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Acute and long COVID-19 symptoms and associated factors in the omicron-dominant period: a nationwide survey via the online platform Wenjuanxing in China

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Abstract

Backgrounds To our knowledge, there is no available nationwide data on omicron symptom patterns in China mainland. We aim to determine the acute and long COVID-19 symptoms in the omicron-dominant period and to evaluate its association with risk factors.

Methods We designed a cross-sectional nationwide study and data about self-reported symptoms were collected by an online platform named Wenjuanxing. Eligible participants were aged 25–65 years and were symptomatic. In this study, the ratios of the number of people of different ages and genders were weighted by the data from the Seventh National Census (2020 years), and validated by a published nationwide representative study through comparing smoking rates. Descriptive indicators were calculated for demographic characteristics, diagnosis ways, and duration time, acute symptoms, hospitalization, severity and long COVID-19 symptoms. And, the associations between risk factors and acute and long COVID-19 symptoms were analyzed by multivariable logistic regression models.

Results A total of 32,528 individuals diagnosed as COVID-19 infection from October 1, 2022 to February 21, 2023 were included. The first three acute symptoms of COVID-19 infection were fever (69.90%), headache (62.63%), and sore throat (54.29%), respectively. The hospitalization rate within 7 days was 3.07% and symptoms disappearance rate within 21 days was 68.84%, respectively. Among 3983 COVID-19 patients with 3 months or more time difference between first infection and participation into the study, the long COVID-19 rate was 19.68% and the primary symptoms were muscle weakness (19.39%), headache (17.98%) and smell/taste disorder (15.18%). Age groups, smoking, marriage status and vaccination were risk factors for numbers of acute phase symptoms and long COVID-19 symptoms. Lastly, female and current smokers also showed more numbers of symptoms during acute infection period.

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Conclusions In Chinese mainland, our respondent indicated that current smokers and women were associated with acute COVID-19 symptoms, which should be treated with caution due to the lack of representative.

Keywords Omicron, COVID-19 symptoms patterns, China mainland, Smoking, Female

Backgrounds

The global pandemic caused by COVID-19 has resulted in enormous economic and health burden. As of 3 May 2023, there have been about 765 million confirmed cases of COVID-19 (coronavirus disease 2019), including about 7 million deaths around the world, reported to World Health Organization (WHO) [1]. More than three years into the global pandemic, WHO has identified several variants of the virus including: alpha, beta, gamma, delta, and omicron [2], which differ in transmissibility, disease symptoms, and severity of symptoms [3]. To date, Omicron including subvariants are generally considered the most important virus variant, given the current prevalence rate among general public [4, 5]. Although most cases caused by this variant of concern resolve within two to four weeks of the initial symptoms' appearance [6], emerging evidence shows virus variants potentially affect the long term health outcomes after infection, often referred to as "long COVID" outcomes [7–9].

COVID-19 is not a disease that can be ignored, although on May 5, 2023, Tan Desai, Director General of the WHO, announced that the COVID-19 epidemic was no longer listed as a public health emergency of international concern (PHEIC) [10]. In other words, the end of the pandemic does not mean that all countries or regions in the world are no longer threatened by the epidemic at the same time. For example, COVID-19 might become a long-term health burden for the United States, because more than 1000 people still die each week even at the current COVID-19 epidemic low point [11]; in addition, the epidemic in Southeast Asia is currently in a rebound period due to the impact of the new Omicron strain. China has shown signs of other Omicron virus strains such as the XBB strain, which may indicate that a second wave of the epidemic is coming [12].

Better understanding of symptoms and long-term health effect of variants of concern may help clinicians, researchers, and policy advisors plan for diagnosis, treatment, and public health efforts of COVID-19. On Nov 26, 2021, Omicron was firstly designated a variant of concern by WHO [13], which has been identified in 210 countries and is now the most prevalent lineage globally [14]. Compared with previously dominant delta variant, the clinical severity, such as hospitalisations and deaths, of omicron infection is lower [15–21]. However, previous studies has indicated that age and vaccination status trigger different clinical presentation for Omicron infection [19, 22]. On the other hand, the cumulative evidence of latest studies also have established the primary symptoms of long COVID, including fatigue, shortness of breath, cough, cognitive impairment and anosmia [6, 23, 24]; and some risk factors have already been identified, such as older age, obesity, history of chronic diseases (cardiovascular disease, chronic lung disease, kidney disease and diabetes) and female sex [25–33].

Population-based studies on acute/long symptoms of Omicron infection are scarce in Chinese mainland. On May 23, 2023, we searched PubMed with the terms (("SARS-CoV-2") AND ("omicron") AND ("symptoms") AND ("China mainland")), with no date or language restrictions. We screened all papers by reading full text, and found that no national data on omicron symptoms was available in China mainland. This might be related with the fact that only a small portion of the people in Chinese mainland were exposed to SARS-CoV-2 prior to November 2022, when 'Dynamic zero-COVID' policy—including mass testing, population vaccination, quarantining and travel restrictions—to protect hundreds of thousands of people from infection and deaths [34]. From November 11 to December 7, 2022, more flexible COVID-19 control measures were conducted, for example, to encourage voluntary stay-at home quarantine, gradual replacement of nucleic acid screening by antigen detection, and the lift of travel restrictions, et al [35]. On December 26, 2022, the National Health Commission announced that the COVID-19 would be changed from category B infectious disease with management of category A to category B disease with management of category B starting from January 8, 2023 [36].

Therefore, to provide data about acute and long-COVID symptoms in individuals in Chinese mainland and explore the effect of risk factors such as sex, age and smoking status, we conducted a nationwide study and collected information on infected patients by online questionnaire survey from January 28 to February 21, 2023.

