

# Decreased eosinophil counts and elevated lactate dehydrogenase predict severe COVID-19 in patients with underlying chronic airway diseases

Dian Chen,<sup>1,2</sup> Shuchen Zhang,<sup>3</sup> Yuchen Feng,<sup>1,2</sup> Wenliang Wu,<sup>1,2</sup> Chenli Chang,<sup>1,2</sup> Shengchong Chen,<sup>1,2</sup> Guohua Zhen <sup>(1,2</sup> Lingling Yi<sup>1,2</sup>

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<sup>1</sup>Department of Internal Medicine, Huazhong University of Science and Technology, Wuhan, China <sup>2</sup>Key Laboratory of Respiratory Diseases, National Health Commission of People's Republic of China, Wuhan, China <sup>3</sup>Department of Allergy,

Huazhong University of Science and Technology, Wuhan, China

### Correspondence to

Dr Lingling Yi, Department of Internal Medicine, Huazhong University of Science and Technology, Wuhan 430030, China;

yilingling20061281@163.com

GZ and LY contributed equally.

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### ABSTRACT

**Background** Several predictors of COVID-19 severity have been reported. However, chronic airway inflammation characterised by accumulated lymphocytes or eosinophils may affect the pathogenesis of COVID-19. **Methods** In this retrospective cohort study, we reviewed the medical records of all patients with

laboratory-confirmed COVID-19 with chronic bronchitis, chronic obstructive pulmonary disease (COPD) and asthma admitted to the Sino-French New City Branch of Tongji Hospital, a large regional hospital in Wuhan, China, from 26 January to 3 April. The Tongji Hospital Ethics Committee approved this study.

Results There were 59 patients with chronic bronchitis, COPD and asthma. When compared with non-severe patients, severe patients were more likely to have decreased lymphocyte counts (0.6×10<sup>9</sup>/L vs 1.1×10<sup>9</sup>/L, p<0.001), eosinopaenia (<0.02×10<sup>9</sup>/L; 73% vs 24%, p<0.001), increased lactate dehydrogenase (LDH) (471.0 U/L vs 230.0 U/L, p<0.001) and elevated interleukin 6 level (47.4 pg/mL vs 5.7 pg/mL, p=0.002) on admission. Eosinopaenia and elevated LDH were significantly associated with disease severity in both univariate and multivariate regression models including the above variables. Moreover, eosinophil count and LDH level tended to return to normal range over time in both groups after treatment and severe patients recovered slower than non-severe patients, especially in eosinophil count.

**Conclusions** Eosinopaenia and elevated LDH are potential predictors of disease severity in patients with COVID-19 with underlying chronic airway diseases. In addition, they could indicate disease progression and treatment effectiveness.

### BACKGROUND

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### SARS-CoV-2 was first identified after sequencing relevant clinical samples in a bunch of unknown viral pneumonia cases in December 2019 in Wuhan, Hubei Province, China. COVID-19, caused by SARS-CoV-2, was subsequently declared a pandemic by the WHO due to its aggressive spread on a large scale in many countries, leading to thousands of confirmed cases worldwide every day. As of 15 November 2020, 53.7 million confirmed cases of COVID-19 and 1.3 million deaths have been reported worldwide, demanding an urgent need for early identification of severe cases.<sup>1</sup> Clinical evidence of SARS-CoV-2 has suggested several transmission routes between humans, with

respiratory aerosol droplets undoubtedly being the main source of infection. SARS-CoV-2 is able to attack the respiratory system by binding to the cell entry receptors ACE2 on airway epithelial cells and results in pneumonia and respiratory failure in critically ill patients.

Chronic bronchitis, chronic obstructive pulmonary disease (COPD) and asthma are common respiratory diseases with chronic airway inflammation.<sup>2-4</sup> Eosinophils, neutrophils and macrophages in innate immune response significantly increase in the airway and lungs during the initial phase of inflammation. Lymphocytopaenia has been reported in severe patients infected with SARS-CoV-2.5 Circulating eosinophil counts have also been reported to be decreased in patients with COVID-19 and associated with severity of the disease.<sup>6</sup> Therefore, patients with underlying COPD, asthma and chronic bronchitis may have different inflammatory states after SARS-CoV-2 infection compared with patients without chronic airway inflammation.

In this retrospective cohort study, we reviewed the medical records of 59 patients with laboratoryconfirmed COVID-19 with underlying chronic airway inflammation and compared the demographic, clinical and radiological characteristics as well as laboratory results between severe and nonsevere patients in this cohort. Potential predictors of disease severity were identified in the abnormal laboratory findings using univariate and multivariate regression models.

### **METHODS**

### Study population and data collection

The subjects of this study were adults with COVID-19 and underlying chronic respiratory diseases (admission date from 26 January to 3 April 2020) at the Sino-French New City Branch of Tongji Hospital. Severe and non-severe patients were included in the case and control groups, respectively. COVID-19 was diagnosed according to WHO interim guideline.<sup>7</sup> Patients with chronic respiratory diseases were diagnosed according to a previous diagnosis. All patients were confirmed by positive findings in reverse-transcriptase PCR assay of SARS-CoV-2 RNA in throat swab specimens. The study was conducted on 15 June.Demographic information, clinical characteristics (including medical history, symptoms, comorbidities, smoking history and allergic history) and radiological results

## **Original research**

of each patient were obtained from the electronic medical record system of the Sino-French New City Branch of Tongji Hospital and analysed by three independent researchers. Severity of COVID-19 was staged according to the guidelines for diagnosis and treatment of COVID-19 published by the Chinese National Health Committee (version 5–7).

### Criteria for severity of COVID-19

Severe COVID-19 was diagnosed when patients met one of the following criteria: (1) respiratory distress with respiratory frequency  $\geq$  30 per minute; (2) pulse oximeter oxygen saturation  $\leq$  93% at rest; and (3) oxygenation index (artery partial pressure of oxygen/inspired oxygen fraction)  $\leq$  300 mm Hg.

### Laboratory testing

Medical laboratory results, including number of leucocytes, lymphocytes, monocytes, eosinophils, basophils, platelets, alanine aminotransferase, aspartate aminotransferase, serum creatine kinase, serum lactate dehydrogenase (LDH), blood urea nitrogen, serum creatinine, cardiac troponin I, concentrations of D-dimer, C reactive protein (CRP), procalcitonin, erythrocyte sedimentation rate, serum ferritin, cytokines (interleukin (IL) 2R, IL-6, IL-8, IL-10, tumour necrosis factor (TNF)- $\alpha$ ) and immune function were collected for each patient from the electronic medical records.

### **Statistical analysis**

All data were analysed with SPSS Statistics Software (V.26). The statistics for categorical variables were summarised as frequencies and percentages and were compared using  $\chi^2$  test or Fisher's exact test between different groups where appropriate. Continuous variables were described using median (IQR) and compared using Mann-Whitney U test. To explore the risk factors associated with disease severity, univariable and multivariable logistic regression models were used to estimate the OR and 95% CI. A two-sided  $\alpha$  of less than 0.05 was considered statistically significant.

### RESULTS

### Demographics and clinical characteristics of patients with non-severe and severe COVID-19 with chronic airway diseases

A total of 1888 patients were admitted. Fifty-nine patients with underlying chronic airway inflammation, including COPD (0.95%), asthma (0.53%) and chronic bronchitis (1.64%), were confirmed to have SARS-CoV-2 infection. Of the patients, 33 were classified as non-severe and 26 were classified as severe. Although COPD was more common in patients with severe COVID-19 when compared with patients with non-severe COVID-19 (42% vs 21%), the difference was not statistically significant.

The median age of all patients was 71 years (IQR, 57–80) and more than half (54%) were over 70 years old. Majority (71%) of the patients were male (table 1). There was no significant difference in age and sex between non-severe and severe patients. Thirty-one (53%) patients had one or more comorbidities besides the three chronic airway diseases, with cardiovascular disease (46%) and endocrine system disease (15%) being the most common comorbidity. There were no significant differences in the presence of these comorbidities between patients with non-severe and severe COVID-19. Half of the patients had smoking histories or were current smokers.

The most common symptoms were fever (83%), cough (73%), fatigue (47%) and dyspnoea (42%). Dyspnoea was more

Table 1	Demographics and clinical characteristics of patients with
COVID-19	with chronic airway inflammation on admission

	All patients (N=59)	Non-severe patients (n=33)	Severe patients (n=26)	P value
Age (years)	71 (57–80)	70 (55–79)	74 (64–82)	0.184
<30	2 (3)	1 (3)	1 (4)	0.726
30–49	5 (8)	4 (12)	1 (4)	
50–69	20 (34)	11 (33)	9 (35)	
≥70	32 (54)	17 (52)	15 (58)	
Sex				
Female	17 (29)	10 (30)	7 (27)	0.776
Male	42 (71)	23 (70)	19 (73)	
Comorbidity	31 (53)	17 (52)	14 (54)	0.859
COPD	18 (30)	7 (21)	11 (42)	0.081
Chronic bronchitis	31 (53)	18 (55)	13 (50)	0.728
Asthma	10 (17)	8 (24)	2 (8)	0.093
Cardiovascular disease	27 (46)	14 (42)	13 (50)	0.562
Cerebrovascular disease	3 (5)	1 (3)	2 (8)	0.418
Digestive system disease	1 (2)	0 (0)	1 (4)	0.441
Endocrine system disease	9 (15)	4 (12)	5 (19)	0.451
Nephrosis	2 (3)	1 (3)	1 (4)	0.863
Urinary system disease	1 (2)	1 (3)	0 (0)	1.000
Viral hepatitis	1 (2)	1 (3)	0 (0)	1.000
Smokers	29 (49)	14 (42)	15 (58)	0.244
Symptoms and signs				
Fever				
<38.5°C	21 (36)	13 (39)	8 (31)	0.407
≥38.5°C	28 (47)	14 (42)	14 (54)	
Cough	43 (73)	21 (64)	22 (85)	0.072
Chest tightness	16 (27)	7 (21)	9 (35)	0.250
Haemoptysis	1 (2)	0 (0)	1 (4)	0.441
Dyspnoea	25 (42)	8 (24)	17 (65)	0.001
Fatigue	28 (47)	15 (45)	13 (50)	0.728
Myalgia	11 (19)	7 (21)	4 (15)	0.568
Nausea	2 (3)	1 (3)	1 (4)	0.863
Anorexia	2 (3)	0 (0)	2 (8)	0.190
Diarrhoea	15 (25)	9 (27)	6 (23)	0.713
Headache	2 (3)	0 (0)	2 (8)	0.190

Data are median (IQR) or n (%).

P values comparing severe with non-severe patients were calculated by  $\chi^2$  test, Fisher's exact test or Mann-Whitney U test, as appropriate.

COPD, chronic obstructive pulmonary disease.

common in severe patients compared with non-severe patients (65% vs 24%, p=0.001) (table 1).

# Laboratory findings of patients with non-severe and severe COVID-19 with chronic airway diseases

When compared with non-severe patients, severe patients were more likely to have elevated neutrophil counts  $(8.2 \times 10^{\circ}/L \text{ vs} 4.1 \times 10^{\circ}/L \text{ p} = 0.001)$ , decreased lymphocyte counts  $(0.6 \times 10^{\circ}/L \text{ vs} 1.1 \times 10^{\circ}/L \text{ p} < 0.001)$ , eosinopaenia ( $< 0.02 \times 10^{\circ}/L \text{ ; 73\%}$  vs 24%, p<0.001), elevated D-dimer ( $> 1 \mu \text{g/mL}$ ; 88% vs 42%, p=0.001), increased LDH (471.0 U/L vs 230.0 U/L, p<0.001), elevated blood urea nitrogen (> 9.5 mmol/L; 42% vs 3%, p<0.001), increased hypersensitive troponin I (> 34 pg/mL; 48% vs 7%, p=0.001), and increased inflammation markers including CRP (126.2 mg/L vs 19.9 mg/L, p<0.001), procalcitonin

( $\geq$ 0.05 ng/mL; 96% vs 43%, p<0.001) and ferritin (1264.2 mg/L vs 293.6 mg/L, p=0.004) (table 2). Of note, significant differences in the expression of inflammation-related cytokines including IL-6, IL-8 and TNF- $\alpha$  were observed between the two groups, which were dramatically increased in severe patients.

