Clinical characteristics of patients infected with novel coronavirus wild strain, Delta variant strain and Omicron variant strain in Quanzhou: A real-world study

HUATANG ZHANG^{1*}, WENHUANG CHEN^{1*}, XIAOYI YE^{2*}, YONGJUN ZHOU^{3,4*}, YIJUAN ZHENG¹, ZHANGYAN WENG¹, JIANFENG XIE⁵, KUICHENG ZHENG⁵, ZHIJUN SU¹, XIBIN ZHUANG² and XUEPING YU¹

Departments of ¹Infection and ²Respiratory Disease, The First Hospital of Quanzhou Affiliated to Fujian Medical University; ³College of Life Sciences and Chemistry and ⁴Institute of Bioengineering and Biotechnology,

Minnan Science and Technology University, Quanzhou, Fujian 362000; ⁵Fujian Provincial Key Laboratory of Zoonosis Research, Fujian Center for Disease Control and Prevention, Fuzhou, Fujian 350001, P.R. China

Received June 11, 2022; Accepted August 12, 2022

DOI: 10.3892/etm.2022.11761

Abstract. This study aimed to investigate the clinical features of patients infected with novel coronavirus wild strains, Delta variant strains and Omicron variant strains to provide a reference for early clinical diagnosis and prognostic assessment. The demographic, clinical symptoms and ancillary examination data of 47 patients with novel coronavirus wild type strain infection, 18 with Delta variant infection and 20 with Omicron variant infection admitted to the First Hospital of Quanzhou affiliated with Fujian Medical University were collected and analyzed. The novel coronavirus wild strain and Delta strain were the predominant clinical types; patients infected with the Omicron strain were mainly asymptomatic. Fever and fatigue were the main clinical manifestations in the wild strain and Delta strain groups, whereas dry cough, nasal congestion, sore throat and fever were common clinical manifestations in the Omicron strain group. The Delta strain and Omicron variant

Correspondence to: Dr Xueping Yu, Department of Infection, The First Hospital of Quanzhou Affiliated to Fujian Medical University, 250 East Street, Licheng, Quanzhou, Fujian 362000, P.R. China E-mail: xpyu15@fudan.edu.cn

Mr. Xibin Zhuang, Department of Respiratory Disease, The First Hospital of Quanzhou Affiliated to Fujian Medical University, 250 East Street, Licheng, Quanzhou, Fujian 362000, P.R. China E-mail: zxbqz@163.com

*Contributed equally

Abbreviations: COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; ALB, albumin; ICU, intensive care unit; VOC, variants of concern; WHO, world health organization; Ig, immunoglobulin; PT, prothrombin time; CT, computed tomography; CRP, C-reactive protein

Key words: novel coronavirus, variant strain, Quanzhou, clinical features, Omicron

groups had fewer comorbidities than the wild-type strain group, but no significant reduction was observed in the negative conversion time of nucleic acids. Significant differences were found in the neutrophil count/lymphocyte count ratio, lymphocyte count, eosinophil count, red blood cell count, hemoglobin level, erythrocyte sedimentation rate, C-reactive protein, prothrombin time, international normalized ratio and plasma D-dimer, PH, PaO₂, lactic acid and albumin levels among the three groups. Patients infected with the Omicron strain in Quanzhou presented with mild symptoms of the upper respiratory tract as the primary clinical manifestation and had few comorbidities and a good prognosis; however, the negative conversion time of the new coronavirus nucleic acid was still considerably long.

Introduction

Novel coronavirus pneumonia [coronavirus disease 2019 (COVID-19)] has rapidly spread in various countries worldwide since its emergence in December 2019 and has now become a major global public health problem (1). The novel coronavirus [severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)] has evolved to produce variant strains with variable transmissibility and virulence, such as Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Delta (B.1.617.2) and Omicron (B.1.1.529) (WHO. Tracking SARS-CoV-2 Variants (EB/OL) 2021-12-06 (available from https://www.who.int/) (2). The Delta variant was first detected in India in October 2020 (3). It quickly replaced the Gamma variant in several countries and regions worldwide and was designated as a variant of concern (VOC) by the World Health Organization (WHO) on May 11, 2021 (4). The P681R mutation in the Delta mutant spike (S) protein is one of the key mutations that enhances the ability of SARS-CoV-2 to fuse with host cells (5). The Omicron mutant strain was first detected in South Africa and reported to the WHO on November 24, 2021 (6). Mutations in more S protein sites in the Omicron mutant strain further enhanced its pathogenicity, infectivity and immune escape ability. The mutant strain was designated as a VOC by the WHO on November 26, 2021

(WHO. Tracking SARS-CoV-2 Variants (EB/OL) 2021-12-06 (available from https://www.who.int/). Due to its enhanced immune escape ability and transmissibility, Omicron has replaced other mutant strains and has become a major epidemic strain in several countries and regions worldwide (7). Omicron induces an asymptomatic or mild infection and is highly transmissible, posing a serious challenge to the prevention and control of the epidemic. In the present study, the demographic data, clinical characteristics and negative conversion time of nucleic acids of the new coronavirus in patients infected with the SARS-CoV-2 wild strain, Delta strain and Omicron strain in Fujian Province, China, were reported for the first time, thus providing a reference for the clinical management of patients infected with new coronary pneumonia in this region.