Methods

Study design

We conducted a nationwide and cross-sectional study, although sample size was not rigorously calculated. Firstly, the 31 provinces/municipalities/autonomous regions of China are divided into five geographical divisions, namely, East China, South China, Central China, North China, West China. Then, according to data from the Seventh National Census (2020 years), the ratios of the number of people of different ages and genders in each divisions to the total number of people in China

Table 1 Characteristics of COVID-19 infected patients included into analysis

	Total (*N*=32,528)	No. (%)
Areas		
North China	6076	18.68
South China	4481	13.78
West China	6951	21.37
East China	9995	30.73
Central China	5025	15.45
Age group, years		
25–34	8559	26.31
35–44	7687	23.63
45–54	9293	28.57
55–65	6989	21.49
Sex		
Male	16,652	51.19
Female	15,876	48.81
Smoking		
Current smoker	8707	26.77
Former smoker	1121	3.45
Never smoker	22,700	69.79
Education		
Primary school or lower	1059	3.26
Middle school	3586	11.02
High school	7432	22.85
College or higher	20,451	62.87
Marriage status		
Unmarried	12,173	37.42
Married	17,587	54.07
Divorced	2768	8.51
Any of the following physical diseases	14,187	43.61
cardiovascular diseases	4473	13.75
diabetes	3022	9.29
chronic respiratory diseases	3793	11.66
Digestive system diseases	2911	8.95
chronic liver disease	1654	5.08
chronic kidney disease	899	2.76
malignancy	636	1.96
Hematological disease	539	1.66
Allergic diseases	1995	6.13
Anxiety or Depression	1928	5.93
Infectious status were determined by which testing		
Self-reported Symptoms	14,228	43.74
Antigen detection tests	11,879	36.52
Nucleic acid based tests	6421	19.74
Vaccinated for COVID-19		
Two vaccine doses	23,525	72.32
Three vaccine doses	9003	27.68
Hospitalization within 7 days	998	3.07
Disappear within 21 days	22,393	68.84
long COVID-19	784	19.68*

*: Only 3983 COVID-19 patients were followed up for 3 months or more

were viewed as weighted rates of sample size (Appendix Table 1). And, the weighted rates were as the basis for sample size allocation. Lastly, we compared the smoking rates in this study with the rates in a published nationwide representative study, and results were shown in the Appendix Table 2.

Study population

The participants were recruited from January 28 to February 21, 2023, and they were required to complete an electronic questionnaire on a survey platform named Wenjuanxing. A total of 88,746 infected individuals participated into the online survey. Of these, 29,024 participants were were excluded due to completing the questionnaire within 2 min or repeatedly submitting questionnaire or logical error. Of the remaining 59,722 participants, we further excluded 3206 individuals aged<25 or >65 years due to low data reliability or small sample size. Based on the weighted sample size rates, 23,988 individuals were randomly excluded. Finally, 32,528 individuals were included into the analysis database. The flowchart was seen in Fig. 1.

Ethical considerations

The study was approved by the institutional review board of the China-Japan Friendship Hospital (2022-KY-183-1). This study complied with the Declaration of Helsinki. Informed consent was obtained for each participant. Study data of individuals are anonymous and there is no compensation for all participants.

Variables

Referring to previous studies [6, 37], we designed online questionnaire including demographic characteristics (gender, age, educational level, marriage and area), history of chronic disease (cardiovascular diseases, cancers, diabetes and chronic respiratory diseases, etc.), smoking and vaccination status. Secondly, questions on COVID-19 infection included date and ways of diagnosis, symptoms and duration of acute phase, and hospitalization or not. Thirdly, questions on long COVID-19 included number of infection, symptoms and duration. The definition of long COVID-19 in our study is consistent with the definition of World Health Organization (WHO), namely that the condition occurs after a history of probable or confirmed SARS-CoV-2 infection [38]. Symptoms usually occur 3 months from the onset of acute COVID-19 symptoms, last for at least 2 months and cannot be explained by an alternative diagnosis. Finally, standardized terminology not only facilitated comparison between studies, but also reduced the subjectivity and variability in symptom perception and reporting [39] (Appendix Table S3).

Table 2 Odds ratios (OR) and 95% confidence intervals (95% CI) for the associations of risk factors and numbers of acute phase symptoms

	Model 1			Model 2		
	OR	95% CI	P value	OR	95% CI	P value
Age group, years						
25–34	—	—				
35–44	1.1	1.03, 1.17	< 0.01	1.10	1.03, 1.17	< 0.01
45–54	0.92	0.87, 0.98	0.01	0.92	0.86, 0.97	< 0.01
55–65	0.8	0.75, 0.86	< 0.01	0.79	0.74, 0.84	< 0.01
Sex						
Male	—	—				
Female	1.16	1.11, 1.22	< 0.01	1.92	1.82, 2.03	< 0.01
Smoking						
Current smoker	—	—				
Former smoker	0.8	0.7, 0.9	< 0.01	0.74	0.65, 0.84	< 0.01
Never smoker	0.5	0.47, 0.52	< 0.01	0.36	0.34, 0.39	< 0.01
Area						
North China	—	—		—	—	
South China	0.91	0.84, 0.98	0.02	0.92	0.85, 1.00	0.04
West China	0.86	0.8, 0.92	< 0.01	0.86	0.80, 0.93	< 0.01
East China	0.87	0.81, 0.92	< 0.01	0.87	0.81, 0.93	< 0.01
Central China	0.99	0.92, 1.07	0.89	0.97	0.89, 1.04	0.4
Education						
Primary school or lower	—	—		—	—	
Middle school	1.98	1.69, 2.33	< 0.01	2.14	1.82, 2.52	< 0.01
High school	2.55	2.2, 2.97	< 0.01	2.84	2.44, 3.33	< 0.01
College or higher	2.94	2.54, 3.4	< 0.01	3.28	2.82, 3.82	< 0.01
Marriage status						
Unmarried	—	—		—	—	
Married	1.04	1, 1.09	0.07	0.95	0.90, 1.00	0.04
Divorced	0.72	0.66, 0.78	< 0.01	0.66	0.60, 0.72	< 0.01
BMI (Kg/m^2)						
18.5–24	—	—		—	—	
< 18.5	0.98	0.92, 1.04	0.54	0.97	0.91, 1.03	0.3
≥ 24	1.05	0.99, 1.11	0.1	1.08	1.02, 1.14	0.01
Vaccinated for COVID-19						
Two doses	—	—		—	—	
Three doses	0.7	0.67, 0.74	< 0.01	0.74	0.70, 0.78	< 0.01
History of chronic diseases						
No	—	—		—	—	
Yes	1.98	1.9, 2.07	< 0.01	1.97	1.88, 2.06	< 0.01