# Predictors of severity of COVID-19 in patients with chronic airway diseases

To identify the predictors of severity of COVID-19 in patients with chronic airway diseases, we analysed the association between abnormal laboratory findings and disease severity with univariate and multivariate logistic regression models. Disease severity was significantly associated with all of the above-mentioned abnormal laboratory findings in univariate logistic regression analyses. In a multivariate regression model that incorporated lymphopaenia, eosinopaenia, elevated LDH and increased IL-6, eosinophil counts <0.02×10%/L (OR per one-unit decrease, 10.115 (95% CI 2.158 to 47.414), p=0.003) and LDH level >225 U/L (OR per one-unit increase, 22.300 (95% CI 2.179 to 228.247), p=0.009) were independent risk factors for disease severity (table 3). Our data suggest that decreased eosinophil counts and increased LDH levels may help clinicians identify severe COVID-19 in patients with chronic airway diseases.

# Eosinophil counts and LDH levels tend to return to normal range over time in non-severe patients

We further analysed the eosinophil counts and LDH levels in patients with non-severe and severe COVID-19 with chronic bronchitis, COPD and asthma, respectively. We found that there was a significant difference in eosinophil counts and LDH levels between severe and non-severe patients with chronic bronchitis and COPD, but not in patients with asthma (figure 1). To observe the dynamic changes of eosinophil counts and LDH levels over time, we collected the eosinophil counts and LDH levels on the 5th, 10th, 15th, 20th, 25th and 30th days after admission. We found that eosinophil counts increased over time both in severe and non-severe patients. Meanwhile, LDH decreased over time (figure 2). Severe patients showed a slower recovery rate than non-severe patients. Of note, both eosinophil counts and LDH levels recovered more slowly in severe patients with COPD than those in severe patients with chronic bronchitis. Our data suggest that, as the disease recovers, eosinophil counts and LDH levels tend to return to normal range both in severe and nonsevere patients, indicating a good therapeutic effect in patients with chronic airway diseases in COVID-19 treatment.

We further performed multivariate analysis for mortality in patients with COVID-19 with chronic airway inflammation using the above four variables and found that eosinophil count  $<0.02 \times 10^{9}$ /L (OR per one-unit decrease, 18.000 (95% CI 1.929 to 167.986), p=0.011) was the only independent risk factor for mortality (online supplemental table 1). Moreover, Kaplan-Meier survival curves indicated that patients with COVID-19 with eosinopaenia or elevated LDH had worse survival probability (p<0.05) (online supplemental figure 1). This suggests that eosinopaenia and elevated LDH are also potential predictors of mortality in patients with COVID-19 with underlying chronic airway diseases.

## DISCUSSION

In this retrospective cohort study, we found that eosinophil counts less than  $0.02 \times 10^{9}$ /L and LDH levels greater than 225 U/L on admission were associated with severity of COVID-19 in patients with underlying chronic bronchitis, COPD and asthma.

Moreover, eosinophil counts and LDH levels tend to return to normal range in severe and non-severe patients after treatment, suggesting their roles as indicators of disease progression and treatment efficacy.

Circulating and tissue-resident eosinophils are associated with a variety of diseases, in which eosinophils participate in the pathological process and play a potent proinflammatory role, such as COPD, asthma and chronic bronchitis. In view of elevated eosinophils in patients with chronic airway inflammation, COPD, asthma and chronic bronchitis have not yet been reported as major risk factors for severity of SARS-CoV-2 infections. Zhang *et al*<sup>8</sup> reported that none had asthma or other comorbid atopic diseases and only two patients had COPD (1.4%) in a cohort of 140 hospitalised patients with COVID-19, more than half of whom (53%) had eosinopaenia on the day of hospital admission. Similarly, Du *et al*<sup>9</sup> analysed the clinical features of 85 fatal cases of COVID-19 and found that 81% of the patients had very low eosinophil counts on admission. In our cohort including 1888 patients, 31 patients had chronic bronchitis (1.64%), 18 patients had COPD (0.95%) and only 10 patients had asthma (0.53%). Meanwhile, eosinopaenia was more common in critically severe patients, suggesting that the resolution of eosinopaenia could be a possible way to improve clinical status.<sup>10</sup> In our study, lower count of eosinophils showed worse survival probability, and eosinophil counts significantly decreased in patients with severe COVID-19 with chronic bronchitis and COPD. No significant difference was observed in patients with asthma, partly due to the limited sample size. Moreover, drastically increased eosinophil counts in the airways of most patients with chronic asthma after bronchoprovocation might be another more important cause. We further explored the dynamic changes of eosinophil counts in patients with chronic airway diseases in the course of COVID-19 and found that eosinophil counts gradually increased over time and returned to normal range in both severe and nonsevere patients, which could be a possible indicator of treatment effectiveness. It remains unclear how eosinopaenia takes place in COVID-19, but the most possible reason could be due to its depletion of antiviral reaction, since Th1 (Type 1 T helper) antiviral response was inhibited in those patients with chronic airway inflammation.

LDH has long been reported to be associated with COPD, asthma and chronic bronchitis and identified as a potential marker of chronic airway inflammation.<sup>11 12</sup> Meanwhile, a large number of studies reported elevated LDH levels in COVID-19, which could be a risk factor for mortality. Zheng et al<sup>13</sup> conducted a systematic literature review and meta-analysis including four studies and found that LDH was statistically significantly higher in severe patients compared with non-severe patients. Elevated LDH in severe cases indicated diffuse lung injury and tissue damage; therefore, we hypothesised that LDH might be another predictor of chronic airway inflammation exacerbation in COVID-19. Kaplan-Meier survival analysis suggested the hazard of elevated LDH levels. Similar to eosinophil, LDH showed elevated levels in patients with severe COVID-19 with chronic bronchitis and COPD and gradually decreased over time in patients with severe and non-severe COVID-19.

Multiple research has highlighted the important roles of eosinopaenia and elevated LDH in facilitating the diagnosis and prognosis of severe COVID-19. Ma *et al*<sup>14</sup> included eosinopaenia to introduce the COVID-19-REAL (radiological image, eosinophils, age, and leukocytes) score, which had a good performance in identifying populations at higher risk of getting COVID-19. Cazzaniga *et al*<sup>15</sup> reported that absolute eosinopaenia in the binary logistic regression analyses was associated with 4-week

