

Coronavirus Disease 2019 Case Series in China: Sequelae and Effectiveness of Vaccination and Antiviral Drugs

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Purpose of the Study: This study investigated post-coronavirus disease 2019 (COVID-19) sequelae among a sample of the Chinese population, and determined the statistical significance of correlations between age, sex, number of COVID-19 vaccinations, number of SARS-CoV-2 infections, development of pneumonia, use of specific drugs (namatevir/ritonavir, azvudine, molnupiravir), chronic underlying diseases, and post-COVID-19 sequelae.

Methods: Data from 869 patients, who visited the Emergency Department of Beijing Shijitan Hospital (Beijing, China) between December 7, 2022 to January 31, 2024, were collected. The criteria for admission: Age ≥ 14 years old, and diagnosed with ≥ 1 positive result on nucleic acid or antigen tests. Retrospectively analyzed the main manifestations of sequelae, statistical analysis of the relationship between age; sex; underlying diseases; number of COVID-19 vaccinations received; use of specific antiviral drugs for COVID-19 and prognosis, and statistical analyses, including logistic regression, were performed. Differences with $P < 0.05$ were considered to be statistically significant. Before entering the model, variables are screened using stepwise regression to ensure that the selected variables are the main ones related to the research question, thereby controlling for confounding factors. SPSS version 27 (IBM Corp. Armonk, NY, USA) was used for statistical analysis. In this study, the duration of sequelae ranged from 2 to 13 months.

Results and Conclusions: This study retrospectively analyzed 869 patients (415 male, 454 female), with an average age of 61.52 ± 23.09 years. There were 401 patients without underlying conditions and 468 patients with one or more underlying conditions. Regarding COVID-19 vaccination status, 320 patients were unvaccinated, while 576 patients received at least one dose of the COVID-19 vaccine. Additionally, 514 patients received antiviral medication, while 355 did not receive antiviral treatment. The primary manifestations of post-COVID-19 included shortness of breath, dizziness and weakness, chronic pneumonia, asthma, and reduced sense of smell. Individuals ≥ 70 years of age were more prone to COVID-19 pneumonia. Patients with underlying disease(s) exhibited statistically higher mortality rates after diagnosis of COVID-19. Vaccination against COVID-19 and the use of specific drugs had a statistically significant effect on mortality and the occurrence of post-COVID-19 sequelae. There was no statistically significant difference in COVID-19 infection rates between males and females, although males were more prone to COVID-19 pneumonia. Young women with COVID-19 often experienced no sequelae, and elderly males exhibited a high mortality rate.

Keywords: novel coronavirus, COVID-19 vaccine, post-COVID-19 sequelae, antiviral drugs

Introduction

Coronavirus disease 2019 (COVID-19) is spreading worldwide. According to data from the World Health Organization (WHO), as of November 8, 2023, the global cumulative number of confirmed COVID-19 cases exceeded 770 million, with > 6.97 million deaths. In China, > 99 million confirmed cases of COVID-19 and $> 120,000$ deaths between January 3, 2020 and November 8, 2023, were reported to the WHO. Although the causative virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has undergone multiple mutations and transmissions, resulting in reduced virulence and decreased transmissibility, it continues to negatively affect human health and quality of life. The

particular study period was chosen because it covers the 13 months following relaxation of dynamic COVID Zero policy, during which nearly everyone in China was infected at some point. At the beginning of China’s epidemic prevention policy, there were many severe cases, and the vast majority of individuals were infected with SARS-CoV-2 at one time or another. Since then, there have been multiple COVID-19 outbreaks, although the virus is currently at a low level of endemicity. In May 2023, the WHO recognized COVID-19 as an established and ongoing health issue, no longer constituting a public health emergency of international concern. The present study mainly examined the characteristics of SARS-CoV-2 infection, COVID-19 vaccines, and specific drugs, analyzing through statistical analysis of clinical data whether they have a statistically significant protective effect on individuals and the main post-COVID sequelae experienced among the Chinese population.