Materials and methods

Source of cases. A total of 47 patients with SARS-CoV-2 wild type strain infection between January 21, 2020 and March 6, 2020, together with 18 patients with Delta strain infection between September 12, 2021 and September 15, 2021 and 20 patients with Omicron strain infection between February 10, 2022 and February 12, 2022, were treated at the Special Ward for Infection Disease, The First Hospital of Quanzhou affiliated with Fujian Medical University.

Inclusion criteria. Patients infected with the SARS-CoV-2 wild type, Delta and Omicron mutant strains were included in this study. SARS-CoV-2 sequencing was conducted at the Center for Disease Prevention and Control of Quanzhou.

Exclusion criteria. Patients with incomplete medical data and suspected cases were excluded.

Diagnostic criteria. According to the New Coronavirus Pneumonia Treatment Protocol (Trial Version 8) issued by the General Office of the National Health Commission and the Office of the National Administration of Traditional Chinese Medicine (8), those with an epidemiological history, clinical manifestations and positive results on pathogenic or serological tests are considered confirmed cases of new coronavirus pneumonia. According to the results of the comprehensive evaluation of clinical manifestations and auxiliary examinations, these cases can be classified into mild, common, severe and critical types. In the present study, an asymptomatic infection carrier was defined as an individual with a positive nucleic acid test result for novel coronavirus but without any associated clinical manifestations.

Discharge criteria. Patients i) whose body temperature returned to normal after more than three days, ii) who demonstrated significant improvement in respiratory symptoms, iii) whose acute exudative lesions identified on lung imaging improved significantly and iv) who showed negative results for two consecutive nucleic acid tests using respiratory specimens (≥ 24 h apart) were discharged from the hospital.

Data collection. The following data were collected: i) Demographic characteristics (sex, age, underlying disease, COVID-19 vaccination status and epidemiological history); ii) clinical typing and clinical symptoms of COVID-19; iii) ancillary tests performed within 48 h after admission [routine blood tests (Coulter LH750 analyzer; Beckman Coulter, Inc.), complete biochemical tests (AU5811; Beckman Coulter, Inc.), humoral immunity (IMMAGE800; Beckman Coulter, Inc.), coagulation screening (ACL-TOP 700; Diamond Diagnostics Inc.), lung computed tomography (CT; SOMATOM Emotion 16; Siemens AG), blood gas analysis (ABL9; Radiometer Medical) and analysis of nucleic acid-negative conversion time for COVID-19 (QuantStudio5; Thermo Fisher Scientific, Inc.)]; and iv) efficacy evaluation (nucleic acid-negative conversion time). The database strictly regulated the use of the data to ensure security and confidentiality.

Statistical analysis. Data analysis was performed using IBM SPSS Statistics for Windows version 23.0 (IBM Corp.). The Kruskal-Wallis rank sum test or Mann-Whitney U test was used to analyze non-normally distributed continuous variables (data are presented as medians with 25 and 75th percentiles). Qualitative data were analyzed using Fisher's exact test and are presented as percentages. P<0.05 was considered to indicate a statistically significant difference.

Results

Study sample and typing. A total of 85 patients were enrolled in the present study. In the SARS-CoV-2 wild type strain group, four patients had mild infection, 40 had common infection and three had severe infection. In the Delta strain group, two patients had mild infection and 16 had a common infection. In the Omicron strain group, six patients had asymptomatic infection, seven had mild infection and seven had common infection.

Demographic and clinical characteristics. In the present study, no significant differences were observed in the age, sex and body mass index among the wild type, Delta and Omicron strain groups. The nucleic acid-negative conversion time was significantly longer in the Omicron strain group than in the wild type (Z=16.301, P=0.037) or Delta strain groups (Z=30.904, P<0.001). The most common clinical manifestations in the wild type and Delta strain groups were fever and malaise, respectively. By contrast, the most common clinical presentation in the Omicron strain group was a dry cough. Fever, nasal congestion and sore throat were common in the Omicron strain group. The COVID-19 vaccination rate of the Delta group was higher and the rates of clinical symptoms of fever, dry cough, sore throat, expectoration, nasal congestion and runny nose in this group were lower than those in other groups. None of the patients in this study developed conjunctivitis, ageusia (taste loss), or anosmia (smell loss). The details of patient characteristics are summarized in Table I.

Hematology results within 48 h after admission. The statistical hematology results of the wild-type strain, Delta strain and Omicron strain groups are shown in Table II. The lymphocyte count, eosinophil count, red blood cell count, hemoglobin

Characteristic	Primitive strain group (n=47)	Delta strain group (n=18)	Omicron strain group (n=20)	χ^2	P-value
Age (years)	38 (31-50)	33 (10-40.5)	35 (30-42)	-	0.137
Sex (male)	24 (51.06)	9 (45.00)	20 (100.0)	9.677	0.200
BMI (kg/m ²)	23.9 (20.7-26.4)	20.42 (17.88-23.22)	22.49 (20.52-23.53)	-	0.195
Nucleic acid-Negative conversion time (days)	22 (15-30)	24 (18-30)	26 (24-30.75)	-	0.001
Vaccination status	0	5 (27.78)	0	-	-
Underlying diseases					
Hypertension	10 (21.28)	0	0	-	-
Diabetes	5 (10.64)	0	0	-	-
Malignant tumors	1 (2.13)	0	0	-	-
Chronic liver disease	11 (23.40)	0	0	-	-
Respiratory disease	4 (8.51)	0	0	-	-
Fever	39 (82.98)	10 (33.33)	7 (35)	139.48	0.000
Dry cough	11 (23.40)	3 (16.67)	8 (40)	140.23	0.000
Sore throat	13 (27.66)	3 (16.67)	7 (35)	111.63	0.000
Weakness	19 (40.43)	6 (33.33)	0	65.22	0.000
Expectoration	26 (55.32)	2 (11.11)	3 (15)	141.53	0.000
Diarrhea	10 (21.28)	0	1(5)	151.52	0.000
Myalgia	7 (14.89)	0	1(5)	146.08	0.000
Nasal congestion	6 (12.77)	3 (16.67)	7 (35)	141.29	0.000
Rhinorrhea	7 (14.89)	2 (11.11)	5 (25)	141.10	0.000

