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Original Article

Prevalence and predictors of Post-COVID syndrome in the Kyrgyz population: a clinical overview

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ABSTRACT

A substantial proportion of the population in many countries has been afflicted with COVID-19 coronavirus infection, frequently accompanied by clinically significant symptoms even after the acute infection was treated. During the acute phase of COVID-19, the illness severity varied from moderate to severe, resulting in the development of widespread organ damage and subsequent multisystem symptoms of post-COVID syndrome. This prospective cohort study involved 358 patients diagnosed with COVID-19. The R-studio software was used to execute the statistical analysis, which included the computation of the p-value, median (IQR), n (%), Wilcoxon rank sum test, and Pearson's Chi-squared test.In our study The average age of COVID-19 acute patients was 56 (range: 15 to 84). Women accounted for 53.1% of cases. Cardiovascular, respiratory, and endocrine illnesses were the most common comorbidities. In the acute phase of COVID-19, fever, tiredness, and malaise were prevalent. Respiratory difficulties and cold symptoms were the main complaints. The severity of the illness was connected to lung tissue destruction in the CT picture and increases in CRP, procalcitonin, D-dimer, and fibrinogen. Polypragmasia (using five or more medicines simultaneously) with antimicrobials, GCS, and other symptomatic treatments was seen in therapeutic approaches. We also found key indicators of post-Covid syndrome, such as severe pneumonia with extensive lung damage (CT-3 and CT-4), high CRP, and self-medication with antibiotics and corticosteroids in the early stages of acute Covid-19. Our study emphasises on postcovid syndrome causes. This result corresponded with female population, having severe acute COVID-19, having a reinfection or breakthrough infection after immunisation, having other concomitant conditions, and self-medicating with various drugs.

Keywords: COVID-19, Pandemic, Post-COVID syndrome, Risk factors, Kyrgyz population

Introduction

Kyrgyzstan, also known as the Kyrgyz Republic, is a country in Central Asia. It is surrounded by Kazakhstan to the north, China to the east, Tajikistan to the south, and Uzbekistan to the west. Bishkek, the capital and largest city of Kyrgyzstan, is situated in the northern region and is home to over 1 million residents as of 2024. Osh, the second largest city, serves as the administrative hub of the southern region, nestled in the scenic Fergana Valley close to the Uzbekistan border [1]. The rapid spread of COVID-19 has posed significant challenges in the healthcare [2] system globally, including in Kyrgyzstan. During the early stages of the pandemic, healthcare workers encountered significant obstacles in delivering efficient medical care for acute infection. However, as time has passed, the attention has now turned towards addressing the treatment of post-COVID syndrome. Based on

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the definition provided by the WHO, individuals may experience a "condition after COVID-19" (known as post-Covid syndrome) following an acute SARS- CoV-2 infection [3]. This typically occurs around 3 months after the onset of COVID-19 and involves symptoms that persist for at least 2 months, without any other explanation [4]. Numerous studies that have been published indicate that typical post-COVID syndrome symptoms include exhaustion, dyspnea, cognitive impairment, and other conditions that disrupt day-to-day activities. After recovering from an acute episode of COVID-19 [5-8], symptoms may appear for the first time or continue from the original illness. One characteristic of post-COVID syndrome is its ability to develop in individuals who have had COVID-19, irrespective of the severity of the illness, including those who did not need respiratory assistance [9]. While young persons were likewise at the highest risk of developing post-COVID syndrome, several studies have identified female gender, advanced age, high viral load, severity of acute COVID-19, and concomitant disorders as risk factors for post-COVID syndrome [10]. To the best of our knowledge, this is the first study based on the Kyrgyz population that examines the relationship between clinical manifestations and changes in laboratory parameters of acute COVID-19 with the development of post–COVID syndrome. The objective of this study is to enhance our comprehension of the enduring effects of SARS-CoV-2 infection in the population of central Asian countries and to pinpoint clinical and laboratory markers of acute COVID-19 at the onset and later stages of the epidemic, which impact the progression of post-COVID syndrome.