Methods

General information and data were collected from 869 patients (415 male, 454 female) who visited the Emergency Department of Beijing Shijitan Hospital (Beijing, China) between December 7, 2022 and January 31, 2024. Information were collected by reviewing patients’ medical records and searching the hospital information system (HIS). The criteria for admission: All participants were ≥ 14 years of age, and diagnostic standards for COVID-19 infection included individuals diagnosed with COVID-19 since December 7, 2022, with ≥ 1 positive result on nucleic acid or antigen tests. The key term in this study is “COVID-19 infection”, which is defined as a positive result for either nucleic acid or antigen testing. There is no specific group of patients that needs to be excluded. Information collected included the following: age; sex; underlying diseases; number of SARS-CoV-2 infections; development or absence COVID-19 pneumonia; use of specific antiviral drugs for COVID-19, such as namatevir/ritonavir, azvudine, molnupiravir; number of COVID-19 vaccinations received; and post-COVID-19 sequelae. In this study, the duration of sequelae ranged from 2 to 13 months. All relevant data were entered into a database using SPSS version 27 (IBM Corporation, Armonk, NY, USA), and statistical analyses, including logistic regression, were performed. The dependent variables in the regression model of this study include whether the patient develops pneumonia after COVID-19 infection, whether there are any sequelae, and whether the patient dies. The independent variables include age, sex, underlying conditions, vaccination status, and whether the patient took antiviral medication. Before variables are entered into the model, stepwise regression is used to screen them, ensuring that the selected variables are the main ones relevant to the research question. Differences with $P < 0.05$ were considered to be statistically significant.

Results

General information and data of 869 participants have no missing date, the general information of the patients is shown in [Table 1](#). The clinical manifestations of acute COVID-19 infection are mainly fever, sore throat, nasal congestion, cough, fatigue, and body aches, with some patients also experiencing diarrhea and reduced sense of smell. Most of these symptoms gradually improve and disappear. However, some acute symptoms may persist or new symptoms may appear during the

Table 1 General Data

Items			
Age, years	61.52±23.09		
Gender, n(%)			
Male	415	47.7%	
Female	454	52.3%	
Number of Underlying Diseases, n(%)			
0 types	401	46.1%	
1 types	220	25.3%	
2 types	102	11.7%	
≥ 2 types	146	16.8%	

(Continued)

Table 1 (Continued).

Items			
Vaccination Status, n(%), Time interval between the last dose of vaccine, months			
0 doses	320	36.8%	–
1 doses	46	5.30%	18
2 doses	162	18.6%	12
3 doses	341	39.2%	6
Antiviral Medication Usage Used, n(%)			
Used	514	59.1%	
Not used	355	40.9%	
Number of COVID-19 Infections, n(%)			
1time	705	81.1%	
2times	143	16.5%	
3times	17	1.96%	
4times	4	0.46%	
COVID-19 Pneumonia Diagnosis, n(%)			
Yes	368	42.3%	
No	501	57.7%	
Deaths, n(%)			
Yes	161	18.5%	
No	708	81.5%	

recovery phase, which are referred to as post-COVID sequelae. In this study, the duration of sequelae ranged from 2 to 13 months. The main post-COVID-19 sequelae in China and their percentages are summarized in Figure 1. Individuals > 70 years of age were more likely to develop COVID-19 pneumonia. Patients were divided into two groups, ≥ 70 and < 70 years of age, to analyze the rate of COVID-19 pneumonia. The results revealed a significant difference (Table 2). Patients with underlying diseases exhibited a significantly higher mortality rate after being diagnosed with COVID-19 ($P < 0.01$).