Table I. Comparisons of demographic and clinical characteristics of the wild strain group, Delta strain group and Omicron strain group.

and albumin (ALB) levels in the Omicron strain group were significantly higher than those in the original strain group (Z=17.905, P=0.013; Z=24.908, P=0.000; Z=19.809, P=0.008; Z=26.687, P=0.007; Z=24.763, P=0.000, respectively). The neutrophil count/lymphocyte count ratio, prothrombin time (PT) and plasma D-dimer levels were significantly lower in the Omicron strain group compared with the original strain group (Z=16.882, P=0.003; Z=34.396, P=0.000; Z=29.553, P=0.000, respectively). The eosinophil count, red blood cell count and hemoglobin levels were significantly higher in the Omicron strain group than in the Delta strain group (Z=35.754, P=0.000; Z=21.218, P=0.001; Z=18.209, P=0.001, respectively). The neutrophil count/lymphocyte count ratio was significantly lower in the Omicron strain group compared with the Delta group (Z=18.000, P=0.015). C-reactive protein (CRP), PT and plasma D-dimer levels were significantly higher in the wild strain group compared with the Delta strain group (Z=17.139, P=0.024; Z=17.642, P=0.017; Z=17.219, P=0.033, respectively). The ALB level was significantly higher in the Delta strain group compared with the wild strain group (Z=23.398, P=0.001).

Comparisons of lung CT results. The incidence of patchy shadows, ground-glass opacities, bronchial inflation signs, halo signs, consolidation shadows and peripheral lesions identified through lung imaging was significantly higher in the wild type group compared with the Delta and Omicron strain groups (Table III).

Comparisons of vaccinated and unvaccinated. The demographic and clinical characteristics and auxiliary examinations of the two groups were statistically analyzed. The vaccinated group displayed higher lymphocyte and eosinophil counts compared with the unvaccinated group. The proportion of lung lesions was significantly lower in the vaccinated group compared with the unvaccinated group (Table IV).

Discussion

The continuous evolution and mutation of SARS-CoV-2, as well as the resulting variant strains with their enhanced transmission, pathogenicity and immune escape have posed serious challenges to the prevention and control of the epidemic in countries and regions worldwide. Through in-depth research, we have gained more knowledge and understanding of the epidemic situation, transmission characteristics and clinical features of the Omicron strain. However, there is a lack of reports on the demographic data, clinical characteristics and prognosis of patients infected with the SARS-CoV-2 wild type, Delta and Omicron strains living in Fujian Province, China. To provides a reference for the prevention and treatment of COVID-19 in this region, the demographic and clinical data of COVID-19 patients living in Quanzhou City, Fujian Province since the outbreak of COVID-19 were obtained in the present study. Patients in the Omicron strain group were younger and had fewer underlying diseases, milder clinical symptoms that predominantly

