiovascular disease, and malignancies were common comorbidities [3]. Another large study, describing data of 5700 hospitalized patients from New York, USA, reported a median age of 63 years (range 1–107 years). There were 40% of females. Common comorbidities were hypertension, obesity, and diabetes. Among patients who were discharged or died (*n* = 2634), 14% required intensive care management. Approximately, 12% of patients needed mechanical ventilation. In total, 21% of patients had died [4].

MATERIALS AND METHODS
Study design
This is a prospective cohort study.

Study period
The period was from December 2020 to April 2021.

Study setting
The study was conducted in Khartoum State COVID-19 Centers. Namely Alia Hospital, Fedail hospital, and Ministry of Health Laboratories.

Study population
Covered all Sudanese asymptomatic patients with SAR – COV 2 positive PCR test.

Study sample and sampling technique
As this study was conducted in a short period, a large number of study subjects were not expected to be enrolled as a total coverage as a sampling technique. According to records, the total number of admitted patients (98) during the study period.

Ethical considerations
Written consent was obtained from the Ministry of Health and provided to the Khartoum State centers for COVID-19 patients. A written ethical clearance and approval for conducting this research were obtained from Sudan Medical Specialization Board ethical Committee. Written permission was obtained from the Administrative Authority of Khartoum State Centers for COVID-19 patients. All subjects were informed that the collected data was used for research purposes only, and the privacy issues were intentional.

DATA COLLECTION
Close-ended structured interview questionnaire constructed for the study was used filled out by resident medical officers under the supervisor. Some information and investigation were collected from the patient records. Confidentiality was obtained by using serial numbers for the patients.

DATA ANALYSIS
The data was analyzed by a computerized program; a statistical package for social sciences (SPSS), and the results were presented in tables and graphs. Chi squire test was used to compare between variables and *P-value* was considered significant if < 0.05.

RESULTS
In this study, a total of 98 patients who attended COVID 19 centers at Khartoum State during the period from January to April 2021 were included to assess the clinical course of asymptomatic and mildly symptomatic patients who had a positive PCR test. The mean age was 49±7.3 years. The common age group was 30 – 39 years 42(62.9%), followed by 20 – 29 years 21(21.4%), 40 – 49 years 18(18.4%), less than 20 years 7(7.1%), 50 – 59 years 5(5.1%) and 60 – 69 years 5(5.1%) (Table 1). Males were 58(59.2%) and females were 40(40.8%). The male to female ratio was 1.5:1. The majority of the patients 76(77.6%) from urban areas and 22(22.4%) are from rural areas. The majority of the patients 78(79.6%) had no medical history of chronic illnesses. The reported chronic illnesses were diabetes mellitus 7(7.1%), hypertension 6(6.1%), bronchial asthma 6(6.1%), and kidney disease 1(1.1%) (Table 2). The majority of the patients 75(76.5%) not on any medications. The patients on medications for chronic illnesses were 15(15.3%), on vitamin C 3(3.1%), vitamin C and D 3(3.1%), and 2(2%) on vitamin D (Table 3). Symptomatic patients before the PCR test were 65(66.3%) and asymptomatic were 33(33.7%). The reported symptoms were fatigability 36(55.4%), fever 20(30.8%), loss of taste 20(30.8%), loss of smell 20(30.8%), headache 16(24.6%), runny nose 10(15.4%), cough 4(6.2%), shortness of breath 2(3.1%), nausea 2(3.1%), diarrhea 2(3.1%) and vomiting 2(3.1%) (Table 4). After the first PCR test, symptomatic patients were 80(81.6%) and asymptomatic were 18(18.4%). The reported symptoms were loss of smell 54(67.5%), loss of taste 50(62.5%), %), fatigability 45(56.3%), fever 41(51.3%), headache 41(51.3%), runny nose 39(48.8%), cough 28(35%), nausea 23(28.8%), shortness of breath 21(26.3%), diarrhea 19(23.8%) and vomiting 13(16.3%) (Table 5). Among symptomatic patients after the PCR test, the time of appearance of symptoms was 1–7 days in 76(95%) and 8 – 14 days after the test in 4(5%). Among symptomatic patients after the first PCR test, the time of disappearance of symptoms was 7 – 14 days in 40(50%), less than 7 days 19(23.8%), 15 – 21 days 12(15%), and 22 – 28 days after appearance 9(11.2%) (Table 6). Of the patients who received COVID-19 protocol 65(66.3%) and 33(33.7%) did not. The second test of PCR was done for 55(56.1%) and not done for 43(43.9%). The result of the test was negative 51(92.7%) and positive 4(7.3%). After 28 days follow up the outcome of the patients was recovery 76(76.6%), remain Asymptomatic 18(18.4%), and remain symptomatic 4(4.0%) (Table 11). It is clear from (Tables 7- 8) that the appearance of symptoms before and after the PCR test was significantly affected by chronic diseases (*P-value* < 0.05), where the patients without a history of chronic diseases were 27(81.8%) and