*: Model 1: Univariate Logistic regression model; Model 2: Multivariate Logistic regression model

Statistical analysis

Continuous variables were summarized as mean and standard deviation and categorical variables as frequencies and percentages. We listed the symptoms distribution during acute phase in all COVID-19 infection patients, and the distribution by sex, age, smoking status. Furthermore, we also analyzed the long COVID-19 symptoms distribution among the symptomatic population, and the distribution by sex, age, smoking status.

In addition, for each of the individual acute phase symptoms, a series of Multivariable Logistic regression models were used to explore the association between each risk factor and symptoms among all infectious patients. For long COVID-19 symptoms, regression models were also built to provide odds ratios (ORs) for each of the risk factors, and symptomatic patients were served as observation group and patients with no report of symptoms as control group. In our study, age groups, sex, smoking status, educational level, marriage, BMI, history of chronic diseases and vaccination status were included into the Multivariable Logistic regression models as risk factors.

Lastly, we divided all subjects into severely (4 symptoms or more) and lightly (less than 4 symptoms)

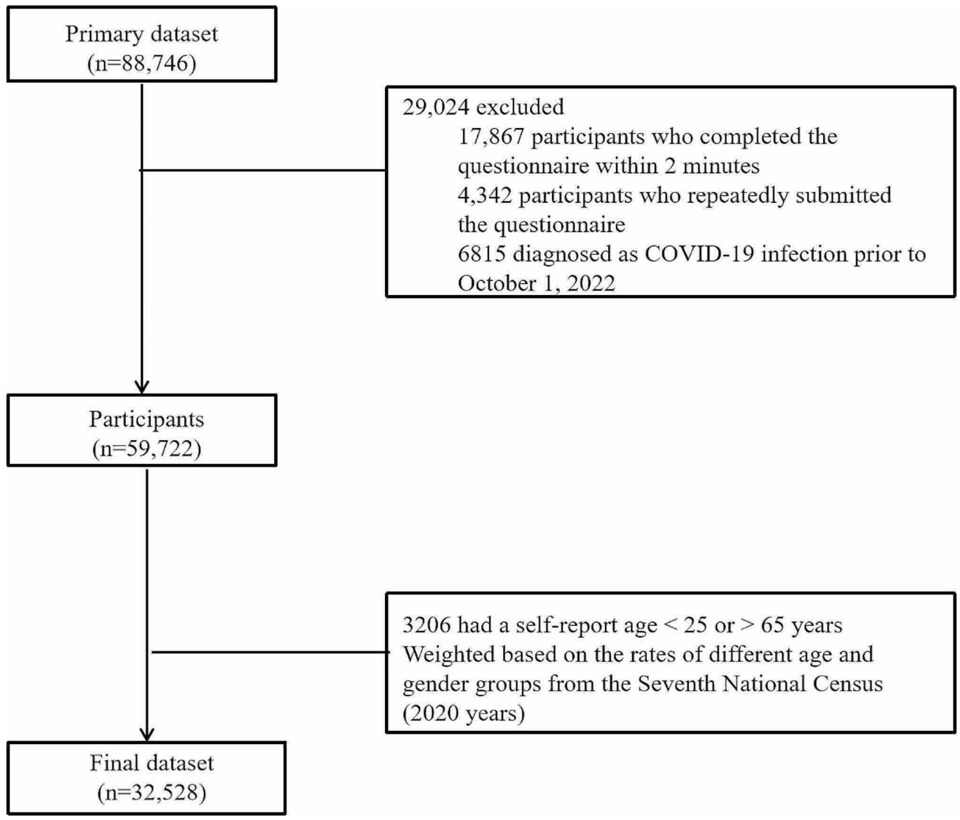


Fig. 1 Flowchart of the COVID-19 study

symptomatic groups, according to the number of symptoms during acute infection phase (the median value was 4). We conducted univariate and Multivariable Logistic regression models to explore the relationship between risk factors and the severity of symptoms during the acute infection period, respectively. All statistical analyses were performed in R software, version 4.2.1.