Ζ	L
	г

Hematological result	Wild strain group (n=47)	Delta strain group (n=18)	Omicron strain group (n=20)	χ^2	P-value
White blood cell count $(x10^{9}/l)$	5.47 (4.40-6.48)	6.19 (5.29-6.59)	6.06 (4.20-6.50)	0.857	0.651
Neutrophil count (x10 ⁹ /l)	3.23 (2.43-3.87)	3.35 (2.78-4.41)	2.93 (1.80-3.65)	4.828	0.089
Lymphocyte count (x10 ⁹ /l)	1.55 (1.10-1.94)	1.54 (0.99-1.89)	1.94 (1.66-2.27) ^b	8.969	0.011
Neutrophil count/lymphocyte count ratio (NLR)	2.10 (1.56-2.92)°	1.90 (1.49-4.65)	1.25 (1.0-2.14) ^a	10.173	0.006
Eosinophil count (x10 ⁹ /l)	0.48 (0.36-0.62)	0.62 (0.50-0.87) ^a	0.08 (0.07-0.18) ^b	34.116	0.000
Platelet count $(x10^{9}/l)$	228 (190-265)	243 (214-170)	243 (221.5-283.5)	2.343	0.310
Red blood cell count $(x10^{12}/l)$	4.64 (4.36-5.1)	4.70 (4.42-5.06) ^a	5.39 (5.12-5.92) ^b	15.286	0.000
Hemoglobin (g/l)	138.5 (129.75-152)	132 (127-141.5) ^a	155 (144.25-159) ^b	15.188	0.001
Erythrocyte sedimentation rate (mm/H)	17 (11-22)	28(25.8-42.5)	14.5 (10.25-15.75)	18.872	0.000
CRP (mg/l)	3.65 (0.51-14.4)°	0.51 (0.49-4.46)	0.56 (0.52-3.10)	7.810	0.020
IL-6 (ng/l)	-	7.05 (2.16-10.24)	2.15 (1.76-5.66)	5.541	0.019
PCT (ng/ml)	-	-	0.04 (0.04-0.04)	11.593	-
PT (S)	11.5 (11-11.8) ^c	10.60 (10.05-11.10)	9.85 (9.35-10.35) ^b	33.599	0.000
D-dimer (ng/ml)	0.32 (0.26-0.47) ^c	0.26 (0.20-0.34)	0.22 (0.18-0.25) ^b	22.921	0.000
INR	1.03 (0.97-1.05)	0.95 (0.90-0.99)	0.86 (0.84-0.93)	27.578	0.000
pH	7.43 (7.40-7.46)	-	7.38 (7.38-7.40)	19.276	0.000
PaO_2 (mmHg)	88.75 (76.23-101.25)	-	103 (99-108.75)	10.175	0.001
Lactic acid (mmol/l)	1.1 (0.95-1.28)	-	0.55 (0.4-0.7)	13.931	0.000
ALB (g/l)	39.2 (36.3-42.1)°	42.4 (41.25-58.65)	43.95 (41.15-46.95) ^b	21.489	0.000
ALT (U/l)	23 (14-34)	16 (12-22.5)	24.5 (16.25-34)	6.054	0.048
AST (U/l)	24 (19-30)	22 (17-23.9)	24.5 (16.25-34)	1.675	0.443
ALP (U/l)	70 (58.5-85.5)	78 (57-139)	69 (50.75-79.75)	1.618	0.445
GGT (U/l)	19 (12-37)	19 (13-33.5)	33.5 (18.25-38.50)	2.778	0.249
TBIL (μ mol/l)	15.9 (11.3-23.9)	14.4 (6.3-17.1)	14.90 (10.7-19.6)	4.214	0.122
C3	0.83 (0.73-0.98)	0.89 (0.78-1.07)	0.86 (0.71-0.99)	2.133	0.334
C4	0.23 (0.18-0.33)	0.30 (0.23-0.36)	0.30 (0.24-0.36)	11.557	0.003
IgA (mg/l)	1.96 (1.44-2.80)	2.31 (1.59-3.15)	2.09 (1.39-2.34)	2.096	0.351
IgM (mg/l)	1.02 (0.77-1.34)	1.28 (1.05-2.00)	0.98 (0.79-1.18)	5.709	0.058
IgG (mg/l)	12.20 (10.35-13.45)	12.25 (10.66-13.65)	11.90 (8.99-12.95)	2.154	0.341

^aSignificant difference Omicron strain group vs. Delta strain group; ^bsignificant difference Omicron strain group vs. original strain group; ^csignificant difference Delta strain group vs. original strain group. CRP, C-reactive protein; PCT, procalcitonin; PT, prothrombin time; INR, international normalized ratio; ALB, albumin; ALT, alanine transaminase; AST, aspartate transferase; ALP, alkaline phosphatase; GGT, gamma-glutamyl transferase; TBIL, total bilirubin; Ig, immunoglobulin.

Table III. Findings of lung	g computed tomog	raphy in the SA	RS-CoV-2 wild strain.	. Delta strain and O	micron strain groups.

Computed tomography finding	Wild strain (n=47)	Delta strain group (n=18)	Omicron strain group (n=20)	χ^2	P-value
Patchy shadows	39 (82.98)	10 (55.56)	3 (15)	124.75	0.000
Ground-glass opacities	29 (61.70)	9 (50)	2 (10)	102.17	0.000
Bronchial inflation sign	22 (46.81)	0	0	-	-
Halo sign	5 (10.64)	0	0	-	-
Consolidation shadows	12 (25.53)	2 (11.11)	1 (5)	139.25	0.000
Peripheral lesions	30 (63.83)	3 (16.67)	3 (15)	97.11	0.000

affect the upper respiratory tract, fewer complications and an improved prognosis compared with patients in the wild type

and Delta strain groups, but the length of hospital stay was not significantly shorter.