13(72.2%) of the asymptomatic patients before and after PCR test respectively. It is clear from **(Tables 9-10)** that the appearance of symptoms before and after the PCR test was significantly affected by medications on use (*P-value* < 0.05), where the patients without a history of medications were 26(78.8%) and 11(61.1%) of the asymptomatic patients before and after PCR test respectively.

Table-1: Distribution of the patients according to ages group

Age group	N	%
Less than 20 years	7	7.1
20 - 29 years	21	21.4
30 - 39 years	42	42.9
40 - 49 years	18	18.4
50 - 59 years	5	5.1
60 - 69 years	5	5.1
Total	**98**	**100**

Table-2: Distribution of the patients according to history of chronic illnesses

Chronic illnesses	N	%
No	78	79.6
Diabetes	7	7.1
Hypertension	6	6.1
Bronchial asthma	6	6.1
Chronic kidney disease	1	1.1
Total	**98**	**100**

Table-3: Distribution of the patients according to medications on use

On medications	*N*	*%*
No	75	76.5
Medications for chronic illness	15	15.3
Vitamin C	3	3.1
Vitamin D	2	2.0
Vitamin C and D	3	3.1
Total	**98**	**100**

Table-4: Distribution of the patients according to presenting symptoms before first PCR test

Symptoms before test	Yes		No		Total	
	N	%	N	%	N	%
Fatigability	36	55.4	29	44.6	65	100
Fever	20	30.8	45	69.2	65	100
Loss of taste	20	30.8	45	69.2	65	100
Loss of smell	20	30.8	45	69.2	65	100
Headache	16	24.6	49	75.4	65	100
Runny nose	10	15.4	55	84.6	65	100
Cough	4	6.2	61	93.8	65	100
SOB	2	3.1	63	96.9	65	100
Nausea	2	3.1	63	96.9	65	100
Diarrhea	2	3.1	63	96.9	65	100
Vomiting	2	3.1	63	96.9	65	100

Table-5: Distribution of the patients according to presenting symptoms after first PCR test

Symptoms after test	Yes		No		Total	
	N	%	N	%	N	%
Loss of smell	54	67.5	26	32.5	80	100
Loss of taste	50	62.5	30	37.5	80	100
Fatigability	45	56.3	35	43.8	80	100
Fever	41	51.3	39	48.8	80	100
Headache	41	51.3	39	48.8	80	100
Runny nose	39	48.8	41	51.3	80	100

Symptoms after test	Yes		No		Total	
	N	%	N	%	N	%
Cough	28	35.0	52	65.0	80	100
Nausea	23	28.8	57	71.3	80	100
SOB	21	26.3	59	73.8	80	100
Diarrhea	19	23.8	61	76.3	80	100
Vomiting	13	16.3	67	83.8	80	100

Table-6: Distribution of the patients according to disappearance of symptoms after first PCR test

Time of disappearance of symptoms	N	%
Less than 7 days after appearance	19	23.8
7 day to 14 days after appearance	40	50.0
15 day to 21 days after appearance	12	15.0
22 day to 28 days after appearance	9	11.2
Total	**80**	**100**