### Table 2 Laboratory findings of patients with COVID-19 with chronic airway inflammation on admission

Multic call count, x10 <sup>1</sup> /L         40.0-0.00 <sup>1</sup> 666 (x34-361)         5.88 (x17-1.43)         9.27 (2.86-1.23.10)         0.004           -4         13 (2)         9 (27)         4 (15)         0.004           -10         13 (2)         2 (6)         11 (42)         -           50         13 (2)         2 (6)         11 (42)         0.000         0.001           ymmophi count, x10 <sup>5</sup> /L         1.86 (3.0-1.20.5-5.20)         8.16 (3.0-1.20.00)         0.001         0.001         0.51 (2.3-6.32)         0.56 (2.3-0.76)         0.000           <1.1         21 (36)         17 (62)         4 (15)         0.001         0.01 (0.0-0.02)         0.000           <1.1         21 (36)         17 (62)         4 (15)         0.001         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01         0.01	, , ,	Normal range	All patients (N=59)	Non-severe patients (n=33)	Severe patients (n=26)	P value
number bound protein         is a room protein           4-10         33 (6)         22 (67)         11 (42)         .           10         13 (50)         22 (67)         11 (42)         .           Neutrophil count, x10 <sup>2</sup> /L         130 (50)         24 (7)         11 (42)         .           Neurophiloge count, x10 <sup>2</sup> /L         130 (53)         41 (2) (55)         0.000         0.001           c.11         21 (86)         17 (52)         41 (5)         .         0.001           c.11         21 (86)         17 (52)         41 (5)         .         0.001           c.10.02         0.01 (0.00         0.01 (0.35-6.05)         0.51 (0.30-6.06)         0.52 (0.33 -0.63)         0.891           Exinghilo count, x10 <sup>1</sup> /L         0.02 -0.20         0.02 (0.00 -0.01)         0.00 (0.00 -0.02)         0.000           c.0.02         0.02         0.00 -0.10         0.01 (0.01 -0.03)         0.01 (0.01 -0.03)         0.01           c.0.02         130 (10,01 -0.23)         0.12 (0.10 (0.01 -0.23)         0.02         1.03         1.03           t.0.02 (11,01 -0.23)         130 (11,01 -0.23)         0.14 (0.30 -00.00         1.14         1.14 </td <td>White cell count ×10<sup>9</sup>/</td> <td>4 00-10 00</td> <td>6 66 (4 54-9 61)</td> <td>5 98 (3 71-7 43)</td> <td>9 27 (5 86–12 83)</td> <td>0.002</td>	White cell count ×10 <sup>9</sup> /	4 00-10 00	6 66 (4 54-9 61)	5 98 (3 71-7 43)	9 27 (5 86–12 83)	0.002
1-0         33 (56)         22 (67)         11 (42)           -10         13 (22)         2 (6)         11 (42)           -10         13 (22)         2 (6)         11 (42)           Nutrophi (court, x10 <sup>2</sup> /L         1.00-2.00         0.001         0.001           Lymphopte court, x10 <sup>2</sup> /L         1.10-2.00         0.40 (5.3-1.44)         1.14 (9.61-1.35)         0.56 (2.2-0.76)         0.001           -11         21 (36)         17 (52)         4 (15)         0.001         0.01         0.01         0.01 (0.01-0.03)         0.01 (0.01-0	<4	1.00 10.00	13 (22)	9 (27)	4 (15)	0.002
10         12 (2)         2 (0)         11 (13)           10         13 (2)         2 (0)         11 (14)           Neutropin (court, x10 <sup>2</sup> /L         1.00–630         4.50 (2.7–7.90)         4.12 (2.86–5.42)         8.16 (2.90–12.00)         0.000           <1.1         1.00–630         4.50 (2.7–7.90)         4.12 (2.86–5.42)         8.16 (2.90–12.00)         0.000           <1.1         21 (36)         17 (4.80–13)         0.55 (0.25–0.20)         0.55 (0.25–0.20)         0.000 (0.00–0.02)         0.000           5.1         21 (36)         0.51 (0.35–0.63)         0.51 (0.35–0.63)         0.01 (0.00–0.02)         0.000           <0.02         0.02 -0.52         0.22 (0.54)         23 (5.4)         25 (7.6)         727           Basephilix x10 <sup>1/1</sup> 0.02–0.52         0.22 (0.54)         3.20 (10.01–0.03)         0.01 (0.01–0.03)         0.01 (0.01–0.03)         0.01 (0.01–0.03)         0.01 (0.01–0.03)         0.01 (0.01–0.03)         0.01 (0.01–0.03)         0.01 (0.01–0.03)         0.01 (0.01–0.03)         0.01 (0.01–0.03)         0.01 (0.01–0.03)         0.01 (0.01–0.03)         0.01 (0.01–0.03)         0.01 (0.01–0.03)         0.01 (0.01–0.03)         0.01 (0.01–0.03)         0.01 (0.01–0.02)         0.03 (0.01–0.03)         0.14 (0.01 (0.01–0.03)         0.01 (0.01–0.03)         0.01 (0.01–0.03)	4–10		33 (56)	22 (67)	11 (42 )	0.001
Nature         Nature<	>10		13 (22)	2 (6)	11 (43)	
interspectation         interspectation         interspectation         interspectation         interspectation         interspectation           interspectation         38 (64)         16 (48)         22 (85)         0.000           interspectation         38 (64)         16 (48)         22 (85)         0.000           interspectation         17 (52)         4 (15)         1           Semophile Journt, x10 <sup>0</sup> /L         0.00-0.60         0.51 (0.35-0.65)         0.52 (0.33-0.63)         0.891           Semophile Journt, x10 <sup>0</sup> /L         0.00-0.52         0.02 (0.00-0.03)         0.04 (0.02-0.11)         0.00 (0.00-0.02)         0.000           i-0.02         22 (54)         25 (75)         7 (77)         7         7           Besophile X10 <sup>0</sup> /L         0.00-100         0.01 (0.01-0.03)	Neutrophil count ×10 <sup>9</sup> /I	1 80-6 30	4 50 (2 73–7 99)	4 12 (2 36-5 42)	8 16 (3 90–12 00)	0.001
spin part account where         in for account of the account of	$\frac{1}{1000} \frac{1}{1000} \frac{1}{1000$	1 10-3 20	0.84 (0.53–1.44)	1 14 (0 80–1 73)	0.56 (0.28–0.76)	0.000
1.1         2.500         16.10         2.600         0.100           2.1.1         2.1.09         17.152         4.153         0.000         0.891           Bacophlages, x10 <sup>0</sup> L         0.10-0.60         0.51 (0.35-0.63)         0.51 (0.35-0.66)         0.52 (0.33-0.63)         0.891           Essiophlic x1, x10 <sup>0</sup> L         0.02-0.52         0.20 (000-0.00         0.04 (0.02-0.17)         0.00 (0.00-0.02)         0.00           2.02         22 (54)         52 (76)         7(27)         885         0.14 (0.01-0.03)         0.14 (0.01-0.03)         0.14 (0.01-0.03)         0.14 (0.01-0.03)         0.14 (0.01-0.03)         0.14 (0.01-0.03)         0.14 (0.01-0.03)         0.14 (0.01-0.03)         0.14 (0.01-0.03)         0.14 (0.01-0.33)         0.14 (0.01-0.33)         0.14 (0.01-0.33)         0.14 (0.01-0.33)         0.14 (0.01-0.33)         0.14 (0.01-0.33)         0.14 (0.01-0.33)         0.14 (0.01-0.33)         0.14 (0.01-0.33)         0.14 (0.01-0.33)         0.14 (0.01-0.33)         0.14 (0.01-0.33)         0.14 (0.01-0.33)         0.14 (0.01-0.33)         0.14 (0.01-0.33)         0.14 (0.01-0.33)         0.14 (0.01)         0.5 (0.31-0.32)         0.5 (0.31-0.32)         0.5 (0.01-0.32)         0.01 (0.32, (0.01-0.32)         0.01 (0.32, (0.01-0.32)         0.01 (0.32, (0.01-0.32)         0.01 (0.32, (0.01-0.32)         0.01 (0.32, (0.01-0.32)         0.01 (0.32, (0.0	<11	1.10 5.20	38 (64)	16 (48)	22 (85)	0.004
International         Internat	>11		21 (36)	17 (52)	4 (15)	0.001
Interspect No. X         DV 002-0.52         DV 002-0.020         DV 002-0.0	Macrophages ×10 <sup>9</sup> /I	0 10-0 60	0 51 (0 35-0 63)	0 51 (0 36–0 66)	0 52 (0 33-0 63)	0 891
concernment         concernment <thconcernment< th=""> <thconcernment< th=""></thconcernment<></thconcernment<>	Fosinophil count $\times 10^{9}$ /l	0.02-0.52	0.02 (0.00-0.08)	0.04 (0.02-0.11)	0.00 (0.00-0.02)	0.000
back         back <th< td=""><td></td><td>0.02 0.52</td><td>27 (46)</td><td>8 (24)</td><td>19 (73)</td><td>0.000</td></th<>		0.02 0.52	27 (46)	8 (24)	19 (73)	0.000
Basophils, x10 <sup>1</sup> /L         0.000-010         0.010 (0.01-0.03)         0.01 (0.01-0.03) <td>&gt;0.02</td> <td></td> <td>32 (54)</td> <td>25 (76)</td> <td>7 (27)</td> <td>0.000</td>	>0.02		32 (54)	25 (76)	7 (27)	0.000
Data part of the section of	$\geq 0.02$ Beconhile $\sim 10^9/I$	0.00-0.10	0.01 (0.01_0.03)	0.01 (0.01_0.03)	0.01 (0.01_0.03)	0.657
Internet optimization         ISBN 1123-11230         ISBN 1123-11230         ISBN 1123-11230         ISBN 1123-11300         ISBN 1123-113000 <thisbn 1123-11300<="" th="">         ISB</thisbn>		130.0-175.0	129.0 (112.0-139.0)	134.0 (116.5-141.0)	125 5 (100 0_134 8)	0.057
Table Cooling A 10 n.C         T2 0.00 (10.0 - 27.2.0)         T10.0 (00.0 - 27.4.0)         0.101 (00.0 - 27.4.0)         0.101 (00.0 - 27.4.0)         0.101 (00.0 - 27.4.0)         0.101 (00.0 - 27.4.0)         0.101 (00.0 - 27.4.0)         0.101 (00.0 - 27.4.0)         0.101 (00.0 - 27.4.0)         0.101 (00.0 - 27.4.0)         0.101 (00.0 - 27.4.0)         0.101 (00.0 - 27.4.0)         0.101 (00.0 - 27.4.0)         0.101 (00.0 - 27.4.0)         0.101 (00.0 - 27.4.0)         0.101 (00.0 - 27.4.0)         0.101 (00.0 - 27.4.0.0)         0.872 (00.0 - 27.4.0.0)         0.873 (00.0 - 27.2.0.0)         0.001 (00.0 - 27.4.0.0)         0.273 (00.0 - 27.2.0.0)         0.001 (00.0 - 27.4.0.0)         0.273 (00.0 - 27.2.0.0)         0.001 (00.0 - 27.2.0.0)         0.001 (00.0 - 27.2.0.0)         0.001 (00.0 - 27.2.0.0)         0.273 (00.0 - 27.2.0.0)         0.0	Platelet count v10 <sup>9</sup> /l	125.0-250.0	213.0 (1/13.0-272.0)	216.0 (166.0-270.5)	176.0 (85.5-244.5)	0.104
$\begin{array}{ c c c c c } & 10(17) & 2(0) & 0(31) & 0(3$	<12E	123.0-330.0	213.0 (143.0-272.0)	210.0 (100.0-273.3)	0 (21)	0.145
2123         30-400         534 (8)         51 (84)         16 (84)           Ferritin, gu/L         30-400         534 (60 (218.00-135.60)         281.55 (201.90-581.00)         264.20 (577.45-1889.55)         0.004           Erythrocyte sedimentation rate, mm/hour         0-15         31.50 (15.00-59.75)         40.00 (16.50-59.50)         26.00 (15.00-74.00)         0.872           D-dimer, gu/mL         ≤0.5         1/37 (0.49-2.74)         0.50 (0.40-2.17)         2.56 (1.44-8.99)         0.001           >0.5 -         1/457 (25)         12/31 (39)         2 (8)         0.001           >0.5 -         1/457 (25)         12/31 (39)         2 (8)         0.001           >1.5 -         1/57 (12)         6 (31 (19)         1 (4)         0.001           <1	<125		10 (17)	2 (0)	0 (31)	0.012
remmi, jpL         sou-doot	≥IZJ	20, 400	49 (03)	202 EE (201 00 E91 00)	10 (09) 1264 20 (E77 4E 1990 EE)	0.004
Pymoregy exeminentation rate, minimour 0 = 3 befiner, µg/mL ≤0.5 1.73 (0.49–2.74) 0.65 (0.40–2.17) 2.69 (1.44–8.99) 0.001 ≤0.5 1.73 (0.49–2.74) 0.55 (0.40–2.17) 2.69 (1.44–8.99) 0.001 >0.5–≤1 77 (12) 631 (19) 1(4) >1 (4) >1 (4) >2 (6) >2 (6) >1 (3 (3 - 47.00) 230.00 (200.00–280.00) 471.00 (291.00–68.00) 0.000 ≤225 +1 (4 (75) 19 (4) >2 (9) >2 (9) >1 (4 (2) 1 (4) >2 (9) >2 (9) >1 (4 (2) 1 (4) >2 (9) >1 (4 (2) 1 (4) >2 (9) >1 (4 (2) 1 (4) >2 (9) >1 (4 (2) 1 (4) >1 (4) >2 (9) >1 (4 (2) 1 (4) >1 (4) >2 (9) >1 (4) >3 (4) (1 (5)–14.15) 33 (4) (45–281.85) 0.001 ≤3 (4) >3 (4) (4) (5 (3) (3 -44.70) 2.10 (1,40–39.50) 2.5 (9) >4 (1 (4) (1,5)–14.15) 33 (4) (45–281.85) 0.001 ≤3 (4) >3 (4) (4) (1 (4) (1,40) 1.95–14.15) 33 (4) (45–281.85) 0.001 ≤3 (4) - (4) (5 (3) (3 -44.70) 2.10 (1,40–39.50) 2.5 (9) - (4) (1 (5) (-10–69.00) 0.205 =3 (4) (1 (	Ferriur, µg/L	30-400	534.60 (219.80-1355.63)	293.55 (201.90-581.00)	1264.20 (577.45-1889.55)	0.004