Results

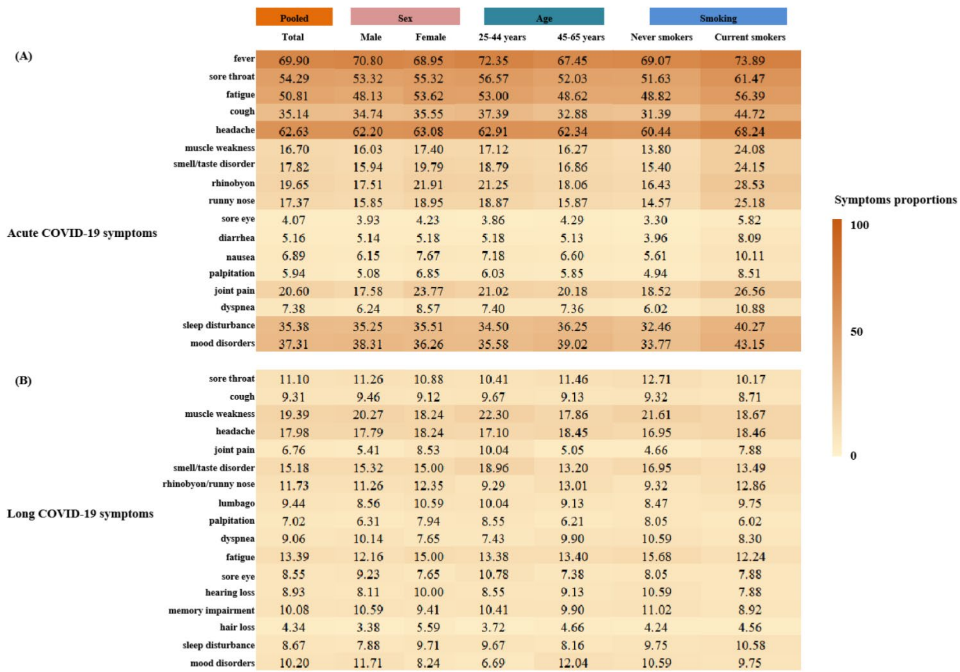
Participants information

As shown in Table 1, among 32,528 COVID-19 patients, there were 6076 (18.68%), 4481 (13.78%), 6951 (21.38%), 9995 (30.73%) and 5025 (15.45%) subjects from North China, South China, West China, East China, Central China, respectively. The proportions of population number in aged 25–34, 35–44, 45–54 and 55–65 were 26.31%, 23.63%, 28.57% and 21.49%, and in male was 51.19%, respectively. Appendix Table 2 shown that smoking rates by age groups and sex were similar to a previous representative and nationwide study, and the overall smoking rate is 26.77%. More than half of participants were married (54.07%), and had a college or higher (62.87%). 14,187 (43.61%) had at least one underlying disease and the most common physical diseases were cardiovascular diseases (13.75%), chronic respiratory diseases (11.66%) and diabetes (9.29%). 56.26% of participants infectious status were determined by nucleic acid based tests (19.74%) or antigen detection tests (36.52%), and 72.32% of all subjects have received two dose of COVID-19 vaccine.

Clinical patterns and influencing factors among all acute COVID-19 patients

Figure 2A present the acute symptoms stratified by sex, age and smoking status. The most common symptoms during the acute phase of infected individuals were fever (69.90%), headache (62.63%), sore throat (54.29%), fatigue (50.81%), cough (35.14%), sleep disturbance (35.38%), mood disorders (37.31%) and joint pain (20.60%). Of the remaining symptoms, the prevalence were lower than 20.00%, such as rhinobyon (19.65%), smell/taste disorder (17.82%), runny nose (17.37%), muscle weakness (16.70%), dyspnea (7.38%), nausea (6.89%), palpitation (5.94%), diarrhea (5.16%) and sore eye (4.07%). Additionally, the rates of hospitalization within 7 days and symptoms disappear within 21 days were 3.07% and 68.84%, respectively (Table 1).

We also did sub-analyses assessing the symptoms prevalence by sex, age and smoking status, and reported that the prevalence of fever, sore throat, fatigue, muscle weakness, smell/taste disorder, rhinobyon, runny nose, nausea, mood disorders were significantly different among



		Pooled	Sex		Age		Smoking	
		Total	Male	Female	25-44 years	45-65 years	Never smokers	Current smokers
(A) Acute COVID-19 symptoms	fever	69.90	70.80	68.95	72.35	67.45	69.07	73.89
	sore throat	54.29	53.32	55.32	56.57	52.03	51.63	61.47
	fatigue	50.81	48.13	53.62	53.00	48.62	48.82	56.39
	cough	35.14	34.74	35.55	37.39	32.88	31.39	44.72
	headache	62.63	62.20	63.08	62.91	62.34	60.44	68.24
	muscle weakness	16.70	16.03	17.40	17.12	16.27	13.80	24.08
	smell/taste disorder	17.82	15.94	19.79	18.79	16.86	15.40	24.15
	rhinobyon	19.65	17.51	21.91	21.25	18.06	16.43	28.53
	runny nose	17.37	15.85	18.95	18.87	15.87	14.57	25.18
	sore eye	4.07	3.93	4.23	3.86	4.29	3.30	5.82
	diarrhea	5.16	5.14	5.18	5.18	5.13	3.96	8.09
	nausea	6.89	6.15	7.67	7.18	6.60	5.61	10.11
	palpitation	5.94	5.08	6.85	6.03	5.85	4.94	8.51
	joint pain	20.60	17.58	23.77	21.02	20.18	18.52	26.56
	dyspnea	7.38	6.24	8.57	7.40	7.36	6.02	10.88
	sleep disturbance	35.38	35.25	35.51	34.50	36.25	32.46	40.27
	mood disorders	37.31	38.31	36.26	35.58	39.02	33.77	43.15
(B) Long COVID-19 symptoms	sore throat	11.10	11.26	10.88	10.41	11.46	12.71	10.17
	cough	9.31	9.46	9.12	9.67	9.13	9.32	8.71
	muscle weakness	19.39	20.27	18.24	22.30	17.86	21.61	18.67
	headache	17.98	17.79	18.24	17.10	18.45	16.95	18.46
	joint pain	6.76	5.41	8.53	10.04	5.05	4.66	7.88
	smell/taste disorder	15.18	15.32	15.00	18.96	13.20	16.95	13.49
	rhinobyon/runny nose	11.73	11.26	12.35	9.29	13.01	9.32	12.86
	lumbago	9.44	8.56	10.59	10.04	9.13	8.47	9.75
	palpitation	7.02	6.31	7.94	8.55	6.21	8.05	6.02
	dyspnea	9.06	10.14	7.65	7.43	9.90	10.59	8.30
	fatigue	13.39	12.16	15.00	13.38	13.40	15.68	12.24
	sore eye	8.55	9.23	7.65	10.78	7.38	8.05	7.88
	hearing loss	8.93	8.11	10.00	8.55	9.13	10.59	7.88
	memory impairment	10.08	10.59	9.41	10.41	9.90	11.02	8.92
	hair loss	4.34	3.38	5.59	3.72	4.66	4.24	4.56
	sleep disturbance	8.67	7.88	9.71	9.67	8.16	9.75	10.58
	mood disorders	10.20	11.71	8.24	6.69	12.04	10.59	9.75

Fig. 2 Proportions of acute and long COVID-19 symptoms among symptomatic patients ✳: means the p-value of subgroup test less than 0.05; For analysis of acute COVID-19 symptoms, there were 32,528 patients; For analysis of long COVID-19 symptoms, there were 784 patients

sex or age groups. Then, in male versus female, another the difference in symptom rates of palpitation, joint pain and dyspnea; there were sleep and disturbance cough in 25–44 years versus 45–65 years. Lastly, the reported rates of all acute symptoms among smokers were significantly higher than those among non-smokers (Fig. 2A and Figure S1).