Materials and Methods

For this study, the Osh city of the Kyrgyz Republic was chosen because to its high population density, 61 individuals per square kilometer; 25.8% of total population. Furthermore, in Kyrgyzstan, the COVID-19 pandemic originated in the aforementioned location and then expanded to other areas [11-13]. To ensure the data was accurate, the research included all COVID-19 patients treated in the Infectious Diseases department of the Osh Interregional Clinical Hospital from 2020 to 2022. The participants were chosen from the registration log; 20 patients were admitted and hospitalized at the start of each month over the research periods, for a total of 480 patients **(Figure 1)**; however, 122 individuals were omitted from the study. Exclusion criteria included 25 patients who died during the acute phase, 19 patients with impairments, 30 patients transferred from other institutions, 17 pregnant women, and 31 foreign nationals. Thus, 358 individuals with acute COVID-19 were included in the research. Those patients were examined clinically, in the laboratory, and with instruments. During long-term follow-up, 252 of 358 patients were monitored to research post-COVID syndrome, whereas 106 patients (mostly adults over 70 years old) dropped out of follow-up owing to patient death (25 people) and refusal (81 people) from frequent hospital or outpatient clinic visits. The primary cause for hospitalization among the examined group of patients was worsening of a patient's health in the presence of any complaints. Blood tests, PCR tests for SARS-CoV-2, disease severity determination (mild, moderate, severe), drug prescription, and diagnosis of post-COVID syndrome were performed in accordance with the recommendations of the Clinical Guidelines for the Diagnosis and Treatment of COVID-19 in the Kyrgyz Republic [14]. In this study, a cohort prospective study and analysis of patients' medical records were conducted according to the following indicators:

1. Demographic data of patients, duration of hospital stay (bed days), frequency of symptoms of the acute stage, severity of the disease, the presence of concomitant diseases, and clinical [15-19] symptoms of long-term consequences;
2. The results of laboratory tests in dynamics: CBC, biochemical [20-22] analyses, coagulation tests (prothrombin time (PT), activated partial thromboplastin time (aPTT), and fibrinogen), and D-dimer;
3. The results of instrumental tests in dynamics: computed tomography and X-ray of the chest, SpO2, ECG, and ultrasound of the abdominal cavity; the amount of lung lesions was measured by CT scan picture using a quantitative evaluation scale of 0 to 5: CT-0 indicates no lesion, CT-1 indicates a lesion <5%, CT-2 indicates 5-25%, CT-3 indicates 26-49%, CT-4 indicates 50-75%, and CT-5 indicates >75% [23].
4. The therapeutic interventions used in the acute period of COVID-19.

Statistical analysis

Patient data were aggregated from the electronic health records for statistical analysis. R-studio software (version 4.0.3) was used for statistical analysis. Comparative evaluation of morbidity rates, clinical features, and laboratory findings, results of patients with post-COVID syndrome were assessed using: Median (IQR); n (%), Wilcoxon rank sum test; Pearson's Chi-squared test.

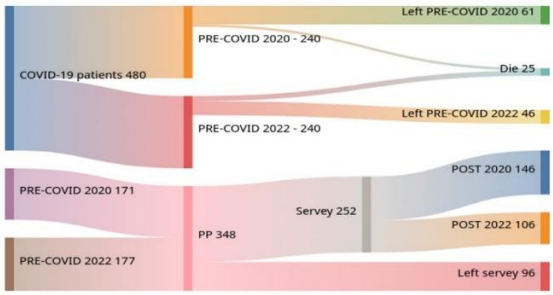

Figure 1. Block diagram of the study population.

Results and Discussion

Characterization of participants

A comparative characterization of demographic, clinical and laboratory parameters of patients in the acute phase of COVID-19 is presented in **Table 1**.