	Erythrocyte sedimentation rate, mm/nour	0-15	31.50 (15.00-59.75)	40.00 (16.50-59.50)	26.00 (15.00-74.00)	0.872
s0.514/57 (25)12/37 (33)2 (8)0.001>0.5757 (2)6/31 (19)1 (4)>136/57 (63)13/31 (42)23 (88)Creatine kinase, U/L $\leq 190$ 85.50 (47.50-196.00)65.00 (38.00-162.25)127.00 (60.50-446.50)0.065Lactate dehydrogenase, U/L135-225260.00 (223.00-471.00)23000 (200.00-280.00)471.00 (291.00-628.00)0.000 $\leq 225$ 15 (25)14 (42)1 (4)0.001>22544 (75)19 (68)25 (96)1Hypersensitive troponin I, pg/mL $\leq 34.2$ 7.60 (3.03-44.70)4.10 (1.95-14.15)33.40 (4.55-281.85)0.001 $\leq 4.2$ $\leq 34.2$ 7.60 (3.03-44.70)4.10 (1.95-14.15)33.40 (4.55-281.85)0.001 $\leq 34.2$ $\leq 40$ 14/54 (26)272 (93)13/25 (52)0.001 $\leq 4.4$ $\leq 14/54$ (26)272 (93)13/25 (52)0.001 $\leq 4.4$ 2400 (15.00-40.00)22.00 (14.00-39.50)24.50 (17.50-69.00)0.205 $\leq 41$ $\leq 40$ 52.00 (19.00-50.00)23.00 (18.50-39.50)45.50 (21.50-89.25)0.003 $\leq 40$ 32.00 (19.00-50.00)23.00 (18.50-39.50)45.50 (21.50-89.25)0.004 $< 40$ 32.00 (19.00-50.00)23.07 (11.0011.000.004 $< 40$ 36.955.10 (3.80-8.30)4.70 (3.75-5.60)7.90 (4.50-15.15)0.004 $< 9.5$ 122.077.21 (61.00-86.50)80.50 (60.00-123.25)0.136 $< 9.5$ 110 (30032.0717.00 (61.00-86.50)<	D-aimer, µg/mL	≤0.5	1.73 (0.49–2.74)	0.65 (0.40-2.17)	2.69 (1.44–8.99)	0.001
>>1         7/5 / 12 / 0         6/3 (19)         1 (4)           >1         36/57 (63)         13/31 (42)         23 (88)           Creatine kinase, U/L         ≤190         85.50 (47.50–196.00)         65.00 (30.00–62.25)         127.00 (60.50–446.50)         0.005           Lactate dehydrogenase, U/L         135–225         260.00 (223.00–471.00)         230.00 (200.00–280.00)         471.00 (291.00–628.00)         0.001           ≤225         15 (25)         14 (42)         1 (4)         0.001           >225         44 (75)         19 (58)         25 (96)         0.001           >34.2         44 (75)         19 (58)         33.40 (455–281.85)         0.001           >34.2         14/54 (26)         229 (7)         1225 (48)         0.001           ≤41         24.00 (15.00–40.00)         2.00 (14.00–39.50)         24.50 (17.50–69.00)         0.205           ≤41         45 (76)         27 (82)         18 (69)         0.203           ≤41         42.00         12.02 (14.00–39.50)         24.50 (17.50–69.00)         0.205           ≤41         42.00         13.00 (18.50–39.50)         45.50 (21.50–89.25)         0.003           ≤40         2.00 (19.00–50.00)         23.00 (18.50–39.50)         45.50 (21.50–89.25)         0.	≤0.5		14/57 (25)	12/31 (39)	2 (8)	0.001
>1365/ (6.3)1/3/1 (4/2)23 (88)Creatine kinase, U/L≤19085.50 (47.50-196.00)65.00 (38.00-162.25)127.00 (60.50-446.50)0.065Lactate dehydrogenase, U/L135-22515 (25)14 (42)1(4)0.001>22544 (75)19 (58)25 (96)Hypersensitive troponin I, pg/mL≤34.27.60 (3.03-44.70)4.10 (1.95-14.15)33.40 (4.55-281.85)0.001≤34.240/54 (74)27/29 (93)13/25 (52)0.001>34.240/54 (74)27/29 (93)13/25 (52)0.001<34.2	>0.5-≤1		//5/ (12)	6/31 (19)	1 (4)	
Creatma kinase, U/L         ≤190         85.50 (47.50-196.00)         65.00 (38.00-162.25)         127.00 (60.50-446.50)         0.005           Lactate dehydrogenase, U/L         135-225         260.00 (223.00-471.00)         230.00 (200.00-280.00)         471.00 (291.00-628.00)         0.001           ≤225         44 (75)         19 (58)         25 (96)            Hypersensitive troponin I, pg/mL         ≤34.2         7.60 (3.03-44.70)         4.10 (1.95-14.15)         33.40 (4.55-281.85)         0.001           ≤34.2         7.60 (3.03-44.70)         4.10 (1.95-14.15)         33.40 (4.55-281.85)         0.001           ≤34.2         7.60 (3.03-44.70)         4.10 (1.95-14.15)         33.40 (4.55-281.85)         0.001           ≤34.2         7.60 (3.03-44.70)         2.129 (93)         13/25 (52)         0.001           ≤34.2         5.41         2.400 (15.00-40.00)         2.20 (14.00-395.00)         2.450 (17.50-69.00)         0.205           ≤41         4.00 (15.00-40.00)         2.00 (14.00-395.00)         24.50 (17.50-69.01)         0.003           ≤40         5.20 (17.00-69.01)         2.300 (18.00-39.50)         45.50 (21.50-89.25)         0.003           ≤40         2.207         7 (21         15 (58)         0.004           ≤9.5         10 (3.00-8.30) </td <td>&gt;1</td> <td>100</td> <td>36/57 (63)</td> <td>13/31 (42)</td> <td>23 (88)</td> <td></td>	>1	100	36/57 (63)	13/31 (42)	23 (88)	
Lactate dehydrogenase, U/L135–225260.00 (223.00–471.00)230.00 (200.00–280.00)471.00 (291.00–628.00)0.000 $\leq 225$ 15 (25)14 (42)1 (4)0.01>22544 (75)19 (58)25 (96)11 $\leq 34.2$ 7.60 (3.03–44.70)4.10 (1.95–14.15)33.40 (4.55–281.85)0.001 $\leq 34.2$ 40/54 (74)27/29 (93)13/25 (52)0.001 $> 34.2$ 14/54 (26)2/29 (7)12/25 (48)0.205 $\leq 41$ 24.00 (15.00–40.00)22.00 (14.00–39.50)24.50 (17.50–69.00)0.205 $\leq 41$ 45 (76)27 (82)18 (69)0.259 $> 41$ 4.00 (15.00–50.00)23.00 (18.50–39.50)45.50 (21.50–89.25)0.003 $\leq 40$ 32.00 (19.00–50.00)23.00 (18.50–39.50)45.50 (21.50–89.25)0.003 $\leq 40$ 32.00 (19.00–50.00)23.00 (18.50–39.50)45.50 (21.50–89.25)0.004 $\leq 40$ 32.00 (19.00–50.00)23.00 (18.50–39.50)45.50 (21.50–89.25)0.004 $\leq 90$ 11 (42)1011 (42)0.004 $\leq 40$ 32.00 (19.00–50.00)23.00 (18.00–31.50)7.90 (4.50–15.15)0.001 $\leq 90$ 3.6–9.55.10 (3.80–8.30)4.70 (3.75–5.60)7.90 (4.50–15.15)0.001 $\leq 9.5$ 12 (20)1 (3)11 (42)110.001 $\leq 9.5$ 10 (17)1 (3)9 (35)0.011 $\leq 9.5$ 10 (17)1 (3)9 (35)0.011 $\leq 104$ $\leq 9-104$ 7.90 (61.00–86.50)8.00 (60.00–123.25)0.136<	Creatine kinase, U/L	≤190	85.50 (47.50–196.00)	65.00 (38.00–162.25)	127.00 (60.50–446.50)	0.065
$\leq 225$ 15 (25)14 (42)1 (4)0.001>22544 (75)19 (58)25 (96)Hypersensitive troponin l, pg/mL $\leq 34.2$ 7.60 (3.03–44.70)4.10 (1.95–14.15)33.40 (4.55–281.85)0.001 $\leq 34.2$ 40/54 (74)27/29 (93)13/25 (52)0.001 $\leq 34.2$ 14/54 (26)27/29 (7)12/25 (8)Alanine aminotransferase, U/L $\leq 41$ 24.00 (15.00–40.00)22.00 (14.00–39.50)24.50 (17.50–69.00)0.205 $\leq 41$ 14 (24)6 (18)8 (31)Aspartate aminotransferase, U/L $\leq 40$ 32.00 (19.00–50.00)23.00 (18.50–39.50)45.50 (21.50–89.25)0.003 $\leq 40$ 37 (63)26 (79)11 (42)0.004>403.6–9.55.10 (3.80–8.30)4.70 (3.75–5.60)7.90 (4.50–15.15)0.004 $\leq 9.5$ 5.10 (3.80–8.30)4.70 (3.75–5.60)7.90 (4.50–15.15)0.004 $\leq 9.5$ 12 (20)1 (3)11 (42) $\leq 9.5$ 5.10 (0.80–8.30)4.70 (0.10–86.50)80.50 (60.00–123.25)0.136 $\leq 9.5$ 10410 (7)1 (3)9 (35) $< 104$ $\leq 0.05$ 0.88 (0.44–0.31)0.04 (0.03–0.07)0.18 (0.88–1.37)0.000 $< 0.05$ $< 0.05$ 0.87 (6.33)17/30 (67)1/25 (4)0.001 $< 0.05$ $< 0.55$ 37.55 (67)13/30 (43)24.25 (96) $< 104$ $< 1.455 (4.33–124.28)$ 19.85 (1.39–34.05)126.15 (7.68–188.43)	Lactate dehydrogenase, U/L	135–225	260.00 (223.00–471.00)	230.00 (200.00–280.00)	471.00 (291.00–628.00)	0.000
>22544 (75)19 (58)25 (96)Hypersensitive troponin I, pg/mL $\leq 34.2$ 7.60 (3.03–44.70)4.10 (1.95–14.15)33.40 (4.55–281.85)0.001 $\leq 34.2$ 40/54 (74)27/29 (93)13/25 (52)0.001 $\geq 34.2$ 14/54 (26)22/9 (7)12/25 (48)12/25 (48)Alanine aminotransferase, U/L $\leq 41$ 24.00 (15.00–40.00)22.00 (14.00–39.50)24.50 (17.50–69.00)0.205 $\leq 41$ 14 (24)6 (18)8 (31)25.90 (14.00–39.50)45.60 (21.50–89.25)0.003 $\leq 40$ 32.00 (19.00–50.00)23.00 (18.50–39.50)45.50 (21.50–89.25)0.004 $> 40$ $\leq 40$ 32.00 (19.00–50.00)23.00 (18.50–39.50)11 (42)0.004 $> 9.5$ 12 (20)1 (3.35–5.60)7.90 (4.50–15.15)0.004 $\leq 9.5$ 12 (20)1 (3)11 (42)11 (42)11 (42)Creatinine, µmol/L59–1047.400 (61.00–94.00)72.00 (61.00–86.50)80.50 (60.00–123.25)0.136 $\leq 104$ 59–10410 (17)1 (3)9 (35)11 (42)11 (42)11 (42) $>104$ 10 (17)1 (3)0.040.050.05 </td <td>≤225</td> <td></td> <td>15 (25)</td> <td>14 (42)</td> <td>1 (4)</td> <td>0.001</td>	≤225		15 (25)	14 (42)	1 (4)	0.001
Hypersensitive troponin I, pg/mL $\leq 34.2$ 7.60 (3.03-44.70)4.10 (1.95-14.15)33.40 (4.55-281.85)0.001 $\leq 34.2$ 40/54 (74)27/29 (93)13/25 (52)0.001 $> 34.2$ 14/54 (26)2/29 (7)12/25 (48)12/25 (48)Alanine aminotransferase, U/L $\leq 41$ 24.00 (15.00-40.00)22.00 (14.00-39.50)24.50 (17.50-69.00)0.205 $\leq 41$ 45 (76)27 (82)18 (69)0.259>4114 (24)6 (18)8 (31)Aspartate aminotransferase, U/L $\leq 40$ 32.00 (19.00-50.00)23.00 (18.50-39.50)45.50 (21.50-89.25)0.003 $\leq 40$ 32.00 (19.00-50.00)25 (79)11 (42)0.004>4022 (37)7 (21)15 (58)0.001 $\leq 9.5$ 5.10 (3.80-8.30)4.70 (3.75-5.60)7.90 (4.50-15.15)0.004 $\leq 9.5$ 47 (80)32 (97)15 (58)0.000 $> 9.5$ 12 (20)1 (3)11 (42)0.001 $\leq 104$ 59-10474.00 (61.00-94.00)72.00 (61.00-86.50)80.50 (60.00-123.25)0.136 $\leq 104$ 59-10474.	>225		44 (75)	19 (58)	25 (96)	
$\leq 34.2$ $40/54$ (74) $27/29$ (93) $13/25$ (52) $0.001$ >34.214/54 (26) $2/29$ (7) $12/25$ (48)Alania aminotransferase, U/L $\leq 41$ $24.00$ (15.00-40.00) $22.00$ (14.00-39.00) $24.50$ (17.50-69.00) $0.259$ $\leq 41$ 45 (76) $7$ (82) $18$ (69) $0.259$ >41 $41$ (24) $6$ (18) $8$ (31) $11$ Aspartate aminotransferase, U/L $\leq 40$ $32.00$ (19.00-50.00) $23.00$ (18.50-39.50) $45.50$ (21.50-89.25) $0.003$ $\leq 40$ $22$ (37) $7$ (21) $11$ (42) $0.004$ >40 $22$ (37) $7$ (21) $15$ (58) $0.001$ $\leq 9.5$ $5.10$ (3.80-8.30) $4.70$ (3.75-5.60) $7.90$ (4.50-15.15) $0.004$ $\leq 9.5$ $47$ (80) $32$ (97) $11$ (42) $0.004$ $\leq 9.5$ $12$ (20) $1$ (3) $11$ (42) $0.001$ $\leq 9.5$ $12$ (20) $1$ (3) $11$ (42) $0.001$ $\leq 9.5$ $12$ (20) $1$ (3) $11$ (42) $0.001$ $\leq 9.5$ $12$ (20) $1$ (3) $11$ (42) $0.001$ $\leq 9.5$ $12$ (20) $1$ (3) $11$ (42) $0.001$ $\leq 9.5$ $12$ (20) $1$ (3) $11$ (42) $0.001$ $\leq 9.5$ $12$ (20) $1$ (3) $11$ (42) $0.001$ $\leq 9.5$ $12$ (20) $1$ (3) $11$ (2) $0.001$ $\leq 104$ $49$ (83) $32$ (97) $15$ (58) $0.001$ $\leq 104$ $49$ (83) $32$ (97) $17$ (65) $0.001$ <t< td=""><td>Hypersensitive troponin I, pg/mL</td><td>≤34.2</td><td>7.60 (3.03–44.70)</td><td>4.10 (1.95–14.15)</td><td>33.40 (4.55–281.85)</td><td>0.001</td></t<>	Hypersensitive troponin I, pg/mL	≤34.2	7.60 (3.03–44.70)	4.10 (1.95–14.15)	33.40 (4.55–281.85)	0.001
>34.214/54 (26)2/29 (7)12/25 (48)Alanine aminotransferase, U/L $\leq$ 4124.00 (15.00-40.00)22.00 (14.00-39.50)24.50 (17.50-69.00)0.205 $\leq$ 4145 (76)27 (82)18 (69)0.259>4114 (24)6 (18)8 (31)Aspartate aminotransferase, U/L $\leq$ 4032.00 (19.00-50.00)23.00 (18.50-39.50)45.50 (21.50-89.25)0.003 $\leq$ 4032.00 (19.00-50.00)23.00 (18.50-39.50)45.50 (21.50-89.25)0.004 $\leq$ 4032.00 (19.00-50.00)23.00 (18.50-39.50)45.50 (21.50-89.25)0.004 $\leq$ 4022 (37)7 (21)15 (58)0.004 $\leq$ 403.6-9.55.10 (3.80-8.30)4.70 (3.75-5.60)7.90 (4.50-15.15)0.004 $\leq$ 9.547 (80)32 (97)15 (58)0.001 $\leq$ 9.512 (20)1 (3)11 (42)11Creatinine, µmol/L59-10474.00 (61.00-94.00)72.00 (61.00-86.50)80.50 (60.00-123.25)0.136 $\leq$ 10449 (83)32 (97)17 (65)0.00111 $<$ 10410 (17)1 (3)9 (35)110.001 $<$ 0.050.08 (0.04-0.31)0.04 (0.03-0.07)0.18 (0.08-1.37)0.000 $<$ 0.0518/55 (33)17/30 (57)1/25 (4)0.000 $<$ 0.0530.55 (4.33-124.28)18.85 (1.93-34.05)126.15 (27.68-188.43)0.002 $<$ 314/58 (24)11/26 (24)3 (12)0.043	≤34.2		40/54 (74)	27/29 (93)	13/25 (52)	0.001