Table IV. The demographic			

Characteristic	Vaccination group (n=5)	Unvaccinated group (n=80)	χ^2	P-value
Age (years)	10 (8.5-35.5)	36 (30.0-48.0)	_	0.028
Sex (male)	3 (60.0)	50(63.3)	4.000	0.261
BMI (kg/m^2)	18.79 (16.17-20.70)	22.85 (20.35-25.64)	-	0.002
Nucleic acid-Negative conversion time (days)	16 (16-19.5)	23 (17-29)	-	0.124
Underlying disease				
Hypertension	0	10 (12.50)	_	-
Malignant Tumors	0	1 (1.25)	_	-
Diabetes	0	5 (6.25)	_	-
Chronic liver disease	0	11 (13.75)	-	-
Respiratory disease	0	4 (5.00)	-	-
Clinical manifestation				
Fever	2 (40.00)	56 (70.00)	1.954	0.321
Dry cough	2 (40.00)	22 (27.50)	0.363	0.618
Sore throat	0	23 (28.75)	-	-
Weakness	1 (20.00)	25 (31.25)	0.178	1.000
Expectoration	1 (20.00)	28 (35.00)		
Diarrhea	0	11 (13.75)	_	-
Myalgia	0	7 (8.75)	_	_
Rhinorrhea	0	14 (17.50)	_	-
Nasal congestion	0	16 (20.00)	-	-
Laboratory examination				
White blood cell count $(x10^{9}/l)$	6.22 (5.70-7.64)	5.79 (4.42-6.60)	_	0.282
Neutrophil count ($x10^{9}/l$)	3.35 (3.00-4.16)	3.37 (2.42-4.30)		0.722
Lymphocyte count $(x10^{9}/l)$	1.74 (1.41-2.34)	1.56 (1.13-1.97)	_	0.421
Neutrophil count/lymphocyte count ratio	1.79 (1.39-3.67)	1.80 (1.30-3.29)	-	0.421
Eosinophil count ($x10^{9}/1$)	0.62 (0.37-1.04)	0.37 (0.15-0.57)	-	0.026
Platelet count $(x10^{9}/l)$	270.00 (240.00-278.50)	236.00 (193.75-263.25)	-	0.020
Red blood cell count $(x10^{12}/l)$	4.70 (4.48-5.12)			0.831
Hemoglobin (g/l)	4.70 (4.48-3.12) 129.00 (126.00-142.50)	4.78 (4.42-5.39)	-	0.831
	, , , , , , , , , , , , , , , , , , , ,	143.00 (130.00-155.25)	-	
Erythrocyte sedimentation rate (mm/H)	27.00 (12.00-44.50)	16.00 (12.00-26.80)	-	0.193
CRP (mg/l)	0.49 (0.48-9.12)	2.25 (0.51-6.14)	-	0.070
IL-6 (ng/l)	8.21 (2.45-8.21)	2.61 (1.95-6.95)	-	0.129
PCT (ng/ml)	0.04 (0.04-0.04)	0.04 (0.04-0.05)	-	1.000
PT (S)	10.90 (10.60-11.10)	10.90 (10.05-11.60)	-	0.488
D-dimer (ng/ml)	0.23 (0.20-0.36)	0.28 (0.22-0.39)	-	0.287
INR	0.97 (0.95-0.99)	0.97 (0.89-1.04)	-	0.425
рН	-	7.40 (7.38-7.44)	-	-
PaO_2 (mmHg)	-	97.50 (83.63-107.00)	-	-
Lactic acid (mmol/l)	-	0.70 (0.50-1.05)	-	-
ALB (g/l)	42.90 (40.00-57.60)	41.30 (38.20-44.30)		0.140
ALT (U/l)	12.00 (10.50-19.50)	22.00 (15.00-31.00)		0.176
AST (U/l)	22.00 (20.00-26.00)	22.00 (17.50-30.00)		0.807
ALP (U/l)	186.00 (74.00-307.00)	69.00 (55.25-82.50)		0.208
GGT (U/l)	13.00 (12.00-53.50)	21.00 (14.00-37.00)		0.923
TBIL (μ mol/l)	7.20 (5.34-14.95)	15.50 (9.90-21.80)		0.088
C3	0.24 (0.19-0.24)	0.85 (0.74-0.99)	-	0.914
C4	0.91 (0.74-0.91)	0.24 (0.19-0.35)	-	0.952
IgA (mg/l)	1.80 (1.48-1.80)	2.14 (1.51-2.84)	-	0.380
IgM (mg/l)	1.43 (1.05-1.43)	1.11 (0.81-1.36)	-	0.083
IgG (mg/l)	10.80 (8.80-10.80)	12.20 (10.53-13.50)	-	0.290

Table IV.	Continued.
-----------	------------

Characteristic	Vaccination group (n=5)	Unvaccinated group (n=80)	χ^2	P-value
Lung computed tomography				
Patchy shadows	1 (20.00)	51 (63.75)	2.174	0.140
Ground-glass opacities	1 (20.00)	39 (48.75)	0.621	0.431
Bronchial inflation sign	0	22 (27.50)	-	-
Halo sign	0	5 (6.25)	-	-
Consolidation shadows	0	14 (17.5)	-	-
Peripheral lesions	0	35 (43.75)	-	-

CRP, C-reactive protein; PCT, procalcitonin; PT, prothrombin time; INR, international normalized ratio; ALB, albumin; ALT, alanine transaminase; AST, aspartate transferase; ALP, alkaline phosphatase; GGT, gamma-glutamyl transferase; TBIL, total bilirubin; Ig, immunoglobulin.

Recent studies have shown a reduced risk of hospitalization and death in the Omicron strain group compared with the Delta strain group; however, morbidity and mortality have significantly increased with age in the Delta and Omicron strain groups, especially in patients aged >70 years (9,10). The high mortality rate among older patients is also a primary concern during the treatment of COVID-19, which may be related to several factors, such as underlying diseases, low vaccination rate and CD8+ T-cell deterioration. The present study found that the median age of patients in the Omicron strain group was higher compared with that of patients in the Delta strain group, but patients in both groups were younger than patients in the original strain group, which indicated a decline in the age of the infected individuals while evolving. Angiotensin-converting enzyme 2 (ACE2) is the key receptor for the integration of SARS-CoV-2 into human target cells (11), the serum concentration of which is higher in men than in women. Therefore, SARS-CoV-2 is more harmful to men and is characterized by increased morbidity and mortality (12). Individuals with obesity and underlying diseases (e.g., hypertension, diabetes and chronic kidney disease) are susceptible to SARS-CoV-2 and are at a higher risk of intensive care unit (ICU) admission, especially those of Asian descent (13). Unlike reports from other countries, the length of hospital stay in the Omicron strain group was not shorter than that in the wild-type strain group, which may be due to the different discharge criteria for patients with COVID-19 in different countries and the fact that none of the patients enrolled in this study had been vaccinated against COVID-19 (14).