Table 1. Demographic characteristics of patients in the acute phase of COVID-19 (n=358)

Indicators	2020 y (n = 176)[1]	2022 y(n = 182)[1]	p-value[2]
gender			>0.9
male	82 (47%)	85 (47%)	
female	94 (53%)	97 (53%)	
Average age	53 (40 - 60)	60 (51 - 70)	<0.001
15-29 years	1 (0.6%)	0 (0%)	0.090
30-44 years	18 (11%)	10 (6.7%)	
45-59 years	38 (23%)	30 (20%)	
60-74 years	62 (37%)	47 (31%)	
75+ years	49 (29%)	65 (43%)	
Concomitant pathology by systems			0.002
Cardiovascular	17 (35%)	49 (45%)	
Endocrine	14 (29%)	18 (17%)	
Respiratory	6 (12%)	33 (30%)	
Gastrointestinal	6 (12%)	2 (1.8%)	
Others	6 (12%)	7 (6.4%)	
Days from symptom onset to hospital admission			0.030
up to 5 days	110 (64%)	109 (62%)	
5-10 days	55 (32%)	49 (28%)	
10 days and more	6 (3.5%)	19 (11%)	
Severity			<0.001
Mild	43 (25%)	2 (1.1%)	
Moderate	62 (36%)	91 (51%)	
Severe	66 (39%)	84 (47%)	

[1]n (%); Median (IQR)

[2]Pearson's Chi-squared test; Fisher's exact test; Wilcoxon rank sum test

The patients' average age was 56 years (15-84), with 167 (46.6%) males and 191 (53.1%) women. There was no significant difference in the male to female ratio. Almost 80% of those admitted to the hospital were above the age of 45 (285 patients, 79.6%). **Table 1** shows how patients' concomitant illnesses were presented by systems. A total of 66 patients (18.4%) were diagnosed with cardiovascular disease, which included arterial hypertension, coronary heart disease, aortic and coronary artery atherosclerosis, and respiratory system pathology (bronchial asthma, chronic obstructive pulmonary disease) (39 patients - 10.9%). Endocrine problems (type 2 diabetes mellitus and obesity) were found in 32 patients (8.9%), whereas gastrointestinal pathology (gastritis, gastric ulcer, and duodenal ulcer) and other systems (urinary, hematopoietic, and central nervous system) were less prevalent (in a few instances). In most instances, patients were admitted to the hospital within 5 days of illness start (219 patients - 61.2%), with 153 patients (42.7%) having moderate disease and 150 patients (41.9%) having severe disease at admission. The clinical symptoms of the acute phase of COVID-19 are presented in **Table 2**.

Table 2. Clinical syndromes in patients with the acute phase of COVID-19 during hospitalization (n=358)

Indicators	2020 y (n = 176)[1]	2022 y (n = 182)[1]	p-value[2]
Fever	176 (100%)	182 (100%)	0.3
Asthenic syndrome	149 (87%)	165 (93%)	0.056
Catarrhal syndrome (sore throat, pharyngeal hyperemia, rhinorrhea, nasal congestion)	146 (85%)	104 (59%)	<0.001
Intoxication syndrome (myalgia, chills, sweating, aching joints, body)	129 (75%)	91 (51%)	<0.001
Respiratory syndrome (cough, shortness of breath, chest pain)	122 (71%)	153 (86%)	<0.001
Neurological syndrome (anosmia, ageusia, headache, dizziness)	40 (23%)	52 (29%)	0.2
Dyspeptic syndrome (diarrhea, anorexia, abdominal pain, nausea)	17 (4.7%)	16 (4.5%)	0.2

Fever was a consistent symptom of COVID-19's acute phase, with the febrile type being the most common (150 patients, 41.9%) [24]. Fever was associated with asthenic (314 patients, 87.7%) and intoxication syndromes (220 patients, 61.5%). COVID-19 infection was present in the majority of patients (275 patients, 76.8%) and caused respiratory and catarrhal symptoms (250 patients, 69.8%). The average respiratory rate was 24 breaths per minute (range: 20-26), with an average SpO2 level of 88% (84-90). In patients with modest disease severity, the amount of lung tissue lesion was assessed and rated as CT-0 and CT-1 with comparable frequency (44%); CT-2 alterations were observed in 11% of instances. CT-2 alterations were observed more often (35%) in individuals with significant COVID-19, followed by CT-1 (27%) and CT-3 (26%) at identical rates [25]. CT-4 alterations were infrequent (8%). Severe patients exhibited a high proportion of lung lesions rated CT-3 (49%) and CT-4 (36%), with an uncommon CT-2 pattern (11%). Neurologic condition was detected in 92 individuals (25.7%), but dyspeptic syndrome was less prevalent (33 patients, 9.2%) [26].