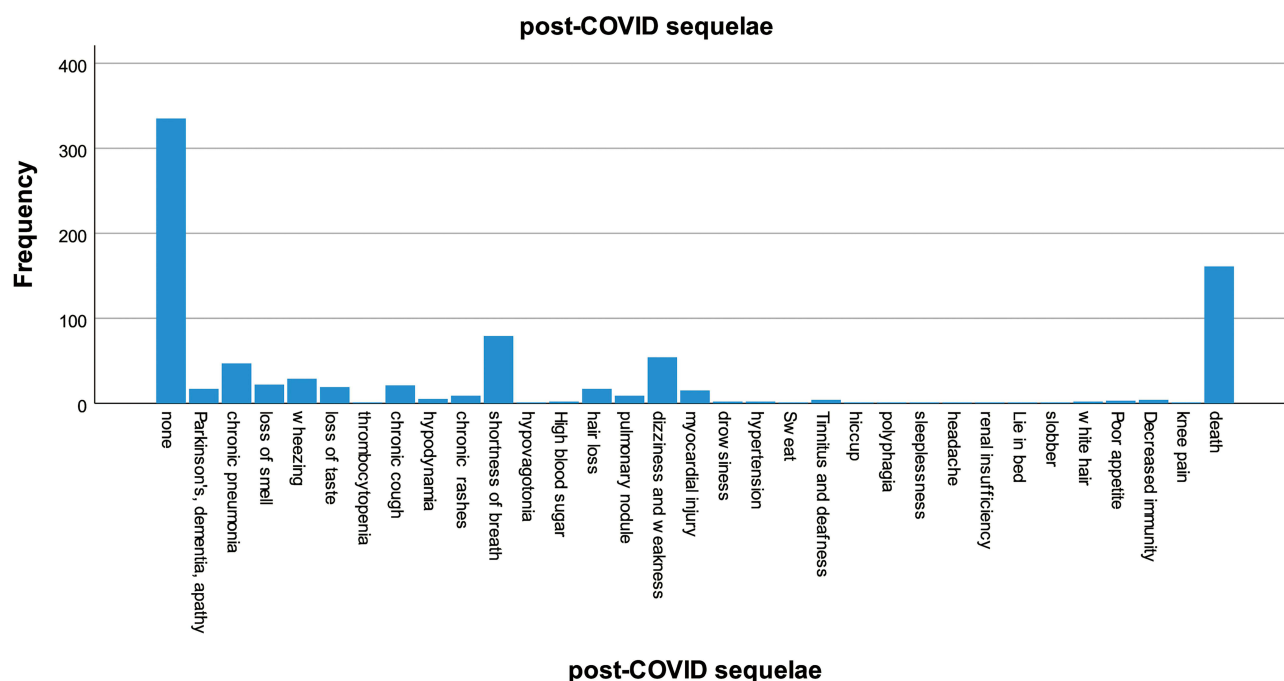


Figure 1 Comparison of the frequencies of sequelae of COVID-19.

Table 2 The Statistical Regression Analysis Output on COVID-19 Infection in Relation to Age ($P < 0.01$)

Variables in the Equation							
		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1 ^a	Age	3.482	0.193	326.731	1	0.000	32.532
	Constant	-5.518	0.313	311.761	1	0.000	0.004

Note: ^aVariable(s) entered on step 1: age.

Patients with underlying diseases exhibited a significantly higher rate of pneumonia ($P < 0.01$) (Table 3). Individuals who received higher number of COVID-19 vaccine doses were significantly less likely to experience sequelae ($P < 0.01$). There was a statistically significant difference in mortality among patients who received a higher number of COVID-19 vaccine doses versus those who did not ($P < 0.01$) (Table 4). The difference in the incidence of sequelae between the group that took antiviral drugs and the group that did was statistically significant ($P < 0.01$). There was a statistical difference in mortality rate between the group that took antiviral drugs and the group that did not ($P < 0.01$) (Table 5). Males were significantly more likely than females to develop COVID-19 pneumonia ($P < 0.01$) (Table 6). The data demonstrated that young females infected with SARS-CoV-2 often did not experience sequelae, whereas older males exhibited a higher mortality rate from COVID-19 after infection (Figure 2). Finally, there was no statistical difference in COVID-19 rates between males and females ($P > 0.05$) (Table 7).