In the present study, fever was the most predominant clinical manifestation in the wild type and Delta strain groups, whereas dry cough was the most common symptom in the Omicron strain group. The incidence of upper respiratory symptoms such as dry cough, nasal congestion, sore throat and runny nose was higher in the Omicron strain group compared with the wild type and Delta strain groups, which agrees with the results found by Iacobucci (15). Omicron is more likely to attack the upper respiratory tract and has the potential to cause explosive transmission events. Therefore, proper wearing of face masks, frequent hand washing and maintenance of good ventilation are effective strategies to prevent the spread of the virus (16). Previous studies (17,18) have shown that the Omicron strain causes significantly lower incidence of pulmonary infection and less severe symptoms than the Delta strain; one explanation is that the Omicron strain frequently colonizes the nasal cavity, rather than the lung. Previous animal experiments reveal (19) that hACE2 mice infected with the Omicron strain have significantly reduced lung lesions and pathological changes compared with those infected with other SARS-CoV-2 variants. A previous study (20) found that the incidence of hyposmia is significantly reduced in the Omicron strain group compared with that in the other variant groups and the incidence of anosmia in those who received booster vaccinations when infected with the Omicron strain decreased to 16.7%, while that of sore throat increased to 70.5%. Due to the relatively small sample size, conjunctivitis or a reduced sense of taste and smell was not observed in the present study.

In the present study, the lymphocyte and eosinophil counts in the Omicron strain group were higher than those in the wild type and Delta strain groups and the differences were significant but still within the normal range. This finding was consistent with the severity of illness in the patients in the present study. An elevated lymphocyte count is commonly observed in patients with viral infections; however, the lymphocyte count decreases in patients with SARS and SARS-CoV-2 infections (21). The lymphocyte count in COVID-19 patients is correlated with the severity of the disease, such that as the disease worsens, the lymphocyte count decreases. A greater decrease in lymphocyte count indicates a more severe lung injury (22). This phenomenon may be related to the fact that during SARS-CoV-2 infection, to avoid being recognized and cleared by the human immune system, the anti-inflammatory response is increased, lymphocytes are negatively regulated, lymphocyte function is inhibited and lymphocyte apoptosis is increased, thus resulting in a decrease in lymphocyte count (23). The early stage of SARS-CoV-2 infection is characterized by a decrease in white blood cell and lymphocyte counts, with varying degrees of elevated CRP levels and erythrocyte sedimentation rates (24). Previous studies have reported that elevated white blood cell count, neutrophil count, IL-6 level and procalcitonin level are independent predictors of disease severity and ICU admission (25,26). Close monitoring of inflammatory indicators is important for assessing the disease severity and prognosis. Significantly elevated levels of D-dimer and fibrin degradation products are valid predictors of mortality in patients with severe COVID-19 and elevated D-dimer levels in patients with COVID-19 are associated with local pulmonary thrombosis, an immunostatic hemostasis response that limits further transmission of SARS-CoV-2 (25,27).

In the present study, no significant differences were found in the complement C3, immunoglobulin (Ig) A, IgG and IgM levels among the three groups; however, significant differences were found in the complement C4 levels between the wild-type strain group and the Delta strain and Omicron strain groups, but all the levels were within the normal range. Lin et al (28) report that an elevated complement C3 level is a valid predictor of delayed discharge in COVID-19 patients. A previous study suggests that low complement C3 levels are associated with a higher risk of clinical deterioration in hospitalized patients with COVID-19 (29). A previous meta-analysis showed that decreased serum C3 and C4 levels suggest excessive complement activation and depletion and are significantly associated with increased disease severity and mortality in patients with COVID-19 (30). Complement activation is the pathophysiological basis of several lung diseases and C3 is the central component of the complement activation pathway. Infection with SARS-CoV-2 induces a virus-specific immune response in the body, producing large amounts of IgA, IgM and IgG in effector B cells, which in turn inhibits viral proliferation, spread and reinfection (31). IgA antibodies secreted by the respiratory and intestinal tracts are the primary mediators of local mucosal immunity and serum IgA regulates anti-inflammatory and proinflammatory activities. Yu et al (32) report relatively high serum IgA levels in patients with severe COVID-19. Serum IgG is the most persistent and important antibody involved in the humoral immune response and could promote phagocytosis by mononuclear macrophages, neutralize bacterial toxins and neutralize viruses. IgM has stronger bactericidal, bacteriolytic, pro-phagocytic and agglutinating effects than IgG and is a first-line defense against microbial invasion (33). Liver injury is often considered one of the typical manifestations of COVID-19 and 58-78% of COVID-19 patients present with varying degrees of liver injury (34). Liver injury is thought to result from the direct action of SARS-CoV-2, along with the inflammatory response, drug cytotoxicity and ischemia-reperfusion injury. Elevated AST, GGT and ALP levels and decreased ALB levels are indicators of poor prognosis in patients with COVID-19 (35,36).

The present study had a few limitations. First, it was conducted at a single center and the number of patients was relatively small; hence, the results should be verified by a multicenter study with a larger sample size and the conclusions should be interpreted with caution. Second, all patients enrolled in the study were treated with traditional Chinese medicine decoction (28), but failed to further analyze the effect of Chinese medicine decoction on hospitalization outcomes.