We presented laboratory parameters of COVID-19 patients on admission depending on CT lung severity score **(Table 3)**. The presented data demonstrate a positive correlation between the changes in laboratory findings and CT lung severity score.

Table 3. Laboratory findings in acute COVID-19 patients on admission, depending on CT lung severity score (n=358)

Indicators	CT-0 n = 26[1]	CT-1 n = 68[1]	CT-2 n = 76[1]	CT-3 n = 115[1]	CT-4 n = 73[1]	p-value[2]
Neutrophils, %	53 (48-62)	60 (56-64)	63 (59-69)	66 (60-75)	68 (63-73)	<0.001
Lymphocytes, %	36 (31-41)	33 (29-36)	32 (25-35)	27 (21-32)	27 (23-32)	<0.001
ESR, mm/h	19 (14-24)	20 (15-28)	20 (15-27)	20 (15-30)	25 (19-30)	0.069
CRP, g/l	50 (41-56)	69 (56-85)	96 (84-128)	149 (119-176)	196 (174-200)	<0.001
Procalcitonin, ng/ml	0.14 (0.08-0.23)	0.25 (0.20-0.36)	0.53 (0.34-0.65)	0.71 (0.53-0.96)	1.02 (0.79-1.23)	<0.001
D-dimer, mcg/ml	0.75 (0.64-1.07)	1.11 (0.67-1.82)	1.05 (0.72-1.60)	1.26 (0.99-1.90)	1.36 (1.20- 2.19)	<0.001
Fibrinogen, mg/l	4666 (4000-5772)	7996 (5662-9772)	8772 (6279-10660)	8882 (6666-10216)	8888 (7104-10216)	<0.001

[1] Median (IQR)
[2]Wilcoxon rank sum test

As seen in **Table 3**, a significant increase in CRP, procalcitonin, D-dimer, and fibrinogen levels was associated with a higher CT lung severity score. Thus, CRP was increased by 33 times, procalcitonin by 10 times, D-dimer by 3 times, and fibrinogen by 2 times, while the complete blood count test components tended to change in accordance with the severity of the condition. The correlation coefficient (r) between CT lung severity score and laboratory parameters in COVID-19 patients is presented in **Table 4**.

Table 4. Correlation coefficient (r) between CT lung severity score and laboratory parameters in COVID-19 patients (n=358)

Indicators	r	Tightness of relationship on the Cheddock scale	Student's t-test	p-value[2]	Coefficient of determination r2
CRP	0.78	high	23.56	<0.001	0.609
Procalcitonin	0.58	noticeable	13.37	<0.001	0.334
Neutrophils	0.45	moderate	9.52	<0.001	0.203
Lymphocytes	-0.36	moderate	7.14	<0.001	0.125
Fibrinogen	0.23	weak	4.42	<0.001	0.052
D-dimer	0.16	weak	3.12	<0.001	0.027

Statistical analysis of the correlation between the CT lung severity score and significant laboratory parameters in COVID-19 showed a high and noticeable association with CRP and procalcitonin and a weak association with coagulogram parameters.