Alanine aminotransferase, U/L $\leq 41$ $24.00 (15.00-40.00)$ $22.00 (14.00-39.50)$ $24.50 (17.50-69.00)$ $0.205$ $\leq 41$ $45 (76)$ $27 (82)$ $18 (69)$ $0.259$ $> 41$ $14 (24)$ $6 (18)$ $8 (31)$ $$ Aspartate aminotransferase, U/L $\leq 40$ $32.00 (19.00-50.00)$ $23.00 (18.50-39.50)$ $45.50 (21.50-89.25)$ $0.003$ $\leq 40$ $\leq 0.001 (19.00-50.00)$ $23.00 (18.50-39.50)$ $45.50 (21.50-89.25)$ $0.003$ $\leq 40$ $\leq 0.001 (19.00-50.00)$ $23.00 (18.50-39.50)$ $45.50 (21.50-89.25)$ $0.003$ $\leq 40$ $\leq 0.01 (19.00-50.00)$ $23.00 (18.50-39.50)$ $45.50 (21.50-89.25)$ $0.003$ $\leq 40$ $\leq 0.01 (19.00-50.00)$ $23.00 (18.50-39.50)$ $45.50 (21.50-89.25)$ $0.003$ $\leq 40$ $\leq 0.01 (19.00-50.00)$ $23.00 (18.50-39.50)$ $45.50 (21.50-89.25)$ $0.003$ $\leq 40$ $\leq 0.01 (19.00-50.00)$ $23.00 (18.50-39.50)$ $45.50 (21.50-89.25)$ $0.003$ $\leq 40$ $\leq 0.97 (11.51)$ $11 (42)$ $0.004$ $\leq 9.5$ $< 7 (80)$ $32 (97)$ $11 (42)$ $0.001$ $\leq 9.5$ $>9.5 (10.0-94.00)$ $72.00 (61.00-86.50)$ $80.50 (60.00-123.25)$ $0.136$ $\leq 104$ $< 9-9.5$ $10 (17.00 (51.00-80.50)$ $80.50 (60.00-123.25)$ $0.136$ $\leq 104$ $< 0.05$ $0.08 (0.04-0.31)$ $0.04 (0.03-0.07)$ $0.18 (0.08-1.37)$ $0.000$ $< 0.05$ $< 0.05 (18.35 (43.3) (17.30 (57))$ $17.50 (57.68-188.43)$ $0.000$ $< 0.05$ $< 31.55 (4.3$	>34.2		14/54 (26)	2/29 (7)	12/25 (48)	
$\leq 41$ 45 (76)27 (82)18 (69)0.259>4114 (24)6 (18)8 (31)Aspartate aminotransferase, U/L $\leq 40$ 32.00 (19.00-50.00)23.00 (18.50-39.50)45.50 (21.50-89.25)0.003 $\leq 40$ 37 (63)26 (79)11 (42)0.004>4022 (37)7 (21)15 (58)Blood urea nitrogen, mmol/L3.6-9.55.10 (3.80-8.30)4.70 (3.75-5.60)7.90 (4.50-15.15)0.004 $\leq 9.5$ 47 (80)32 (97)15 (58)0.000 $\leq 9.5$ 12 (20)1 (3)11 (42)0.001 $\leq 104$ 59-10474.00 (61.00-94.00)72.00 (61.00-86.50)80.50 (60.00-123.25)0.136 $\leq 104$ 49 (83)32 (97)17 (65)0.001 $< 104$ 10 (17)1 (3)9 (35)0.001 $< 0.05$ 0.08 (0.04-0.31)0.04 (0.03-0.07)0.18 (0.88-1.37)0.000 $< 0.05$ 18/55 (33)17/30 (57)1/25 (4)0.000 $< 0.05$ 37/55 (67)13/30 (43)24/25 (96)0.000 $< 0.05$ 37/55 (67)13/30 (43)24/25 (96)0.000 $< 3$ $< 14/58 (24)$ 11/32 (34)3 (12)0.033	Alanine aminotransferase, U/L	≤41	24.00 (15.00–40.00)	22.00 (14.00–39.50)	24.50 (17.50–69.00)	0.205
>4114 (24)6 (18)8 (31)Aspartate aminotransferase, U/L $\leq 40$ $32.00 (19.00-50.00)$ $23.00 (18.50-39.50)$ $45.50 (21.50-89.25)$ $0.003$ $\leq 40$ $37 (63)$ $26 (79)$ $11 (42)$ $0.004$ >40 $22 (37)$ $7 (21)$ $15 (58)$ Blood urea nitrogen, mmol/L $3.6-9.5$ $5.10 (3.80-8.30)$ $4.70 (3.75-5.60)$ $7.90 (4.50-15.15)$ $0.004$ $\leq 9.5$ $47 (80)$ $32 (97)$ $15 (58)$ $0.000$ > 9.5 $12 (20)$ $1 (3)$ $11 (42)$ $1162$ Creatinine, µmol/L $59-104$ $74.00 (61.00-94.00)$ $72.00 (61.00-86.50)$ $80.50 (60.00-123.25)$ $0.136$ $\leq 104$ $49 (83)$ $32 (97)$ $17 (65)$ $0.001$ $> 104$ $10 (17)$ $1 (3)$ $9 (35)$ $0.001$ $< 0.05$ $0.08 (0.04-0.31)$ $0.04 (0.03-0.07)$ $0.18 (0.08-1.37)$ $0.000$ $< 0.05$ $37/55 (67)$ $13/30 (43)$ $24/25 (96)$ $11/42 (24)$ $3 (12)$ $0.003$ $< 3$ $< 14/58 (24)$ $11/42 (24)$ $3 (12)$ $0.043$	≤41		45 (76)	27 (82)	18 (69)	0.259
Aspartate aminotransferase, U/L $\leq 40$ $32.00 (19.00-50.00)$ $23.00 (18.50-39.50)$ $45.50 (21.50-89.25)$ $0.003$ $\leq 40$ $37 (63)$ $26 (79)$ $11 (42)$ $0.004$ > $40$ $22 (37)$ $7 (21)$ $15 (58)$ $0.004$ Blood urea nitrogen, mmol/L $3.6-9.5$ $5.10 (3.80-8.30)$ $4.70 (3.75-5.60)$ $7.90 (4.50-15.15)$ $0.004$ $\leq 9.5$ $47 (80)$ $32 (97)$ $15 (58)$ $0.000$ > $9.5$ $12 (20)$ $1 (3)$ $11 (42)$ $11 (42)$ Creatinine, µmol/L $59-104$ $74.00 (61.00-94.00)$ $72.00 (61.00-86.50)$ $80.50 (60.00-123.25)$ $0.136$ $\leq 104$ $49 (83)$ $32 (97)$ $17 (65)$ $0.001$ $>104$ $10 (17)$ $1 (3)$ $9 (35)$ $11 (42)$ Procalcitonin, ng/mL $<0.05$ $0.08 (0.04-0.31)$ $0.04 (0.03-0.07)$ $0.18 (0.08-1.37)$ $0.000$ $< 0.05$ $37/55 (67)$ $13/30 (43)$ $24/25 (96)$ $11/32 (34)$ $24/25 (96)$ High-sensitivity C reactive protein, mg/L $<1$ $30.55 (4.33-124.28)$ $9.85 (1.93-34.05)$ $126.15 (27.68-188.43)$ $0.000$ $<3$ $3 (12)$ $0.043$	>41		14 (24)	6 (18)	8 (31)	
$\leq 40$ $37 (63)$ $26 (79)$ $11 (42)$ $0.004$ >40 $22 (37)$ $7 (21)$ $15 (58)$ Blood urea nitrogen, mmol/L $3.6-9.5$ $5.10 (3.80-8.30)$ $4.70 (3.75-5.60)$ $7.90 (4.50-15.15)$ $0.004$ $\leq 9.5$ $47 (80)$ $32 (97)$ $15 (58)$ $0.000$ >9.5 $12 (20)$ $1 (3)$ $11 (42)$ $11 (42)$ Creatinine, µmol/L $59-104$ $74.00 (61.00-94.00)$ $72.00 (61.00-86.50)$ $80.50 (60.00-123.25)$ $0.136$ $\leq 104$ $49 (83)$ $32 (97)$ $17 (65)$ $0.001$ >104 $10 (17)$ $1 (3)$ $9 (35)$ $11 (42)$ Procalcitonin, ng/mL $<0.05$ $0.08 (0.04-0.31)$ $0.04 (0.03-0.07)$ $0.18 (0.08-1.37)$ $0.000$ $< 0.05$ $18/55 (33)$ $17/30 (57)$ $1/25 (4)$ $0.000$ $\geq 0.05$ $15 (57)$ $37/55 (67)$ $13/30 (43)$ $24/25 (96)$ High-sensitivity C reactive protein, mg/L $<1$ $30.55 (4.33-124.28)$ $19.85 (1.93-34.05)$ $126.15 (27.68-188.43)$ $0.000$ $< 3$ $41/58 (24)$ $11/32 (34)$ $3 (12)$ $0.043$	Aspartate aminotransferase, U/L	≤40	32.00 (19.00–50.00)	23.00 (18.50–39.50)	45.50 (21.50–89.25)	0.003
>40       22 (37)       7 (21)       15 (58)         Blood urea nitrogen, mmol/L       3.6–9.5       5.10 (3.80–8.30)       4.70 (3.75–5.60)       7.90 (4.50–15.15)       0.004         ≤9.5       47 (80)       32 (97)       15 (58)       0.000         >9.5       12 (20)       1 (3)       11 (42)         Creatinine, µmol/L       59–104       74.00 (61.00–94.00)       72.00 (61.00–86.50)       80.50 (60.00–123.25)       0.136         ≤104       49 (83)       32 (97)       17 (65)       0.001         >104       10 (17)       1 (3)       9 (35)       0.000         <0.05	≤40		37 (63)	26 (79)	11 (42)	0.004
Blood urea nitrogen, mmol/L         3.6–9.5         5.10 (3.80–8.30)         4.70 (3.75–5.60)         7.90 (4.50–15.15)         0.004           ≤9.5         47 (80)         32 (97)         15 (58)         0.000           >9.5         12 (20)         1 (3)         11 (42)           Creatinine, µmol/L         59–104         74.00 (61.00–94.00)         72.00 (61.00–86.50)         80.50 (60.00–123.25)         0.136           ≤104         49 (83)         32 (97)         17 (65)         0.001           >104         10 (17)         1 (3)         9 (35)         0.001           <0.05         0.08 (0.04–0.31)         0.04 (0.03–0.07)         0.18 (0.08–1.37)         0.000           <0.05         18/55 (33)         17/30 (57)         1/25 (4)         0.000           ≥0.05         37/55 (67)         13/30 (43)         24/25 (96)         0.000           <3         14/58 (24)         11/32 (34)         3 (12)         0.043	>40		22 (37)	7 (21)	15 (58)	
	Blood urea nitrogen, mmol/L	3.6–9.5	5.10 (3.80–8.30)	4.70 (3.75–5.60)	7.90 (4.50–15.15)	0.004
>9.512 (20)1 (3)11 (42)Creatinine, µmol/L59–10474.00 (61.00–94.00)72.00 (61.00–86.50)80.50 (60.00–123.25)0.136≤10449 (83)32 (97)17 (65)0.001>10410 (17)1 (3)9 (35)Procalcitonin, ng/mL<0.05	≤9.5		47 (80)	32 (97)	15 (58)	0.000
Creatinine, µmol/L         59–104         74.00 (61.00–94.00)         72.00 (61.00–86.50)         80.50 (60.00–123.25)         0.136           ≤104         49 (83)         32 (97)         17 (65)         0.001           >104         10 (17)         1 (3)         9 (35)         0.136           Procalcitonin, ng/mL         <0.05         0.08 (0.04–0.31)         0.04 (0.03–0.07)         0.18 (0.08–1.37)         0.000           <0.05         37/55 (67)         13/30 (43)         24/25 (96)         10000           ≥0.05         30.55 (4.33–124.28)         19.85 (1.93–34.05)         126.15 (27.68–188.43)         0.000           <3         14/58 (24)         11/32 (34)         3 (12)         0.043	>9.5		12 (20)	1 (3)	11 (42)	
≤104       49 (83)       32 (97)       17 (65)       0.001         >104       10 (17)       1 (3)       9 (35)         Procalcitonin, ng/mL       <0.05	Creatinine, µmol/L	59–104	74.00 (61.00–94.00)	72.00 (61.00-86.50)	80.50 (60.00–123.25)	0.136
>104       10 (17)       1 (3)       9 (35)         Procalcitonin, ng/mL       <0.05       0.08 (0.04–0.31)       0.04 (0.03–0.07)       0.18 (0.08–1.37)       0.000         <0.05       18/55 (33)       17/30 (57)       1/25 (4)       0.000         ≥0.05       37/55 (67)       13/30 (43)       24/25 (96)         High-sensitivity C reactive protein, mg/L       <1       30.55 (4.33–124.28)       19.85 (1.93–34.05)       126.15 (27.68–188.43)       0.000         <3       14/58 (24)       11/32 (34)       3 (12)       0.043	≤104		49 (83)	32 (97)	17 (65)	0.001
Procalcitonin, ng/mL         <0.05         0.08 (0.04–0.31)         0.04 (0.03–0.07)         0.18 (0.08–1.37)         0.000           <0.05	>104		10 (17)	1 (3)	9 (35)	
<0.05       18/55 (33)       17/30 (57)       1/25 (4)       0.000         ≥0.05       37/55 (67)       13/30 (43)       24/25 (96)         High-sensitivity C reactive protein, mg/L       <1	Procalcitonin, ng/mL	<0.05	0.08 (0.04–0.31)	0.04 (0.03–0.07)	0.18 (0.08–1.37)	0.000
≥0.05 37/55 (67) 13/30 (43) 24/25 (96) High-sensitivity C reactive protein, mg/L <1 30.55 (4.33–124.28) 19.85 (1.93–34.05) 126.15 (27.68–188.43) 0.000 <3 14/58 (24) 11/32 (34) 3 (12) 0.043	<0.05		18/55 (33)	17/30 (57)	1/25 (4)	0.000
High-sensitivity C reactive protein, mg/L       <1       30.55 (4.33–124.28)       19.85 (1.93–34.05)       126.15 (27.68–188.43)       0.000         <3	≥0.05		37/55 (67)	13/30 (43)	24/25 (96)	
<3 14/58 (24) 11/32 (34) 3 (12) 0.043	High-sensitivity C reactive protein, mg/L	<1	30.55 (4.33–124.28)	19.85 (1.93–34.05)	126.15 (27.68–188.43)	0.000
	<3		14/58 (24)	11/32 (34)	3 (12)	0.043
≥3 44/58 (76) 21/32 (66) 23 (88)	≥3		44/58 (76)	21/32 (66)	23 (88)	
IL-1β, pg/mL <5 5.00 (5.00–5.00) 5.00 (5.00–5.00) 0.245	IL-1β, pg/mL	<5	5.00 (5.00-5.00)	5.00 (5.00–5.00)	5.00 (5.00–5.00)	0.245
IL-2R, U/L 223-710 645.00 (406.50-1068.00) 499.50 (337.25-734.25) 973.00 (602.00-1919.00) 0.000	IL-2R, U/L	223–710	645.00 (406.50–1068.00)	499.50 (337.25–734.25)	973.00 (602.00–1919.00)	0.000
IL-6, pg/mL <7 11.59 (2.34–57.00) 5.68 (1.83–29.56) 47.42 (8.64–167.20) 0.002	IL-6, pg/mL	<7	11.59 (2.34–57.00)	5.68 (1.83–29.56)	47.42 (8.64–167.20)	0.002
IL-8, pg/mL <62 14.40 (7.90–47.10) 11.20 (5.40–21.05) 34.10 (12.95–81.00) 0.001	IL-8, pg/mL	<62	14.40 (7.90–47.10)	11.20 (5.40–21.05)	34.10 (12.95-81.00)	0.001
IL-10, pg/mL <9.1 5.00 (5.00–7.20) 5.00 (5.00–5.00) 6.30 (5.00–19.45) 0.001	IL-10, pg/mL	<9.1	5.00 (5.00–7.20)	5.00 (5.00–5.00)	6.30 (5.00–19.45)	0.001
TNF-α, pg/mL <8.1 9.20 (5.75–12.90) 7.65 (4.60–10.83) 11.80 (7.50–17.30) 0.021	TNF- $\alpha$ , pg/mL	<8.1	9.20 (5.75–12.90)	7.65 (4.60–10.83)	11.80 (7.50–17.30)	0.021