We conducted multivariable logistic regression analysis and found that non-smokers had a lower proportion rate of each acute symptoms than smokers, as shown in Fig. 3. Of the remaining 16 symptoms (except for fever), female had a higher risk than male. And age was a risk factor for acute symptoms of fever, sore throat, fatigue, cough, headache, smell/taste disorder, rhinobyon and runny nose, but not for symptoms of muscle weakness, sore eye, diarrhea, nausea, palpitation, joint pain, dyspnea, sleep disturbance and mood disorders.

Risk factors of numbers of acute phase symptoms and long COVID-19

We also explored the risk factors of numbers of acute phase symptoms and long COVID-19. and results were shown in Table 2 and Table 3. After adjusting for educational level, marriage, BMI, history of chronic diseases and vaccination status, multivariable logistic regression results indicated that female had a higher risk of serious acute phase symptoms (OR 95%CI: 1.92, 1.82–2.03), while non-smokers had a lower risk (OR 95%CI: 0.36, 0.34–0.39). Finally, compared with individuals aged 25–34 years, people aged 35–44 years was a risk factor for serious acute symptoms (OR 95%CI: 1.10, 1.03–1.17) but those aged 45–54 years and 55–65 years were protective factors (OR 95%CI: 0.92, 0.86–0.97, OR 95%CI: 0.79, 0.74–0.84, respectively).

Clinical patterns and influencing factors among long COVID-19 individuals

Among 3983 COVID-19 patients, the date difference between first infection and participation into this study was 3 months or more, and the rates of long COVID-19 in Chinese population was 19.68% (784/3983), as shown in Table 1. Figure 2B and Figure S1 showed the distribution of long COVID-19 symptoms. The frequently observed symptoms were muscle weakness (19.39%), headache (17.98%), smell/taste disorder (15.18%), fatigue (13.39%), rhinobyon/runny nose (11.73%), sore throat (11.10%), memory impairment (10.08%) and mood disorders (10.02%). Moreover, the prevalence of symptoms of lumbago, cough, dyspnea, hearing loss, sleep disturbance, sore eye, palpitation, joint pain and hair loss were 9.44%, 9.31%, 9.06%, 8.93%, 8.67%, 8.55%, 7.02%, 6.76% and 4.34%, respectively.

The results of subgroup analysis suggested that there were no significant differences in symptoms distribution between male and female, smokers and non-smokers. In addition, the joint pain and smell/taste disorders were significantly more prevalent among individuals aged 25–44 years, while mood disorders were more common among those aged 55–65 years (Fig. 2B).