Table 3 The Statistical Regression Analysis Output on Death and COVID-19 Infection in Relation to Underlying Diseases ($P < 0.01$)

Variables in the Equation							
		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1 ^a	Underlying diseases or not	1.911	0.237	64.726	1	0.000	6.757
	Constant	-2.791	0.215	168.861	1	0.000	0.061
Step 1 ^a	Underlying diseases or not	2.501	0.175	204.445	1	0.000	12.198
	Constant	-1.830	0.145	158.805	1	0.000	0.160

Note: ^aVariable(s) entered on step 1: underlying diseases or not.

Table 4 The Statistical Regression Analysis Output on Death and Post-COVID-19 Sequelae in Relation to COVID-19 Vaccination ($P < 0.01$)

Variables in the Equation							
		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1 ^a	Number of COVID-19 vaccinations received,	-0.558	0.058	92.382	1	0.000	0.572
	Constant	1.439	0.132	119.207	1	0.000	4.218
Step 1 ^a	Number of COVID-19 vaccinations received,	-0.912	0.088	106.736	1	0.000	0.402
	Constant	-0.461	0.112	16.859	1	0.000	0.631

Note: ^aVariable(s) entered on step 1: number of COVID-19 vaccinations received.

Table 5 The Statistic Regression Analysis Output on Death and Post-COVID-19 Sequelae in Relation to Antiviral Medication Usage. ($P < 0.01$)

Variables in the Equation		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1 ^a	Use of specific drugs	3.397	0.258	172.950	1	0.000	29.886
	Constant	-0.471	0.091	26.995	1	0.000	0.625
Step 1 ^a	Use of specific drugs	6.050	1.007	36.115	1	0.000	423.918
	Constant	-6.242	1.001	38.890	1	0.000	0.002

Note: ^aVariable(s) entered on step 1: use of specific drugs.

Table 6 The Statistical Regression Analysis Output on COVID-19 Infection in Relation to Gender ($P < 0.01$)

Variables in the Equation		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1 ^a	Gender	1.113	0.143	60.769	1	0.000	3.044
	Constant	-1.984	0.228	75.448	1	0.000	0.138

Note: ^aVariable(s) entered on step 1: gender.

Discussion

Results of the present study indicate that the primary manifestations of post-COVID conditions include breathlessness, fatigue, dizziness, chronic pneumonia, wheezing, loss of smell, chronic pneumonia, loss of taste, Parkinson's disease, dementia, apathy, hair loss, myocardial damage, chronic rashes, lung nodules, decreased physical strength, tinnitus and deafness, decreased immunity, loss of appetite, increased blood sugar levels, sleepiness, increased blood pressure, graying of hair, reduced platelet count, renal insufficiency, weakened vagus nerve, excessive sweating, insomnia, headaches, hiccups, knee pain, bedridden state, were the most common. Results of the present study indicate that young adult females often do not experience post-COVID-19 conditions, although elderly males have a high mortality rate from COVID-19, and COVID-19 vaccines and specific drugs have a statistically significant protective effect on the population. The novel coronavirus (ie, SARS-CoV-2) is highly transmissible among humans and severely affects human health. All deaths ($n = 161$) in this study were caused by severe COVID-19 pneumonia in patients who were treated in the Emergency Department of Beijing Shijitan Hospital during the early stages of the pandemic policy, from December 7, 2022, to January 31, 2024. Most of these patients were > 70 years of age and had underlying disease(s). Various degrees of post-COVID-19 sequelae have affected contemporary life. Reducing the infection rate of SARS-CoV-2 and its sequelae has become a global issue.