Table-7: Distribution of the patients according to correlation between appearance of symptoms before PCR test and chronic diseases

Chronic illnesses	Symptoms before test			
	Symptomatic		Asymptomatic	
	N	%	N	%
No	51	78.5	27	81.8
Diabetes	5	7.7	2	6.1
Hypertension	4	6.2	2	6.1
Bronchial asthma	4	6.2	2	6.1
Chronic kidney disease	1	1.5	0	0.0
Total	**65**	**100.0**	**33**	**100**

P-value = 0.011 < 0.05 *significant*

Table-8: Distribution of the patients according to correlation between appearance of symptoms after PCR test and chronic diseases

Chronic illnesses	Symptoms after test			
	Symptomatic		Asymptomatic	
	N	%	N	%
No	65	81.3	13	72.2
Diabetes	6	7.5	1	5.6
Hypertension	4	5.0	2	11.1
Bronchial asthma	4	5.0	2	11.1
Chronic kidney disease	1	1.3	0	0.0
Total	**80**	**100.0**	**18**	**100**

P-value = 0.017 < 0.05 *significant*

Table-9: Distribution of the patients according to correlation between appearance of symptoms before PCR test and medications on use

On medications	Symptoms before test			
	Symptomatic		Asymptomatic	
	N	%	N	%
No	49	75.4	26	78.8
Medications for chronic illness	10	15.4	5	15.2
Vitamin C	3	4.6	0	0.0
Vitamin D	1	1.5	1	3.0
Vitamin C and D	2	3.1	1	3.0
Total	**65**	**100.0**	**33**	**100**

Table-10: Distribution of the patients according to correlation between appearance of symptoms after PCR test an d medications on use

On medications	Symptoms after test			
	Symptomatic		Asymptomatic	
	N	%	N	%
No	64	80.0	11	61.1
Medications for chronic illness	10	12.5	5	27.8
Vitamin C	2	2.5	1	5.6
Vitamin D	2	2.5	0	0.0
Vitamin C and D	2	2.5	1	5.6
Total	80	100.0	18	100

Table-11: Distribution of the patients according to outcome after 28 days follows up

OUTCOME	N	%
Recovered	76	77.6
Remain A symptomatic	18	18.4
Remain symptomatic	4	4.0
Total	98	100