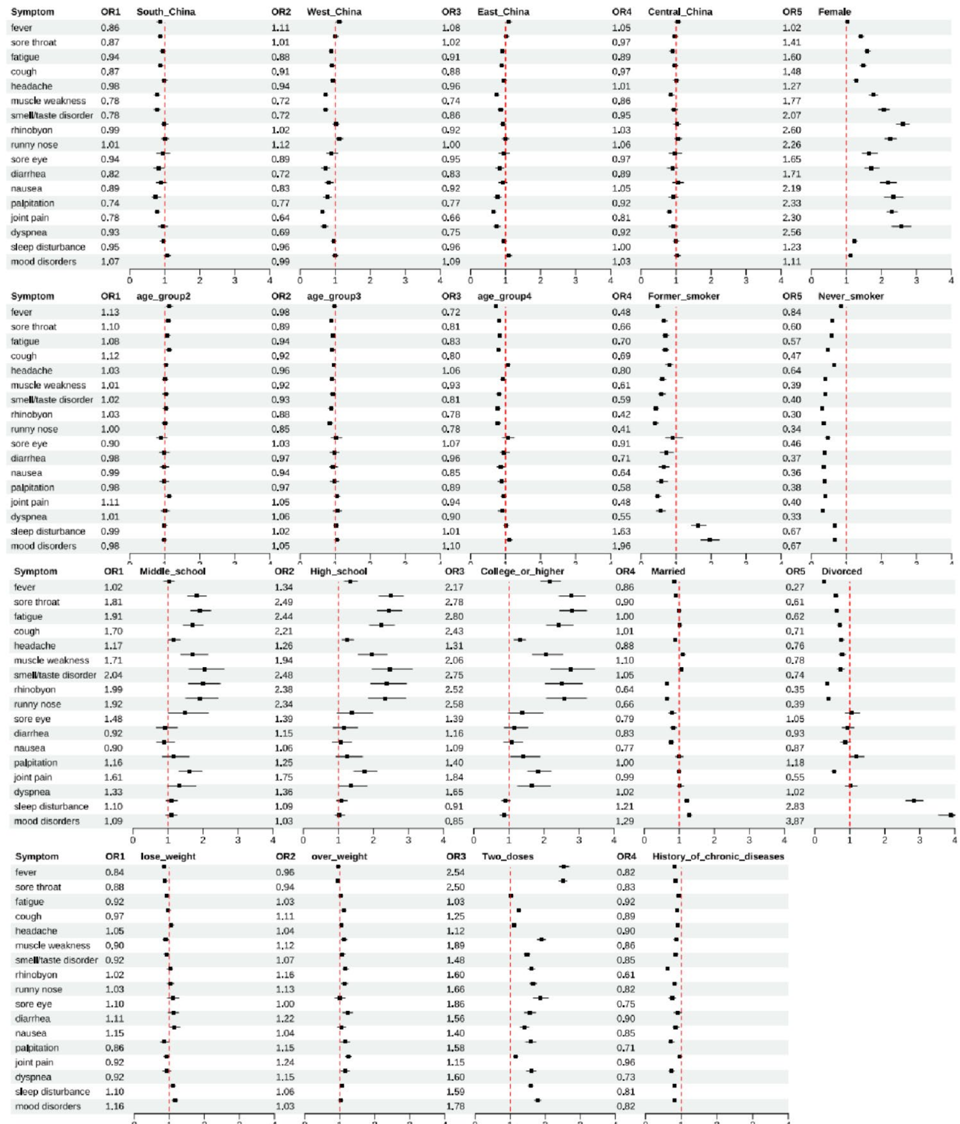


Fig. 3 Association between risk factors and acute COVID-19 symptoms ✳: age group2: 35–44 years, age group3: 45–54 years, age group4: 55–65 years; Those lived in North China, male, 25–34 years, current smokers, primary school, unmarried, 18.5–24 kg/m^2, three vaccine doses and no history of chronic diseases were analyzed as reference groups. For analysis of acute COVID-19 symptoms, there were 32,528 patients

Figs 3 and 4 present the effect of risk factros on acute COVID-19 symptoms and long COVID-19 symptoms, respectively Compared with male, female had higher incidence risks for rhinobyon (OR 95%CI: 2.6, 2.42–2.8)/ runny nose (OR 95%CI: 2.26, 2.1–2.43), dyspnea (OR 95%CI: 2.56, 2.3–2.84) and palpitation (OR 95%CI: 2.33, 2.08–2.62) et al. In addition, non-smokers was a protective factor for rhinobyon (OR 95%CI: 0.3, 0.28–0.33), dyspnea.(OR 95%CI: 0.33, 0.3–0.37) and runny nose (OR 95%CI: 0.34, 0.32–0.37).

Discussion

In general, our findings on the clinical patterns of acute/ long COVID-19 infection in Chinese population were consistent with prior studies from other countries. For acute symptoms of Omicron, the most frequently reported symptoms in our study were fever (69.90%), headache (62.6%), sore throat (54.3%), fatigue (50.8%) and cough (35.1%), while results from the ZOE COVID Study showed that they were runny nose (76.5%), headache (74.7%), sore throat (70.5%), sneezing (63.0%) and persistent cough (49.8%), respectively [19]. Although the main symptoms were similar in the above two studies, the incidence of symptoms was lower in the Chinese study. In addition, the evidence that the clinical severity of infection is lower for omicron than for previously dominant delta variant has been well established [20].

We found that among Omicron infected individuals, female and smokers had higher proportion of acute symptoms than male and non-smoker. In early period of

Table 3 Odds ratios (OR) and 95% confidence intervals (95% CI) for the associations of risk factors and long COVID-19 symptoms

	Model 1			**Model 2**		
	OR	95% CI	P value	OR	95% CI	P value
Age group, years						
25–34	—	—		—	—	
35–44	1.03	0.78, 1.35	0.85	1.06	0.80, 1.40	0.7
45–54	1.47	1.19, 1.82	< 0.01	1.42	1.14, 1.77	< 0.01
55–65	1.6	1.29, 1.99	< 0.01	1.56	1.25, 1.95	< 0.01
Sex						
Male	—	—		—	—	
Female	0.85	0.73, 1.00	0.06	1.11	0.92, 1.34	0.3
Smoking						
Current smoker	—	—				
Former smoker	1.2	0.88, 1.65	0.25	1.17	0.84, 1.61	0.4
Never smoker	0.59	0.5, 0.69	< 0.01	0.58	0.48, 0.71	< 0.01
Area						
North China	—	—		—	—	
South China	1.04	0.77, 1.41	0.8	1.13	0.83, 1.55	0.4
West China	0.89	0.69, 1.16	0.4	0.91	0.70, 1.19	0.5
East China	0.87	0.68, 1.09	0.23	0.98	0.77, 1.25	0.9
Central China	0.82	0.61, 1.1	0.18	0.83	0.61, 1.11	0.2
Education						
Primary school or lower	—	—		—	—	
Middle school	1.33	0.94, 1.89	0.1	1.25	0.88, 1.79	0.2
High school	1.31	0.94, 1.82	0.11	1.25	0.90, 1.76	0.2
College or higher	0.98	0.71, 1.34	0.88	0.97	0.71, 1.35	0.9
Marriage status						
Unmarried	—	—		—	—	
Married	1.47	1.23, 1.77	< 0.01	1.40	1.16, 1.69	< 0.01
Divorced	1.76	1.4, 2.2	< 0.01	1.59	1.26, 2.01	< 0.01
BMI (Kg/m^2)						
18.5–24	—	—		—	—	
< 18.5	0.98	0.79, 1.21	0.85	1.04	0.84, 1.30	0.7
≥ 24	1.16	0.96, 1.4	0.13	1.16	0.96, 1.41	0.13
Vaccinated for COVID-19						
Two doses	—	—		—	—	
Three doses	0.88	0.74, 1.04	0.14	0.79	0.65, 0.94	< 0.01
History of chronic diseases						
No	—	—		—	—	
Yes	1.22	1.05, 1.43	0.01	1.08	0.92, 1.27	0.3