Data are median (IQR), n (%) or n/N (%), where N is the total number of patients with available data.

P values comparing severe with non-severe patients were calculated by  $\chi^2$  test, Fisher's exact test or Mann-Whitney U test, as appropriate.

IL, interleukin; TNF- $\alpha$ , tumour necrosis factor- $\alpha$ .

Unable NotesName<	Table 3         Predictors of severity of COVID-19 i	n patients with chronic airway diseases			
Luboacty nt/01Z36 (1.68 Ya 1.54.0)0.0044-101.087 (0.233 to 3.542)0.687<		Univariable OR (95% CI)	P value	Multivariable OR (95% CI)	P value
	Laboratory findings				
c40889 (0.221 0.35.02)0.0574-101.000 (2.088 to 38.519)0.005Neutraphi count, x1 <sup>0</sup> /1.1.307 (1.18 to 1.718)0.002Variboyte count, x1 <sup>0</sup> /1.0.010 (0.086 to 0.051)0.0051.15.444 (1.64 to 2.07.12)0.006 <td>White cell count, ×10<sup>9</sup>/L</td> <td>1.296 (1.087 to 1.546)</td> <td>0.004</td> <td>-</td> <td>-</td>	White cell count, ×10 <sup>9</sup> /L	1.296 (1.087 to 1.546)	0.004	-	-
4-101(mb>101000 (268 to 85.57)0.005Upmpbore curr, 10%0.394 (0.661 to 615)0.0051.10.204 (0.661 to 615)0.0052.11.11 (eff-0.0053.11 (eff-0.0050.115 (1.58 to 47.414)0.0010.0150.024.0028.42 (2.615 to 27.515)0.0010.115 (1.58 to 47.414)0.021	<4	0.889 (0.223 to 3.542)	0.867	_	-
>101000 (2008 (> 8519)0.050Neutophil (court, x10 <sup>1</sup> ).1.397 (1.136 to 1.718)0.0601.15.340 (1.640 to 20.712)0.065X1.11040 (0.668 to 0.515)0.030	4–10	1 (ref)	-	-	-
Nutrophonylacount, x10 <sup>1</sup> /L1397 (1.13 to 17.18)0020	>10	11.000 (2.068 to 58.519)	0.005	_	-
jymphope court, xtl0 <sup>1</sup> /L0.204 (0.08 to 0.51)0.005<1.1	Neutrophil count, ×10 <sup>9</sup> /L	1.397 (1.136 to 1.718)	0.002	_	-
1544 (1.64b to 20.712)0.006a.1.11 (ref)<	Lymphocyte count, $\times 10^{9}$ /L	0.204 (0.068 to 0.615)	0.005	_	-
11 (ref)Macophages, ×10%10.792 (0.084 to 7.486)0.839 <td>&lt;1.1</td> <td>5.844 (1.649 to 20.712)</td> <td>0.006</td> <td>_</td> <td>-</td>	<1.1	5.844 (1.649 to 20.712)	0.006	_	-
Macopplages, 10 <sup>9</sup> /L0,039Exampline Count, x10 <sup>9</sup> /L**0,031 (10°1 (3.052×10°1 (0.064))0.0190.003±0.026.452 (2.615 to 27.515)0.0011.0115 (2.158 to 47.414)0.003±0.021 (ref)Platelet count, x10 <sup>9</sup> /L0.003 (4.131*10 <sup>-16</sup> 10.1040.10 <sup>10</sup> )0.117*1256.889 (1.317 to 5.042)0.022*1256.889 (1.317 to 5.042)0.011*1251.001 (0.900 to 1.003)0.011*1251.001 (0.900 to 1.03)0.067±1251.001 (0.930 to 1.03)0.067±0.5-5-11.001 (0.930 to 1.03)0.067±0.5-51.001 (0.930 to 1.325 )0.050±0.5-51.001 (0.930 to 1.325 )0.050 </td <td>≥1.1</td> <td>1 (ref)</td> <td>-</td> <td>_</td> <td>-</td>	≥1.1	1 (ref)	-	_	-
Eosinophi count, ×10 <sup>9</sup> /L*5031×10. <sup>9</sup> (5.962×10. <sup>14</sup> to 0.064)0.0190.0020.028.482 (2.51 5r.27.515)0.00010.115 (2.158 to 47.414)0.0320.021 (ref)-1 (ref)Baxophi, x10 <sup>9</sup> /L0.036 (4.819×10 <sup>-16</sup> to 1.044x10 <sup>10</sup> )0.61121256.889 (1.31 7r.036.042)0.02121251 (ref) </td <td>Macrophages, ×10<sup>9</sup>/L</td> <td>0.792 (0.084 to 7.486)</td> <td>0.839</td> <td>_</td> <td>-</td>	Macrophages, ×10 <sup>9</sup> /L	0.792 (0.084 to 7.486)	0.839	_	-
	Eosinophil count, ×10 <sup>9</sup> /L*	5.031×10 <sup>-8</sup> (3.962×10 <sup>-14</sup> to 0.064)	0.019	-	_
±0.021 (ref)-1 (ref)-Basophik, x10 <sup>1</sup> /L0.003 (A.819×10 <sup>-16</sup> to 1.044×10 <sup>10</sup> )0.691<125	<0.02	8.482 (2.615 to 27.515)	0.000	10.115 (2.158 to 47.414)	0.003
Basophils, x10 <sup>9</sup> /L0.003 (A 819×10 <sup>-16</sup> to 10.404×10 <sup>19</sup> )0.691Platele court, x10 <sup>9</sup> /L0.990 (0.990 to 1.001)0.117<125	≥0.02	1 (ref)	-	1 (ref)	-
Platelet count, x10 <sup>9</sup> /L0.996 (0.990 to 1.001)0.117<125	Basophils, $\times 10^9$ /L	$0.003 (4.819 \times 10^{-16} \text{ to } 10.404 \times 10^{10})$	0.691	_	-
<1256.889 (1.317 to 36.042)0.022s1251 (ref)Ferritin, pg/L1.002 (1.000 to 1.003)0.011Erythrocyte sedimentation rate, mm/hour1.001 (0.980 to 1.23)0.896>.05.51 (ref)>.05.51 (ref) <td>Platelet count, ×10<sup>9</sup>/L</td> <td>0.996 (0.990 to 1.001)</td> <td>0.117</td> <td>_</td> <td>-</td>	Platelet count, ×10 <sup>9</sup> /L	0.996 (0.990 to 1.001)	0.117	_	-
\$1251 (ref)Ferritn, rgul1.000 (1.000 to 1.023)0.011Erythrocyte sedimentation rate, mm/hour1.001 (0.900 to 1.023)0.866\$0.51 (ref)\$0.5-511.000 (0.075 to 13.87)1.000\$0.5-511.000 (0.075 to 13.87)0.005 <td>&lt;125</td> <td>6.889 (1.317 to 36.042)</td> <td>0.022</td> <td>_</td> <td>-</td>	<125	6.889 (1.317 to 36.042)	0.022	_	-
Ferritin, pg/L1.002 (1.000 to 1.003)0.011Erythrooyte sedimentation rate, mm/hour1.010 (0.980 to 1.23)0.886s.0.51 (ref)<	≥125	1 (ref)	-	_	-
Erythrocyte sedimentation rate, mm/hour         1.001 (0.980 to 1.023)         0.896         -         -           D-dimer, upfmL         1.305 (0.981 to 1.736)         0.67         -         -           >6.5         1 (ef)         -         -         -           >0.5 -s1         1.000 (0.075 to 13.367 )         1.000         -         -           >1         1.001 (0.075 to 13.367 )         0.000         -         -           Creatine kinase, U/L         1.005 (0.015 to 54.954)         0.000         -         -           Lactate delytrogenase, U/L*         1.014 (1.006 to 1.022)         0.000         -         -         -           >2225         1 (ef)         -         1 (ref)         -         -         -         -           >34.2         1 (ef)         -         -         -         -         -         -           >40         0.080 (0.016 to 41.2)         0.005         -         -         -         -           >40         1.061 (1.021 to 1.069)         0.005         -         -         -         -           >40         1.062 (1.061 to 1.504)         0.007         -         -         -         -         -           >40	Ferritin, µg/L	1.002 (1.000 to 1.003)	0.011	-	-
D-dimer, pgml.         1.305 (0.981 to 1.736)         0.667         -         -           s0.5         1 (ref)         -         -         -           >0.5-s1         1.000 (0.75 to 13.367)         1.005         -         -           >1         1.0515 (0.51 to 54.954)         0.050         -         -           >1         1.0515 (0.591 to 54.954)         0.050         -         -           S225         1 (ref)         -         1 (ref)         -         -           >225         1 (ref)         0.007         2.300 (2.179 to 228.247)         0.009           Hypersensitive troponin I, pg/ml.         1.012 (0.998 to 1.027)         0.603         -         -           >34.2         1 (ref)         -         -         -         -           >40         0.600 (0.016 to 0.412)         0.003         -         -         -           >40         1.040 (1.012 to 1.059)         0.005         -         -         -           >40         1.626 (1.618 to 15.853)         0.007         -         -         -           >40         1.626 (1.016 to 1.549)         0.010         -         -         -           >400         1.626 (1.026 to 1.549)         0	Erythrocyte sedimentation rate, mm/hour	1.001 (0.980 to 1.023)	0.896	_	-
$\leq 0.5$ $  (ref)$ $   -$ >0.5-511.000 (0.075 to 13.367)1.000 $ -$ >11.06.15 (2.051 to 54.954)0.005 $ -$ Creatine kinase, U/L1.05 (0.999 to 1.101)0.990 $ -$ Lactate dehydrogenase, U/L*1.014 (1.006 to 1.022)0.000 $  \leq 225$ 1. (ref) $-$ 1. (ref) $  \geq 225$ 1.8.421 (2.23 to 152.647)0.00722.300 (2.179 to 228.247)0.009Hypersensitive troponin I, pg/mL1.012 (0.998 to 1.027)0.085 $  \leq 34.2$ 1. (ref) $    \leq 40$ 1. (ref) $    \leq 40$ 1. (ref) $    \leq 0.05$ 1. (ref) $    > 0.5$ 2.3.467 (2.769 to 198.859)0.007 $  < 0.05$ 1. (ref) $    > 0.5$ 2.3.467 (2.769 to 198.859)0.004 $  < 104$ 1.022 (1.001 to 1.044)0.010 $  < 104$ 1.021 (1.0024 (1.937 to 145.160)0.010 $  < 104$ 1.069 $    < 0.05$ 3.385 (3.742 to 263.235)0.001 $  < 0.05$ 3.385 (3.742 to 263.235)0.001 $  < 3.3$ 0.106 (0.983 to 15.400)0.053 $-$	D-dimer, µɑ/mL	1.305 (0.981 to 1.736)	0.067	-	-
$>05-=11$ 1000 (0.075 to 13.367)1.000 $ -$ >110.615 (2.051 to 54.954)0.005 $ -$ Creatine kinase, U/L10.005 (0.999 to 1.010)0.000 $  =$ Lactate delydrogenase, U/L*1.040 (1.060 to 1.022)0.000 $  \leq$ 2251 (ref) $-$ 1.(ref) $  >$ 2251 (ref) $    \leq$ 34.21 (ref) $    \leq$ 34.21 (ref) $    \leq$ 34.20.080 (0.016 to 0.12)0.005 $  \leq$ 401 (ref) $    \leq$ 401 (ref) $    \leq$ 401 (ref) $    \leq$ 401 (ref) $    \leq$ 401 (ref) $    \leq$ 401 (ref) $    \leq$ 401 (ref) $    \leq$ 401 (ref) $    \leq$ 401 (ref) $    \leq$ 401 (ref) $    \leq$ 401 (ref) $    <$ 50.51 (321 (10.10 1.0.44)0.010 $   <$ 401 (ref) $    -$ <td>≤0.5</td> <td>1 (ref)</td> <td>_</td> <td>_</td> <td>-</td>	≤0.5	1 (ref)	_	_	-
>1         10.615 (2.051 to 54.954)         0.005         -         -           Creatine kinase, U/L         1.005 (0.999 to 1.010)         0.900         -         -           Lactate dehydrogenase, U/L*         1.014 (1.006 to 1.022)         0.000         -         -           ≤225         1 (ref)         -         1 (ref)         0.007         2.300 (2.179 to 228.247)         0.009           Hypersensitive troponin I, pg/mL         1.012 (0.998 to 1.027)         0.085         -         -         -           ≤34.2         1 (ref)         -         -         -         -         -           ≤34.2         0.080 (0.016 to 0.412)         0.003         -         -         -           ≤40         1 (ref)         -         -         -         -         -           ≥40         1 (ref)         -         -         -         -         -           ≥40         1 (ref)         -         -         -         -         -           ≥40         1 (ref)         -         -         -         -         -         -           ≤40         1 (ref)         -         -         -         -         -         -         -         -	>0.5-≤1	1.000 (0.075 to 13.367)	1.000	_	_
Creatine kinace, U/L       1.005 (0.999 to 1.010)       0.090       -       -         Lactate dehydrogenase, U/L*       1.014 (1.005 to 1.022)       0.000       -       - $\leq 225$ 1 (ref)       -       1 (ref)       0.003       -       - $\leq 34.2$ 1 (ref)       -       0.003       -       -       - $\leq 34.2$ 0.080 (0.016 to 0.412)       0.005       -       -       - $\leq 44.2$ 1 (ref)       -	>1	10.615 (2.051 to 54.954)	0.005	-	-