DISCUSSION

This study aimed to assess the clinical course of asymptomatic COVID-19 patients who had a positive PCR test in multicenter December 2020 to April 2021. To fulfill the objectives of the study a total of 98 patients attended these centers were included. The mean age was 49 ± 7.3 years. Males were 58(59.2%) and females were 40(40.8%). The male to female ratio was 1.5: 1. Similar to Peckham and his colleagues meta-analysis of 3,111,714 reported global cases to demonstrate that, whilst there is no difference in the proportion of males and females with confirmed COVID-19, male patients have almost three times the odds of requiring intensive treatment unit (ITU) admission (OR = 2.84; 95% CI = 2.06, 3.92) and higher odds of death (OR = 1.39; 95% CI = 1.31, 1.47) compared to females [5]. On the other hand, Hu, and his colleagues reported that the age-dependent correlation between people over 65 years of age with IRC was higher in females, while the correlation between age distribution and CFRC as well as MRC was higher in males ($p < 0.0001$ for all). Besides, we found that age-gender-dependent differences were correlated to IRC in places with high income and associated with CFRC in non-high income countries/territories [6]. The frequency of symptomatic patients' COVID-19 positive test results from experience symptoms was 80(81.6%), while the frequency of asymptomatic patients was 18(18.4%). The most common symptoms were loss of smell 54(67.5%), loss of taste 50(62.5%), %), fatigability 45(56.3%), fever 41(51.3%), headache 41(51.3%), runny nose 39(48.8%), cough 28(35%), nausea 23(28.8%), shortness of breath 21(26.3%), diarrhea 19(23.8%) and vomiting 13(16.3%). A similar study in South Korea showed that only 31 (4.9%) were symptomatic at diagnosis; 44 (7.0%) were asymptomatic at diagnosis but developed symptoms by the time they were admitted to the CTC. Among patients who were asymptomatic at the time of admission, 186 (29.4%) developed symptoms during CTC admission and 371 (58.7%) remained asymptomatic [7]. A study by Al-Qahtani and his colleagues showed that 136/188 tested positive, with 44/188 (23.4%) symptomatic and 92/188 (48.9%) asymptomatic. All 92 patients remained asymptomatic and were retested every 2 days until viral clearance [8]. The study named Follow-up of asymptomatic patients with SARS- CoV-2 infection, Shanghai Public Health Clinical Center, Fudan University; Shanghai, China stated that asymptomatic patients have completely different significance for the disease spectrum and natural history of COVID-19. If we can make a diagnosis early enough, we should be able to detect patients in the incubation period. In our cohort, three patients developed symptoms later and became typical COVID-19 patients. They also found that 2.7% of patients (9/328) continued asymptomatic even with pulmonary involvement [9]. Regarding the time and duration of appearance of symptoms among COVID 19 patients, the study showed that among symptomatic patients after the PCR test, the time of appearance of symptoms was 1–7 days in 76(95%) and 8 – 14 days after test in 4(5%). Similar to the previous study found that the median period of asymptomatic patients from viral nucleic acid positive to negative was 9.5 days, the longest was up to 21 days among the 24 asymptomatic cases [10]. Then another study found that the median period from contact to diagnosis and the last positive nucleic acid test was 19 days (8–24 days) and 21.5 days (10–36 days), respectively[11]. The median period from diagnosis to negative nucleic acid test was 7.5 days (2–20 days) with normal or atypical chest CT infections and 12.5 days (8–22 days) with typical CT findings. However, an asymptomatic infection should be quarantined for 14 days until now [54]. Faes and his colleagues study reported that the time between symptom onset and hospitalization or diagnosis are similar, with the median length between symptom onset and hospitalization ranging between 3 and 10.4 days, depending on the age of the patient (longest delay in the age group 20–60 years) and whether or not the patient

lives in a nursing home (additional 2 days for patients from the nursing home). The median loss in the hospital varies between 3 and 10.4 days, with the Loss increasing with age [55]. After 28 days follow up the outcome of the patients was recovery 76(76.6%), remain Asymptomatic 18(18.4%), and remain symptomatic 4(4.0%). The study showed that the appearance of symptoms before and after the PCR test was significantly affected by chronic diseases (*P-value* < 0.05), where the patients without a history of chronic diseases were 27(81.8%) and 13(72.2%) of the asymptomatic patients before and after PCR test respectively. On the other hand, the appearance of symptoms before and after the PCR test was significantly affected by medications on use (*P-value* < 0.05), where the patients without a history of medications were 26(78.8%) and 11(61.1%) of the asymptomatic patients before and after PCR test respectively. Similar to Profili in Italy assessed to evaluate the role of chronic diseases on the risk to develop clinically evident (at least mild symptomatic) forms of SARS-CoV-2 infection in the population of the LHU Toscana Centro. Among the 1,840 cases, compared to the general population, the presence of males and over-60-year-old people is greater. Almost all the considered chronic diseases are more frequent among the cases, compared to the general population. A chronic patient has a 68% greater risk to be positive with at least mild symptoms. Many of the considered diseases show an effect on the risk of getting COVID-19 in asymptomatic form, which remains even adjusting to other comorbidities. The main ones include heart failure, psychiatric disorders, Parkinson's disease, and rheumatic diseases [58].

CONCLUSION

The study showed that among COVID 19 patients, the proportion of symptomatic patients rose after the second test and the most common period between the appearance of symptoms and disappearance after the test was 7 – 14 days. After 28 days follow up the majority of the patients were recovers, 18 remained asymptomatic and 4 symptomatic.

RECOMMENDATION

1) People with asymptomatic COVID-19 are infectious but might be less infectious than symptomatic cases; however, there is a need to apply required screening for COVID 19.
2) It is important to put more regulations and address the role of keeping suitable distance and taking the required precautions among the public and health workers.

FUNDING

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