*: Model 1: Univariate Logistic regression model; Model 2: Multivariate Logistic regression model

the outbreak of epidemic, data suggested that severe or deceased COVID-19 cases were more common in male [40–42]. But the high absolute number of male might be related with more exposure chance for COVID-19 viruses, such as frequent social activities and long business trips. However, in the omicron-dominant period, both male and female would face the same risk of infection because non-pharmaceutical public health intervention (NPI) measures—including quarantining and travel restriction—has been revised based on the fact that omicron variant seems to be much more transmissible [18, 21, 43, 44] and less severe [45] than previous variants and high population vaccination rates [35, 36, 46]. Therefore, higher proportion and more number of acute symptoms for female provided a clue that female should be given more attention during omicron prevalence. Similarly, our data also indicated that smokers should be viewed as high risk population susceptible to Omicron symptoms. Extensive previous research has shown smokers were at greater risk of developing severe disease after infection than are non-smokers such as hospital admission, ICU admission and death [47–50], although cigarette smoking on COVID-19 infection are conflicting [51]. This might be related with the evidence that smoking induces substantial lung injury, because harmful substances in tobacco smoke damage epithelial cells

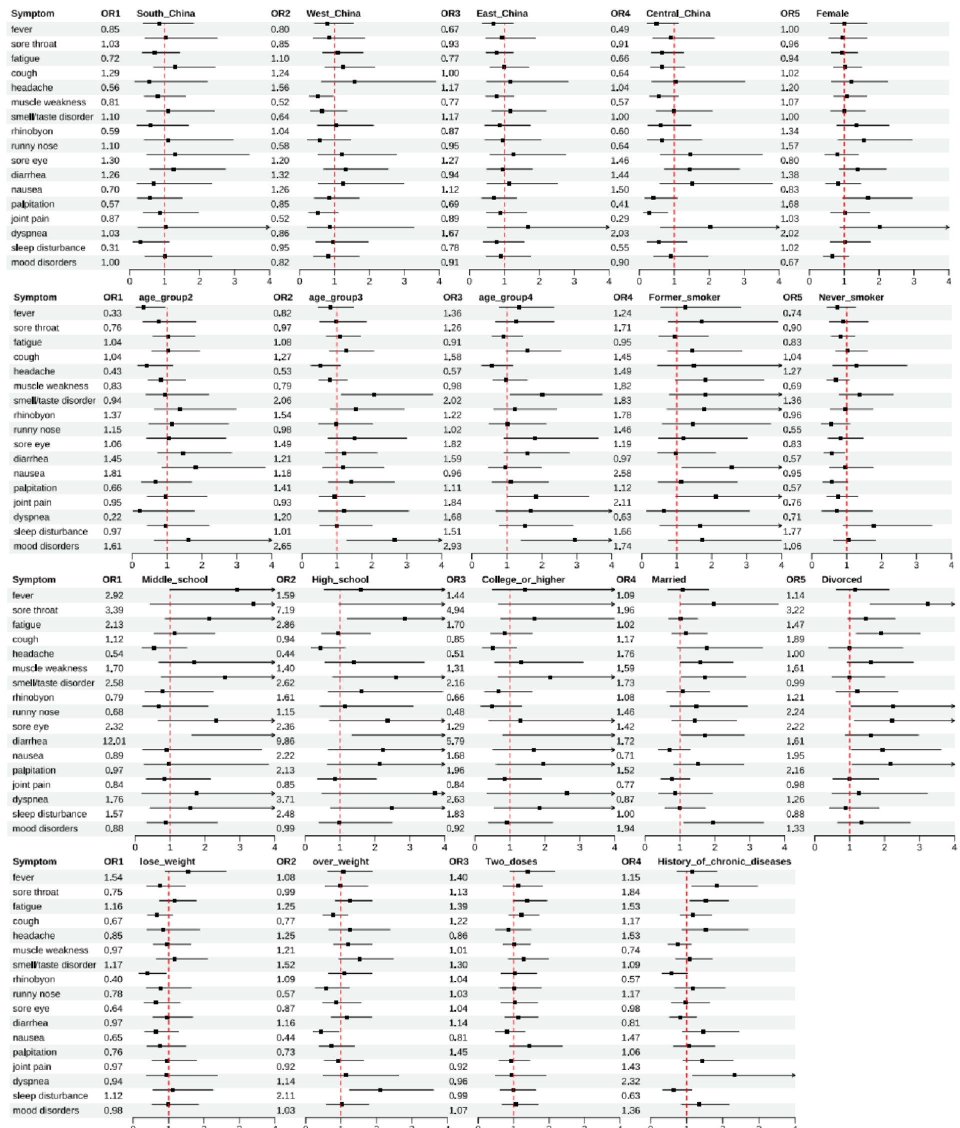


Fig. 4 Association between risk factors and long COVID-19 symptoms ✳: age group2: 35–44 years, age group3: 45–54 years, age group4: 55–65 years; Those lived in North China, male, 25–34 years, current smokers, primary school, unmarried, 18.5–24 kg/m^2, three vaccine doses and no history of chronic diseases were analyzed as reference groups. For analysis of long COVID-19 symptoms, there were 3983 patients

and further compromise the epithelial barrier and mucociliary clearance [52]. Lastly, prior evidence have established that disease severity, hospital admission, and death of COVID-19 were dependent on age [22]. In our study, the highest number of Omicron symptoms were reported in the 35–44 years subgroup and Omicron had age-specific symptoms pattern, which might be helpful to better understanding of the different courses in the age groups.