This study included data from severely ill patients with pneumonia infected with SARS-CoV-2, who visited the Emergency Department of Beijing Shijitan Hospital at the beginning of China's commencement of epidemic control policies, which resulted in a higher mortality rate. Subsequently, with several small-scale low-level outbreaks, both the incidence and mortality rates of severe pneumonia decreased significantly. Research indicates that the lungs are the primary target organs affected by coronaviruses.¹ Extensive studies have shown that persistent breath-holding, shortness of breath, and other respiratory difficulties are among the most common symptoms in discharged patients.² A study involving 110 non-critical patients revealed that lung function tests at discharge revealed varying degrees of impaired lung diffusion.³ Three months after discharge, approximately 55.7% of patients exhibited residual lung lesions (primarily ground-glass opacities [44.1%]), with 34.8% exhibiting impaired lung diffusion capacity, and 9.5% exhibiting other lung function abnormalities.⁴ These lung lesions and functional abnormalities remained prevalent during the six-month

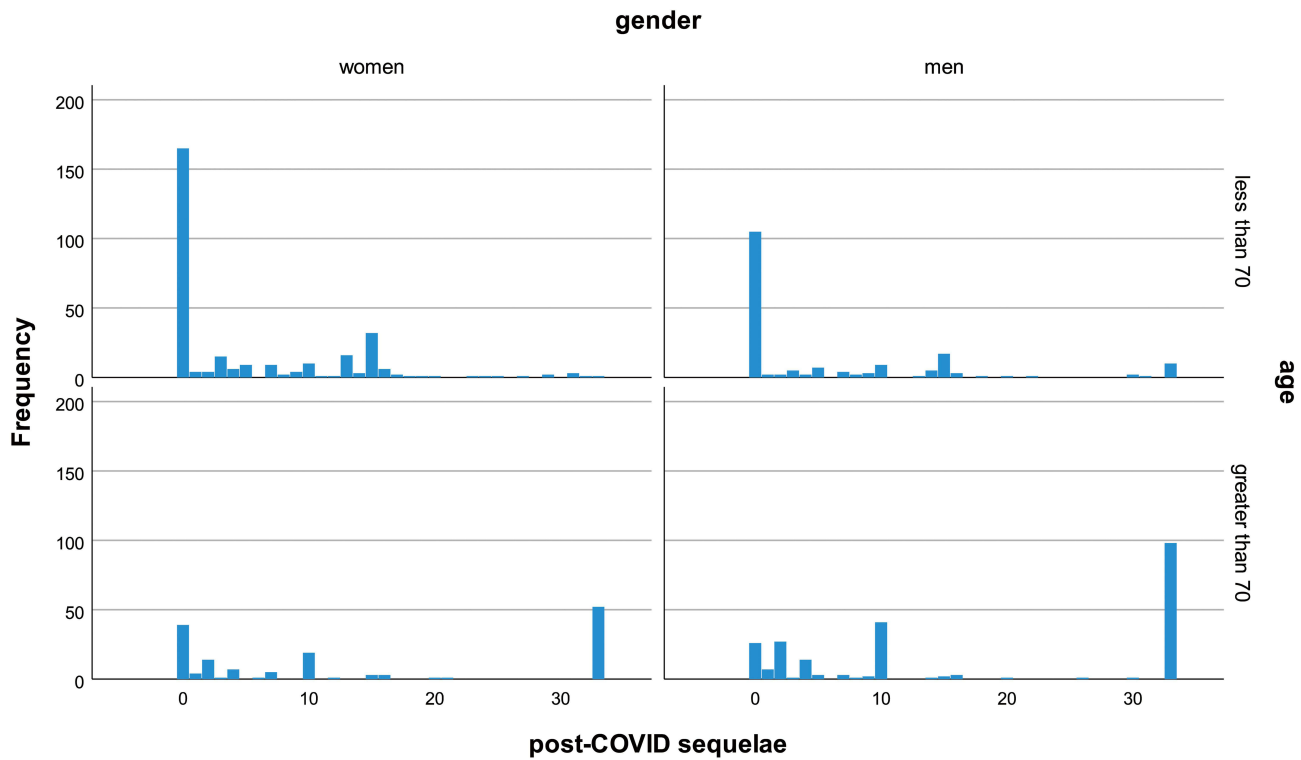


Figure 2 Comparison of the frequencies of sequelae in COVID-19 patients of different Genders and Ages.
Notes: 0, no sequelae; 1, Parkinson's disease, dementia, apathy; 2, chronic pneumonia; 3, loss of taste; 4, wheezing; 5, loss of taste; 6, thrombocytopenia; 7, chronic cough; 8, hypodynamia; 9, chronic rashes; 10, shortness of breath; 11, hypovagotonia; 12, high blood sugar; 13, hair loss; 14, pulmonary nodule; 15, dizziness and weakness; 16, myocardial injury; 17, drowsiness; 18, hypertension; 19, sweat; 20, tinnitus and deafness; 21, hiccup; 22, polyphagia; 23, sleeplessness; 24, headache; 25, renal insufficiency; 26, lie in bed; 27, slobber; 28, stomach discomfort; 29, white hair; 30, poor appetite; 31, decreased immunity; 32, knee pain; 33, death.

follow-up.⁵ In addition to respiratory symptoms, post-COVID sequelae often include reduced or loss of smell and taste. Research has shown that oral epithelial cells and taste buds highly express the angiotensin-converting enzyme 2 (ie, “ACE2”) receptor, leading to taste disturbances when the oral mucosa and taste buds are infected by SARS-CoV-2.