The analysis of therapeutic measures indicated a widespread polypragmasia (simultaneous use of 5 or more drugs) in the observed patients (79.6%), including antimicrobials, GCS, nonsteroidal anti-inflammatory drugs (NSAIDs), antipyretics, bronchodilators, mucolytics, hemostatic agents, proton pump inhibitors, hypoglycemic drugs, and cardiovascular remedies [27, 28]. Antibacterial drugs were the most often recommended medications, with ceftriaxone serving as a first-line treatment in both monotherapy and combination with azithromycin or levofloxacin. In circumstances with minimal severity, 42% of patients got antibiotics, and 9.4% received a combination of two and three antibiotics [29]. In cases of moderate and severe severity, antibiotics were given to all patients, and combination treatment was used in 59.5% and 69.3% of cases, respectively [30].

Long-term follow-up of 252 patients who underwent COVID-19 at the beginning and end of the pandemic shows the

development of post-COVID syndrome in 174 (69%) patients, despite recovery **(Table 5)**.

Table 5. Risk factors for post-COVID syndrome in COVID-19 survivors at the beginning and end of the pandemic, n=252

Indicators	Post-COVID syndrome n = 174[1]	Non post-COVID, n = 78[1]	p-value[2]
Age	46 (34-64)	44 (35-57)	0.14
Gender			0.2
male	76 (44%)	27 (35%)	
female	98 (56%)	51 (65%)	
Years			<0.001
2020	86 (49%)	60 (77%)	
2022	88 (51%)	18 (23%)	
After vaccination	42 (24%)	6 (7.7%)	<0.001
Severity			<0.001
Mild	53 (30%)	59 (76%)	
Moderate	82 (47%)	16 (21%)	
Severe	39 (22%)	3 (3.8%)	
Number of comorbidities n=84			<0.001
1	34 (40.5%)	4 (4.8%)	
2	34 (40.5%)	2 (2.4%)	
3	8 (9.5%)	2 (2.4%)	
Pneumonia	96 (55%)	14 (18%)	<0.001
CT			
CT-0	0 (0%)	1 (1.3%)	
CT-1	17 (9.8%)	22 (29%)	
CT-2	42 (24,1%)	26 (33,3%)	
CT-3	81 (46,5%)	21 (28%)	<0.001
CT-4	33 (19%)	6 (7.6%)	<0.001
Fibrinogen	7,996 (6,968-10,216)	7,329 (6,660-9,772)	0.034
CRP	143 (95-168)	96 (83-134)	<0.001
The number of antibiotics received during the acute period			<0.001
1	35 (20%)	17 (24%)	
2	59 (34%)	11 (16%)	
3	63 (36%)	17 (24%)	
Corticosteroids taken during the acute period	137 (78,7%)	16 (20,5%)	<0.001

The average age of patients with and without post-COVID syndrome ranged from 34 to 64 years. Women are significantly more likely to develop the effects of COVID-19 (56%) but prevail in the group without post-COVID syndrome (65%), whereas men have a higher frequency of long-term consequences (44% and 35%, respectively). At the end of the pandemic (2022), patients were twice as likely to experience postcovid syndrome. In vaccinated people, the probability of re-infection with long-term repercussions was three times greater. The severity of the illness, the existence of concurrent pathology, and the number of cases in the acute phase all had a direct influence on the development of postcovid syndrome. Patients with severe pneumonia and substantial lung injury (CT-3 and CT-4), along with a high level of inflammation (CRP), were more likely to have long-term effects [31]. According to our findings, self-medication with antibiotics and corticosteroids early on had a significant influence on the development of long-term implications in the majority of instances.

The current study aims to establish the parameters of acute COVID-19 that have been associated with the emergence of post-COVID syndrome. To the best of our knowledge, this is the first study conducted in Kyrgyzstan. The age range of patients diagnosed with acute COVID-19 varied from 15 to 84 years. However, those over 60 years old were most often experiencing severe lung lesions, with a nearly equal occurrence at the beginning and the end of the pandemic (63% and 61.5%, respectively). In terms of gender distribution, there were no statistically significant differences; however, there was a trend for women to dominate (53.1%, p>0.9). Initially, the primary concurrent diseases during the pandemic were those affecting the cardiovascular and endocrine systems [32]. By the end of the pandemic, respiratory system diseases were also detected. Hospitalization occurred in 93.8% of cases within the first ten days after the disease began in 2020 and in 3.5% of cases after the tenth day. In 2022, 11% of patients were admitted to the hospital within ten days after the disease began, suggesting a higher

frequency of outpatient treatment towards the end of the epidemic. At the onset of the pandemic, the acute COVID-19 infection in hospitalized patients varied in intensity, ranging from mild to severe [33]. However, by the conclusion of the pandemic, only individuals who needed inpatient treatment were hospitalized, accounting for 96.2% of the admitted patients.