In conclusion, the patients in the Omicron strain group presented with mild symptoms that were mainly associated with the upper respiratory tract and had good prognosis due to their young age and fewer comorbidities; however, the nucleic acid-negative conversion time was not found to be significantly shortened.

Acknowledgements

Not applicable.

Funding

The present study was supported by the Major Health Research Project of Fujian Province (grant no. 2021ZD01001), the Scientific and Technological Development of Project Central Government shall guide local (grant no. 2021L3018), the Young and Middle-aged Talents Training Project of the Fujian Provincial Health Commission (grant no. 2020GGA076) and the Science and Technology Innovation Joint Project of Fujian Province (grant no. 2019Y9048).

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

XYu, YoZ, XYe, ZS and XZ designed the present study. HZ and WC performed analyses. YiZ, ZW, JX and KZ provided materials and obtained data. HZ, WC and XYu wrote the manuscript. XYu, YoZ, XYe, ZS and XZ critically reviewed and revised the manuscript. All authors read and approved the final manuscript. XYu and ZS confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of the Fujian Medical University Affiliated Quanzhou First Hospital (approval number Quanyilun 2020 No. 124). All participants including the guardians of juveniles provided written informed consent.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

- 1. Bigdelou B, Sepand MR, Najafikhoshnoo S, Negrete JAT, Sharaf M, Ho JQ, Sullivan I, Chauhan P, Etter M, Shekarian T, *et al*: COVID-19 and preexisting comorbidities: Risks, synergies, and clinical outcomes. Front Immunol 13: 890517, 2022.
- WHO: Tracking SARS-CoV-2 variants [EB/OL]. https:// www.who.int/en/activities/tracking-SARS-CoV-2-variants/. Accessed December 9, 2021.
- 3. Yadav PD, Kumar G, Mukherjee A, Nyayanit DA, Shete AM, Sahay RR, Kumar A, Majumdar T, Patil S, Pandit P, *et al*: Delta variant SARS-CoV-2 infections in pediatric cases during the second wave in India. J Microbiol Immunol Infect 2: S1684-S1182, 2022.
- 4. Pal R and Yadav U: Resurgence of COVID-19 in India: Time for introspection. Postgrad Med J 98: e86-e87, 2022.

- 5. Calistri P, Amato L, Puglia I, Cito F, Di Giuseppe A, Danzetta ML, Morelli D, Di Domenico M, Caporale M, Scialabba S, *et al*: Infection sustained by lineage B.1.1.7 of SARS-CoV-2 is characterised by longer persistence and higher viral RNA loads in nasopharyngeal swabs. Int J Infect Dis 105: 753-755, 2021.
- 6. Jansen L, Tegomoh B, Lange K, Showalter K, Figliomeni J, Abdalhamid B, Iwen PC, Fauver J, Buss B and Donahue M: Investigation of a SARS-CoV-2 B.1.1.529 (Omicron) variant cluster-nebraska, November-December 2021. MMWR Morb Mortal Wkly Rep 70: 1782-1784, 2021.
- 7. Ulloa AC, Buchan SA, Daneman N and Brown KA: Estimates of SARS-CoV-2 Omicron variant severity in Ontario, Canada. Jama 327: 1286-1288, 2022
- 8. National Health and Wellness Commission of the People's Republic of China. Treatment protocol for novel coronavirus pneumonia (trial version, eighth edition, revised): 81-88, 2020. Accessed August 18, 2020.
- 9. Nyberg T, Ferguson NM, Nash SG, Webster HH, Flaxman S, Andrews N, Hinsley W, Bernal JL, Kall M, Bhatt S, et al: Comparative analysis of the risks of hospitalisation and death associated with SARS-CoV-2 Omicron (B.1.1.529) and delta (B.1.617.2) variants in England: A cohort study. Lancet 399: 1303-1312, 2022.
- 10. Smith DJ, Hakim AJ, Leung GM, Xu W, Schluter WW, Novak RT, Marston B and Hersh BS: COVID-19 mortality and vaccine coverage-Hong Kong special administrative region, China, January 6, 2022-March 21, 2022. MMWR Morb Mortal Wkly Rep 71: 545-548, 2022.
- 11. Bechmann N, Barthel A, Schedl A, Herzig S, Varga Z, Gebhard C, Mayr M, Hantel C, Beuschlein F, Wolfrum C, *et al*: Sexual dimorphism in COVID-19: Potential clinical and public health implications. Lancet Diabetes Endorincol 10: 221-230, 2022
- 12. Sama IE, Ravera A, Santema BT, van Goor H, Ter Maaten JM, Cleland JGF, Rienstra M, Friedrich AW, Samani NJ, Ng LL, et al: Circulating plasma concentrations of angiotensin-converting enzyme 2 in men and women with heart failure and effects of renin-angiotensin-aldosterone inhibitors. Eur Heart J 41: 1810-1817, 2020.
- 13. Wan YI, Apea VJ, Dhairyawan R, Puthucheary ZA, Pearse RM, Orkin CM and Prowle JR: Ethnic disparities in hospitalisation and hospital-outcomes during the second wave of COVID-19 infection in east London. Sci Rep 12: 3721, 2022.
- 14. Maslo C, Friedland R, Toubkin M, Laubscher A, Akaloo T and Kama B: Characteristics and outcomes of hospitalized patients in South Africa during the COVID-19 omicron wave compared with previous waves. JAMA 327: 583-584, 2022.
- 15. Iacobucci G: Covid-19: Runny nose, headache, and fatigue are commonest symptoms of omicron, early data show. BMJ 375: n3103, 2021.
- 16. Kupferschmidt K and Vogel G: Omicron threat remains fuzzy as cases explode. Science 375: 9-10, 2022.
- 17. Graham F: Daily briefing: Omicron struggles to infect the lungs. Nature 6: 1038, 2022.
- Cowper A: Omicron: Who needs action when you've got plan B? 18. BMJ 376: 015, 2022
- 19. Halfmann PJ, Iida S, Iwatsuki-Horimoto K, Maemura T, Kiso M, Scheaffer SM, Darling TL, Joshi A, Loeber S, Singh G, et al: SARS-CoV-2 Omicron virus causes attenuated disease in mice and hamsters. Nature 603: 687-92, 2022.
- 20. Menni C, Valdes AM, Polidori L, Antonelli M, Penamakuri S, Nogal A, Louca P, May A, Figueiredo JC, Hu C, et al: Symptom prevalence, duration, and risk of hospital admission in individuals infected with SARS-CoV-2 during periods of Omicron and delta variant dominance: A prospective observational study from the ZOE COVID study. Lancet 399: 1618-1624, 2022.
- 21. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, et al: Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 323: 1061-1069, 2020.