^{6,7} Numerous studies have indicated that SARS-CoV-2 infection can cause olfactory and taste disorders, which are correlated.^{8,9} This aligns with the findings of the present study; however, the underlying mechanisms require further investigation. Fatigue, cough, and loss of smell are the most common lingering symptoms of COVID-19, although organ-specific damage has also been reported.^{10–12} A large cohort study including > 11 million samples was conducted. It has been confirmed that the risk to the cardiovascular system increases after SARS-CoV-2 infection, leading to various conditions such as arrhythmias, myocarditis, pericarditis, acute coronary artery disease, thromboembolic disorders, heart failure, and cardiac arrest.¹² In addition to post-COVID conditions affecting the respiratory system, sense of smell and taste, and cardiovascular system, there can also be varying manifestations of sequelae in the kidneys, digestive system, hematological system, endocrine system, nervous system, immune system, skin, hair, and physical strength. These

Table 7 The Statistical Regression Analysis Output on Novel Coronavirus Infection in Relation to Gender (P>0.05)

Variables in the Equation		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1 ^a	Gender	0.386	0.288	1.796	1	0.180	1.471
	Constant	2.160	0.425	25.805	1	0.000	8.675

Note: ^aVariable(s) entered on step 1: gender.

conditions significantly affect the health and quality of life of the general population. Medical professionals must consider protecting vulnerable populations, preventing infections, reducing infection rates, and decreasing the incidence of severe cases and mortality rates.

Results of the present study revealed that individuals > 70 years of age were more susceptible to COVID-19 pneumonia. Patients with underlying conditions were prone to developing COVID-19 pneumonia and had a higher mortality rate after infection, with all results showing statistically significant differences. In clinical practice, patients with COVID-19 pneumonia are mostly elderly, especially those with chronic underlying diseases. Other studies have reported that critically ill patients with COVID-19 are typically older, with an average age of 63 years, and have a higher risk for death due to hypertension, diabetes, and other underlying diseases, confirming that they are a high-risk group for novel coronavirus pneumonia.¹³