Presenting in decreasing order: fever, asthenic, intoxication, respiratory, catarrhal, neurological, and dyspeptic. In our research, we categorized symptoms of acute COVID-19 into syndromes to establish clinical indications of the post-COVID syndrome [34] . CT scan images using a quantitative scale score matched the degree of severity and connected with important laboratory [35-37] values of acute COVID-19, thereby assessing the amount of lung lesions [38, 39]. A significant connection between CRP and procalcitonin was found in patients with severe pneumonia and large lung lesions (CT-3 and CT-4), therefore suggesting the degree of systemic inflammatory response of bacterial origin [40, 41].

We examined patients who had acute COVID-19 at the start and end of the pandemic to estimate their probability of acquiring post-COVID syndrome. Follow-up extended from 2020 to 2024; all patient visits to healthcare facilities with any complaints—even if only one visit was noted—were noted. Patients with post-COVID syndrome fell in age between 34 and 64 years. Although elderly people [42, 43] are known to be at the highest risk of developing post-COVID syndrome and higher risk of COVID-19 mortality, in our study, among those over 70 years of age, 81 people refused a continuous health care visit and 25 people died; hence, the study did not include competing risk of death [44].

Patients at the end of the pandemic were more likely to develop post-COVID syndrome, which was linked to the circulating SARS-COV-2 (omicron) strain and reinfections or breakthrough COVID-19 infection after vaccination [45]. In our analysis, the most significant risk variables determining the high likelihood of developing post-COVID syndrome were female gender, severity of acute COVID-19, and the existence of concurrent disorders, regardless of their number, which is consistent with the literature. Chronic illnesses such as arterial hypertension, obesity, and COPD were linked to hospitalization and an increased chance of developing the post-COVID-19 syndrome [46, 47].

According to our results, severe pneumonia with extensive lung damage (CT-3 and CT-4), as well as a high inflammatory index (CRP) and self-treatment with antibiotics and corticosteroids in the early phase of acute COVID-19 with polypharmacy, were linked to long-term COVID-19 complications in a large proportion of cases.

Conclusion

Globally, health systems' inadequate readiness caused COVID-19 to spread into a pandemic and become more severe. High-income countries (HICs) should assist low- and middle-income countries (LMICs) by means of resource sharing so as to enhance testing capacity, provide therapies and vaccinations, and provide significant financial assistance. By means of establishing funding systems, LMICs will be able to generate locally customized, evidence-based policies. Particularly considering the extensive problems of post-COVID syndrome, a poorly known disorder with a broad spectrum of symptoms impacting many bodily systems, this worldwide collaboration is very essential. Our investigation has helped to pinpoint risk variables linked to post-COVID syndrome, including high inflammatory (CRP) scores, severe pneumonia with great lung lesion volume (CT-3 and CT-4), and polypharmacy with antibiotics and corticosteroids during the acute phase of COVID-19. Lack of medications with established effectiveness combined with high in-hospital mortality usually results in the use of many drugs and their combinations, which should be closely controlled by medical practitioners. While the world works on these challenges, it needs to understand the necessity of sharing life-saving resources depending on need and underline the important need for unity and shared responsibility at this crucial period.

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Conflict of interest: None

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Ethics statement: The Local Ethics Committee of the Osh State University of the Ministry of Health of the Kyrgyz Republic approved the study (Protocol No. 9-FHD/01.03.24). Informed permission was waived since the culture findings were obtained anonymously from the laboratory's computerized database, with no patient characteristics identified.

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