Lactate dehydrogenase, U/L*1.014 (1.006 to 1.022)0.000≤2251 (ref)-1 (ref)-1 (ref)->22518.421 (2.223 to 152.647)0.00722.300 (2.179 to 228.247)0.007ybpersensitive troponin I, pg/mL11/20 (9.98 to 1.027)0.085≤34.21 (ref)>34.20.080 (0.016 to 0.412)0.003≤401 (ref)>405.065 (1.618 to 15.853)0.005≥9.51 (ref)≤9.51 (ref)≤9.51 (ref)≤9.51 (ref)0.010≤1041.022 (1.001 to 1.044)0.011<104	Creatine kinase, U/L	1.005 (0.999 to 1.010)	0.090	-	_
≤225         1 (ref)         -         1 (ref)         -           >225         18.421 (2.223 to 152.647)         0.007         22.300 (2.179 to 228.247)         0.009           Hypersensitive troponin I, pg/mL         1.012 (0.998 to 1.027)         0.005         -         -           ≤34.2         1 (ref)         -         -         -         -           >34.2         0.080 (0.016 to 0.412)         0.005         -         -         -           Aspartate aminotransferase, U/L         1.040 (1.012 to 1.069)         0.005         -         -         -           ≤40         1 (ref)         -         -         -         -         -         -           ≤40         1 (ref)         -	Lactate dehydrogenase, U/L*	1.014 (1.006 to 1.022)	0.000	-	-
>22518.421 (2.23 to 152.647)0.0072.300 (2.179 to 228.247)0.009Hypersensitive troponin I, pg/mL1.012 (0.998 to 1.027)0.085 $\leq$ 34.21 (ref)>34.20.080 (0.016 to 0.12)0.003 $\leq$ 401 (ref) $\leq$ 401 (ref) $\leq$ 401 (ref) $\leq$ 401 (ref) $\leq$ 9.51 (ref) $\leq$ 9.51 (ref) $\leq$ 9.523.467 (2.769 to 198.859)0.004 $\leq$ 1041 (ref) $\leq$ 1041 (ref) $<$ 0.0531.385 (1.993 to 76 464.041)0.027 $<$ 0.0531.385 (1.993 to 76 464.041)0.027 $<$ 0.0531.385 (3.742 to 263.235)0.011 $<$ 0.0531.385 (3.742 to 263.235)0.011 $<$ 0.0531.385 (3.742 to 263.235)0.011 $<$ 31 (ref)<	≤225	1 (ref)	_	1 (ref)	-
Hypersensitive troponin I, pg/mL       1.012 (0.998 to 1.027)       0.085       -       -         ≤34.2       1 (ref)       -       -       -         >34.2       0.080 (0.016 to 0.412)       0.003       -       -         Aspartate aminotransferase, U/L       1.040 (1.012 to 1.069)       0.005       -       -         >40       5.065 (1.618 to 15.853)       0.005       -       -         Slood urea nitrogen, mmol/L       1.269 (1.068 to 1.508)       0.007       -       -         >9.5       1 (ref)       -       -       -       -         >9.5       23.467 (2.769 to 198.859)       0.004       -       -       -         <104	>225	18.421 (2.223 to 152.647)	0.007	22.300 (2.179 to 228.247)	0.009
34.2       1 (ref)       -       -       -         >34.2       0.080 (0.016 to 0.412)       0.003       -       -         Aspartate aminotransferase, U/L       1.040 (1.012 to 1.069)       0.005       -       -         ≤40       1 (ref)       -       -       -       -         >40       5.065 (1.618 to 15.853)       0.005       -       -       -         >40       1 (ref)       -       -       -       -       -         >40       1.269 (1.068 to 15.853)       0.007       -       -       -         s9.5       1 (ref)       -       -       -       -       -         >9.5       23.467 (2.769 to 198.859)       0.004       -	Hypersensitive troponin I, pg/mL	1.012 (0.998 to 1.027)	0.085	-	-
>34.20.0800.016 to 0.412)0.003Aspartate aminotransferase, U/L1.0401.0400.005 $\leq 40$ 1 (ref)>405.0651.618 to 15.0810.007Blood urea nitrogen, mmol/L1.2690.007 $\leq 9.5$ 1 (ref)>9.523.4672.769 to 198.859)0.004Creatinine, µmol/L1.0221.001 to 1.044)0.041 $\leq 104$ 1 (ref)>10416.9411.933 to 76464.041)0.027 $< 0.05$ 1 (ref) $\geq 0.05$ 31.3853.742 to 263.235)0.001 $\leq 3$ 1 (ref) $\geq 0.05$ 31.38510.010 to 1.036)0.001 $\leq 3$ 1 (ref) $\geq 3.401$ 1.0231.010 to 1.036)0.001 $\leq 3$ 1 (ref) $\leq 3.411$ 1.0231.003 to 1.04010.055 $\leq 3.4514$ 1.003 to 1.04010.052 $< 7$ 1 (ref) $< 3.4214$ 1.003 to 1.04010.052	≤34.2	1 (ref)	_	_	-
Aspartate aminotransferase, U/L1.040 (1.012 to 1.069)0.005 $\leq$ 401 (ref)>405.065 (1.618 to 15.853)0.005Blood urea nitrogen, mmol/L1.269 (1.068 to 1.508)0.007 $\leq$ 9.51 (ref)>9.523.467 (2.769 to 198.859)0.004 $\leq$ 1041.022 (1.001 to 1.044)0.041 $\leq$ 1041 (ref)>10416.941 (1.977 to 145.160)0.010 $<$ 0.051 (ref) $<$ 1041.023 (1.010 to 1.036)0.001 $<$ 20.51 (ref) $<$ 31 (ref) $<$ 31 (ref) $<$ 31 (ref) $<$ 31 (ref) $<$ 71 (ref) $<$ 71 (ref) $<$ 71 (ref) $<$ 71 (	>34.2	0.080 (0.016 to 0.412)	0.003	-	-
s40         1 (ref)         -         -         -           >40         5.065 (1.618 to 15.853)         0.005         -         -           Blood urea nitrogen, mmol/L         1.269 (1.068 to 1.508)         0.007         -         -           \$9.5         1 (ref)         -         -         -         -           >9.5         23.467 (2.769 to 198.859)         0.004         -         -           Creatinine, µmol/L         1.022 (1.001 to 1.044)         0.041         -         -           \$104         1 (ref)         -         -         -         -           \$104         1 (ref)         -         -         -         -           \$20.05         1 (ref)         -         -         -         -           \$20.05         1 (ref)         -         -         -         -           \$20.05         1 (ref)         -         -         -         -           \$3         1 (ref)         -         -         -         -           \$3         1 (ref)         -         -         -         -           \$3         1 (ref)         -         -         -         -         -         -	Aspartate aminotransferase, U/L	1.040 (1.012 to 1.069)	0.005	_	-
>405.065 (1.618 to 15.853)0.005Blood urea nitrogen, mmol/L1.269 (1.068 to 1.508)0.007 $\leq 9.5$ 1 (ref)>9.523.467 (2.769 to 198.859)0.004Creatinine, µmol/L1.022 (1.001 to 1.044)0.041 $\leq 104$ 1 (ref)>10416.941 (1.977 to 145.160)0.010Procalcitonin, ng/mL390.345 (1.993 to 76.464.041)0.027<0.05	≤40	1 (ref)	_	-	-
Blod urea nitrogen, mmol/L         1.269 (1.068 to 1.508)         0.007         -         - $\leq 9.5$ 1 (ref)         -         -         -           >9.5         23.467 (2.769 to 198.859)         0.004         -         -           Creatinine, µmol/L         1.022 (1.001 to 1.044)         0.041         -         - $\leq 104$ 1 (ref)         -         -         -         -           >104         16.941 (1.977 to 145.160)         0.010         -         -         - $< 0.05$ 1 (ref)         -	>40	5.065 (1.618 to 15.853)	0.005	_	-
≤9.5       1 (ref)       -       -       -       -         >9.5       23.467 (2.769 to 198.859)       0.004       -       -         Creatinine, µmol/L       1.022 (1.001 to 1.044)       0.041       -       -         ≤104       1 (ref)       -       -       -       -         >104       16.941 (1.977 to 145.160)       0.010       -       -       -         <0.05	Blood urea nitrogen, mmol/L	1.269 (1.068 to 1.508)	0.007	_	-
>9.5         2.47 (2.769 to 198.859)         0.004         -         -           Creatinine, µmol/L         1.022 (1.001 to 1.044)         0.041         -         -           \$104         1 (ref)         -         -         -         -           \$104         16.941 (1.977 to 145.160)         0.010         -         -         -           \$0.05         303.345 (1.993 to 76464.041)         0.027         -         -         -           \$0.05         1 (ref)         -         -         -         -         -           \$0.05         31.385 (3.742 to 263.235)         0.001         -         -         -           \$104         1.023 (1.010 to 1.036)         0.001         -         -         -           \$3         1 (ref)         -         -         -         -         -           \$3         4.016 (0.983 to 16.400)         0.055         -	≤9.5	1 (ref)	-	_	-
Creatinine, µmol/L         1.022 (1.001 to 1.044)         0.041         -         -           ≤104         1 (ref)         -         -         -         -           >104         16.941 (1.977 to 145.160)         0.010         -         -           Procalcitonin, ng/mL         390.345 (1.993 to 7646.041)         0.027         -         -           <0.05	>9.5	23.467 (2.769 to 198.859)	0.004	_	-
≤104       1 (ref)       -       -       -         >104       16.941 (1.977 to 145.160)       0.010       -       -         Procalcitonin, ng/mL       390.345 (1.993 to 76 464.041)       0.027       -       -         <0.05	Creatinine, µmol/L	1.022 (1.001 to 1.044)	0.041	_	-
>104       16.941 (1.977 to 145.160)       0.010       -       -         Procalcitonin, ng/mL       390.345 (1.993 to 76 464.041)       0.027       -       -         <0.05	≤104	1 (ref)	-	_	-
Procalcitonin, ng/mL       390.345 (1.993 to 76 464.041)       0.027       -       -         <0.05	>104	16.941 (1.977 to 145.160)	0.010	_	-
<0.05	Procalcitonin, ng/mL	390.345 (1.993 to 76 464.041)	0.027	-	-
≥0.05       31.385 (3.742 to 263.235)       0.001       -       -         High-sensitivity C reactive protein, mg/L       1.023 (1.010 to 1.036)       0.001       -       -         <3	<0.05	1 (ref)	-	_	-
High-sensitivity C reactive protein, mg/L       1.023 (1.010 to 1.036)       0.001       -       -         <3	≥0.05	31.385 (3.742 to 263.235)	0.001	_	-
<3	High-sensitivity C reactive protein, mg/L	1.023 (1.010 to 1.036)	0.001	_	-
≥3       4.016 (0.983 to 16.400)       0.053       -       -         IL-2R, U/mL       1.003 (1.001 to 1.004)       0.005       -       -         IL-6, pg/mL       1.003 (1.001 to 1.004)       0.022       -       -         <7	<3	1 (ref)	-	_	-
IL-2R, U/mL       1.003 (1.001 to 1.004)       0.005       -       -         IL-6, pg/mL       1.023 (1.003 to 1.044)       0.022       -       -         <7	≥3	4.016 (0.983 to 16.400)	0.053	_	-
IL-6, pg/mL       1.023 (1.003 to 1.044)       0.022       -       -         <7	IL-2R, U/mL	1.003 (1.001 to 1.004)	0.005	_	-
<7	IL-6, pg/mL	1.023 (1.003 to 1.044)	0.022	_	-
≥7       8.000 (1.908 to 33.537)       0.004       -       -         IL-8, pg/mL       1.026 (1.002 to 1.051)       0.030       -       -         IL-10, pg/mL       1.166 (0.999 to 1.363)       0.052       -       -         TNF-α, pg/mL       1.178 (1.024 to 1.355)       0.022       -       -	<7	1 (ref)	-	-	-
IL-8, pg/mL     1.026 (1.002 to 1.051)     0.030     -     -       IL-10, pg/mL     1.166 (0.999 to 1.363)     0.052     -     -       TNF-α, pg/mL     1.178 (1.024 to 1.355)     0.022     -     -	≥7	8.000 (1.908 to 33.537)	0.004	-	-
IL-10, pg/mL     1.166 (0.999 to 1.363)     0.052     -     -       TNF-α, pg/mL     1.178 (1.024 to 1.355)     0.022     -     -	IL-8, pg/mL	1.026 (1.002 to 1.051)	0.030	-	-
TNF-α, pg/mL 1.178 (1.024 to 1.355) 0.022 – – –	IL-10, pg/mL	1.166 (0.999 to 1.363)	0.052	-	-
	TNF-α, pg/mL	1.178 (1.024 to 1.355)	0.022	-	-