COVID-19 has become one of the most critical global public health emergencies in recent years, posing a severe threat to the health and lives of populations worldwide. Vaccination against the novel coronavirus (ie, COVID-19 vaccine) is the most cost-effective measure for protecting vulnerable populations, reducing the incidence of severe cases and mortality, and mitigating the harm caused by the virus. Countries are actively developing and administering COVID-19 vaccines, with recombinant proteins, viral vectors, inactivated vaccines, and mRNA vaccines dominating the market. As the transmissibility and immune evasion capabilities of variants increase, the effectiveness and durability of COVID-19 vaccines have become the focal points of current research, which indicates that a higher number of COVID-19 vaccinations is associated with lower morbidity and mortality rates from COVID-19, with the results demonstrating statistically significant differences. Research has shown that vaccination is one of the most effective measures for protecting vulnerable populations and reducing the severity and mortality of COVID-19. The ideal outcome of vaccination is prevention of infection; however, even when complete prevention is not possible, vaccination plays a significant role in reducing hospitalizations, and mitigating severe illness, and death.¹⁴ A recent study from Israel¹⁵ indicated that, among individuals who received 2 doses of the COVID-19 vaccine, the incidence of long-term COVID symptoms was significantly higher in the unvaccinated group 4 months post-infection than in the vaccinated group. The study also found that vaccination alleviated symptoms in infected individuals to the extent that the differences in “long COVID” symptoms between the vaccinated and non-infected groups were not statistically significant. Additionally, a study from the United States¹⁶ found that vaccination reduced the risk for persistent symptoms 28 days after infection. A study from the United Kingdom¹⁷ also suggested that the proportion of vaccinated patients developing long COVID symptoms 12 weeks post-infection was reduced by approximately 35% compared with non-vaccinated individuals.

This study indicates that the use of specific antiviral drugs significantly affects mortality and the occurrence of sequelae, there is a statistically significant difference. The National “Diagnosis and Treatment Protocol for Novel Coronavirus Infection (Trial Version 10)” specifies that nirmatrelvir tablets/ritonavir tablets and molnupiravir capsules are suitable for adult patients with mild to moderate symptoms within 5 days of onset who have high risk factors for progression to severe illness; azvudine tablets are used to treat adult patients with moderate COVID-19 infection.¹⁸ The National “Diagnosis and Treatment Protocol for Severe Cases of Novel Coronavirus Infection (Trial Version 4)” states that for patients with severe symptoms, especially those with a short duration of illness and a high viral load (Ct < 30), the aforementioned drugs can also be used.¹⁹ Currently, there are no drugs that can prevent COVID-19. These drugs do not prevent SARS-CoV-2 from invading healthy cells or directly kill the virus but work by blocking the virus’ polyprotein hydrolysis process after it invades human cells, thereby inhibiting viral replication and exerting an antiviral effect.

This study indicates there is no significant difference in infection rates between males and females; however, males are more likely than females to develop COVID-19 pneumonia, there is a significant difference. Young adult females with COVID-19 rarely experience sequelae, whereas older males exhibit higher mortality rates. Results of the present study are consistent with research related to the Wuhan epidemic, revealing no differences in the susceptibility and clinical symptoms of COVID-19 between males and females. However, males are more likely to experience severe inflammatory responses after developing COVID-19 pneumonia, and the absorption of lung lesions is slower in males than in females.²⁰

This study has certain limitations due to time and sample size, and needs to be validated by large-scale research.

Conclusion

Sequelae of COVID-19 involve multiple systems addition to post-COVID conditions affecting the respiratory system, sense of smell and taste, and cardiovascular system, as well as varying manifestations of sequelae in the kidneys, digestive, hematological, endocrine, nervous, and immune systems, skin, hair, and physical strength. Young adult females often do not experience post-COVID-19 conditions, although elderly males have a high mortality rate from COVID-19, and COVID-19 vaccines and specific drugs have a statistically significant protective effect on the population, which should be promoted in clinical practice.

This information can provide guidance in clinical practice. Protective measures for elderly individuals with underlying diseases and the protective effects of COVID-19 vaccination and antiviral drugs merit promotion.

Data Sharing Statement

Data used in this study are available from the corresponding author upon reasonable request.

Ethical Statement

This study was approved by the Ethics Committee of Beijing Shijitan Hospital, Capital Medical University (Approval Number: IIT2024-147-002). Patient consent to review their medical records was not required by the IRB, and the reason for the exemption is that this study was a retrospective case analysis without any intervention. Patient data in this study database are strictly confidential and comply with the Declaration of Helsinki.

Disclosure

The author declares no conflicts of interest in this work.

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