- 22. Wang F, Hou H, Yao Y, Wu S, Huang M, Ran X, Zhou H, Liu Z and Sun Z: Systemically comparing host immunity between survived and deceased COVID-19 patients. Cell Mol Immunol 17: 875-877, 2020.
- 23. Refaat L, Abdellateif MS, Bayoumi A, Khafagy M, Kandeel EZ and Nooh HA: Detection of abnormal lymphocytes in the peripheral blood of COVID-19 cancer patients: Diagnostic and prognostic possibility. Hematology 27: 745-756, 2022.
- 24. Li R, Tian J, Yang F, Lv L, Yu J, Sun G, Ma Y, Yang X and Ding J: Clinical characteristics of 225 patients with COVID-19 in a tertiary hospital near Wuhan, China. J Clin Virol 127: 104363, 2020.
- 25. Milenkovic M, Hadzibegovic A, Kovac M, Jovanovic B, Stanisavljevic J, Djikic M, Sijan D, Ladjevic N, Palibrk I, Djukanovic M, et al: D-dimer, CRP, PCT, and IL-6 levels at admission to ICU can predict in-hospital mortality in patients with COVID-19 pneumonia. Oxid Med Cell Longev 2022: 8997709, 2022
- 26. Fang S, Wang H, Lu L, Jia Y and Xia Z: Decreased complement C3 levels are associated with poor prognosis in patients with COVID-19: A retrospective cohort study. Int İmmunopharmacol 89: 107070, 2020.
- 27. Tang N, Li D, Wang X and Sun Z: Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemos 18: 844-847, 2020.
- 28. Lin P, Chen W, Huang H, Lin Y, Cai M, Lin D, Cai H, Su Z, Zhuang X and Yu X: Delayed discharge is associated with higher complement C3 levels and a longer nucleic acid-negative conversion time in patients with COVID-19. Sci Rep 11: 1233, 2021.
- 29. Jiang H, Chen Q, Zheng S, Guo C, Luo J, Wang H, Zheng X and Weng Z: Association of complement C3 with clinical deterioration among hospitalized patients with COVID 19. Int J Gen Med 15: 849-857, 2002.
- 30. Zinellu A and Mangoni AA: Serum complement C3 and C4 and COVID-19 severity and mortality: A systematic review and metaanalysis with meta-regression. Front Immunol 12: 696085, 2021.
- 31. Lin Y, Zhao Z, Zheng J, Liu J and Huang A: Realization of humoral immunity against SARS-CoV-2 infections. J Fundamental Research 1: 186-188, 2021.
- 32. Yu HQ, Sun BQ, Fang ZF, Zhao JC, Liu XY, Li YM, Sun XZ, Liang HF, Zhong B, Huang ZF, et al: Distinct features of SARS-CoV-2-specific IgA response in COVID-19 patients. Eur Respir J 56: 2001526, 2020.
- 33. Zhou C, Bu G, Sun Y, Ren C, Qu M, Gao Y, Zhu Y, Wang L, Sun L and Liu Y: Evaluation of serum IgM and IgG antibodies in COVID-19 patients by enzyme linked immunosorbent assay. J Med Virol 93: 2857-2866, 2021.
- 34. Xu L, Liu J, Lu M, Yang D and Zheng X: Liver injury during highly pathogenic human coronavirus infections. Liver Int 40: 998-1004, 2020.
- 35. Diaz-Louzao C, Barrera-Lopez L, Lopez-Rodriguez M, Casar C, Vazquez-Agra N, Pernas-Pardavila H, Marques-Afonso A, Vidal-Vazquez M, Montoya JG, Andrade AH, et al: Longitudinal relationship of liver injury with inflammation biomarkers in COVID-19 hospitalized patients using a joint modeling approach. Sci Rep 12: 5547, 2022
- 36. Lui VC, Hui KP, Babu RO, Yue H, Chung PH, Tam PK, Chan MCW and Wong KKY: Human liver organoid derived intra-hepatic bile duct cells support SARS-CoV-2 infection and replication. Sci Rep 12: 5375, 2022.



This work is licensed under a Creative Commons International (CC BY-NC-ND 4.0) License.