The long COVID-19 rates were varied in different studies, which might be related with observation periods of sequelae of COVID-19, virus variants and vaccination status. For example, the UK's Office for National Statistics found that of triple-vaccinated participants, the socio-demographically adjusted prevalence of self-reported long COVID four to eight weeks after a first COVID-19 infection was 8.5% for Delta and 8.0% for Omicron BA.1. and 9.1% for Omicron BA.2 [53]. When they extended follow-up period to 12 to 16 weeks, there were 5.0% for Delta, 4.5% for Omicron BA.1 and 4.2% for Omicron BA.2, respectively. In addition, data from a multicenter prospective cohort study suggested that among the COVID-positive cohort, self-reported prolonged symptoms at 3 months were 52.6% in the pre-Delta group, 41.5% in the Delta and 41.5% in the Omicron, respectively, but not all participants of this study have vaccination (18.4% in the pre-Delta, 74.1% in the Delta and 98.4% in the Omicron) [54]. Moreover, in Eastern India, researchers found that 29.2% self-reported having long COVID symptoms 4 weeks after diagnosis [55], however they also found that the prevalence on long COVID after infection with only Omicron variant was 8.2% [56]. Lastly, prior studies have also supported that vaccination could reduce the risk of the post-acute sequelae of COVID-19 [57–59]. Findings from a nationwide cohort study indicated that compared with unvaccinated patients, those with vaccination had significantly lower risk for dyspnoea up to three months after infection [6]. This is in accordance with studies showing that vaccination before COVID-19 breakthrough infection partially reduced the risk of post-acute sequalae [57]. For long COVID-19 symptoms, muscle weakness, smell/taste disorder and fatigue in Chinese people has been repeatedly evident by previous studies including Alpha strain, Delta strain and Omicron strain, even on a small scale or periods longer than one year [60–62].

Our study showed that long COVID-19 symptoms were associated with the age groups, which was consistent with prior study [6]. Furthermore, data from Chinese population supported that both smoking and female were associated with an risk of fatigue, which was repeatedly reported by previous studies [32, 37, 63–65]. Notably, our findings demonstrated the associations between factors (age, gender and smoking) and outcomes (COVID-19 symptoms) rather than robust causal links, because this cross-sectional survey collected both factors and outcomes simultaneously. The causal links should be validated in future cohort studies.

Given the evolving nature of Long-COVID studies, different definitions of Long-COVID would lead to variations in the findings of the research. Compared with the definition of the Centers for Disease Control and Prevention (CDC) in the United States, the main difference is the onset time of Long-COVID after after infection (3 months in our definition and 4 weeks in CDC) [38]. Longer time span from the end of acute infection to the start of long COVID and would lead to the loss of long COVID cases, further underestimating our results. In contrast, the rate of long COVID in our study is overestimated, because the latest definition excluded the patients with history of 25 WHO-listed symptoms 180 days before infection [66]. In addition, the latest time interval is between 90 and 365 days after the date of a PCR-positive test or clinical diagnosis of COVID-19, which has no bias on our results due to the follow-up time of our study within 1 year.

The non-respondents to online surveys led to our underestimation of the severity of COVID-19 in Chinese population. Previous evidence showed that higher education levels were more likely to participate into online questionnaires [67], which was supported by our data that 62.87% of our respondents had a college degree or above (a higher level than the average of nation). However, increased adverse COVID-19 outcomes among the poor and low educational status patients has also been reported in studies from India [68], Brazil [69], USA [70], South Korea [71] and African countries [72]. This could be explained by greater load of infection and longer exposure to the virus due to crowded environments, limited housing, large household sizes, low quality jobs, unsafe commute and undernutrition [73, 74]. Therefore, the non-respondents to our online study led to a high educational level of participants, which was related with less adverse COVID-19 events.

We held that the protective effect of the increased age was the results of survivorship bias reported in previous COVID-19 survey [75]. We believe the main reason is survivorship bias that the older age group (55–65 years old) is more likely to be mild patients, because severe patients may have already died or been hospitalized. Accumulating evidence supported that aging itself was a prominent risk factor for severe disease and death from COVID-19, which might be related with age-related decline and dysregulation of immune function [76, 77]. In our study, patients aged 55 to 65 with severe acute COVID-19 symptoms may not respond to the online survey due to death or hospitalization, resulting in the occurrence of survivorship bias. In addition, less severe patients in older age group also led to the low level of association between the increased age and acute COVID-19 symptoms, thus this findings should be treated with caution.

To our knowledge, this is the largest study to date to firstly report on the symptom patterns of acute and long COVID-19 infection in Chinese mainland, during Omicron period. Strengths of the study include the use of a nationwide patients, which is weighted by age ratios by gender from the Seventh National Census (2020 years) and is also validated by smoking rates from a prior study. The large sample size of over 30 thousand people provide enough statistical power to support stratified analyses. According to the data of the Chinese Center for Disease Control and Prevention, from September 26, 2022 to April 27, 2023, COVID-19 genome effective sequences of 43,777 local cases in China mainland were Omicron variants, and all participants in our study was from October 1, 2022 to February 21, 2023 [78].

However, there are several limitations. Firstly, we have limited age range to 25 to 65 years old, which limit the generalization of our findings. Secondly, only about 56% of infected patients was diagnosed by objective molecular tests, such as nucleic acid or antigen detection. In the early stages of the COVID-19 epidemic, limited medical resources could not meet testing needs of a large number of symptomatic individuals. In this study, the combination of symptoms and epidemiological history was also viewed as diagnostic criteria of COVID-19, which might bias our results. Thirdly, there may be health seeking bias in the self-reported symptom data, because some participants might be more active in maintaining their health and be more likely to report symptoms than others. Forthly, our study had survivorship bias, because severe patients might not respond to the online survey due to death or hospitalization. Lastly, we also can not distinguish long COVID-19 symptoms from similar clinical manifestations that occur normally or following infections with other pathogens, but our main findings on long COVID-19 are consistent with other studies with a control group.

In conclusion, our findings indicated that among our respondent, current smokers and women had a higher proportion for each acute symptom, and were also associated with more number of symptoms during acute period.

Supplementary Information

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Supplementary Material 1

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Author contributions

Conceptualization and design, CW and DX; Data collection, XM Z, YL, XX, QQS, JXL, RQ, ZL and LZ; Formal analysis, ZS and XW W; Writing - original draft, ZS and XWW. All authors read and approved the final manuscript.

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Data availability

All data in this study are not publicly available, but could be accessed by inquiring the corresponding author.

Declarations

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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