\*Per one-unit increase. IL, interleukin; ref, reference; TNF- $\alpha$ , tumour necrosis factor- $\alpha$ .



**Figure 1** Clinical characteristics of eosinophil and LDH in patients with COVID-19 with chronic airway inflammation. (A) Eosinophil counts in different subgroups. Eosinophil counts were significantly decreased in patients with severe COVID-19 with chronic bronchitis and COPD. (B) LDH levels in different subgroups. LDH levels were significantly decreased in patients with severe COVID-19 with chronic bronchitis and COPD. Values for non-severe and severe patients are presented with open and closed circles, respectively. Mann-Whitney U test was used. \*P<0.05, \*\*P<0.01, \*\*\*P<0.001, \*\*\*\*P<0.0001. COPD, chronic obstructive pulmonary disease; LDH, lactate dehydrogenase.

mortality and clinical outcomes in patients with COVID-19 pneumonia.<sup>15</sup> Guan *et al*<sup>16</sup> and Feng *et al*<sup>17</sup> both proposed LDH as a significant predictor of COVID-19 mortality and adverse outcomes with the simple-tree XGBoost model, which may help identify high-risk COVID-19 cases. Eosinopaenia and elevated LDH have been identified as risk factors for severe COVID-19 cases; however, it is noteworthy that in our study they were also associated with severity of COVID-19 in patients with chronic airway diseases.

There is growing concern regarding the association between COVID-19 and pulmonary function. Previous reports have concentrated on respiratory follow-up after hospitalisation for COVID-19. Trinkmann *et al*<sup>18</sup> found that symptomatic patients

had a significantly lower forced expiratory volume in 1 s, vital capacity and transfer factor of the lung for carbon monoxide  $(T_{LCO})$  compared with asymptomatic patients. Riou *et al*<sup>19</sup> found that patients with critical disease had lower total lung capacity and  $T_{LCO}$ . However, how the pre-existing pulmonary function impairment impacted the COVID-19 outcome has not yet been fully elucidated. Currently, related literature is scarce, possibly due to limited pulmonary function testing laboratories during the COVID-19 pandemic. Morgenthau *et al*<sup>20</sup> found that mortality in patients with COVID-19 with sarcoidosis was associated with moderate or severe impairment in pulmonary function. He *et al*<sup>21</sup> reported that a longer history of COPD increased the risk of



**Figure 2** Dynamic changes of eosinophil counts and LDH levels in patients with COVID-19 with chronic airway diseases. (A–D) Eosinophil counts increased over time in non-severe and severe patients with COVID-19 with chronic bronchitis (n=31), COPD (n=18) and asthma (n=10). (E–H) LDH levels decreased over time in non-severe and severe patients with COVID-19 with chronic bronchitis (n=31), COPD (n=18) and asthma (n=10). Values for non-severe and severe patients are presented with open and closed circles, respectively. Mann-Whitney U test was used. \*P<0.05, \*\*P<0.01, \*\*\*P<0.001, \*\*\*P<0.001, compared with the eosinophil counts or LDH levels between severe and non-severe patients. COPD, chronic obstructive pulmonary disease; LDH, lactate dehydrogenase.

death and negative outcomes of patients with COVID-19, which was consistent with He's work.<sup>21</sup> In our cohort, the impaired lung function of patients with COVID-19 with underlying chronic airway diseases might have a significant impact on the outcome. However, the analysis could not be conducted due to unavailable data, which was a limitation of this study.

Previous treatment regimens might contribute to the outcome of patients with COVID-19 with underlying chronic airway diseases. Inhaled corticosteroids (ICS) (with or without longacting β-agonist) are applied directly to the respiratory epithelium in the intervention of stable COPD and asthma to reduce airway inflammation. ICS could decrease the expression of both ACE2 and transmembrane protease serine 2 (TMPRSS2) on airway epithelial cells, subsequently protecting them from being invaded by SARS-CoV-2.<sup>22</sup> In addition, the proliferation of coronavirus and cytokine production could also be suppressed by the usage of ICS.<sup>23</sup> However, whether the use of regular ICS before the pandemic had an impact on COVID-19 outcomes remains controversial. Bloom et al reported that patients with asthma older than 50 years could benefit from the use of ICS within 2 weeks of admission, while patients with other chronic pulmonary diseases could not.<sup>24</sup> Schultze et al<sup>25</sup>'s work denied the positive role of regular ICS use in protecting against severe outcome of COVID-19, both in patients with asthma and in patients with COPD. In our cohort, only one patient with COPD and two patients with asthma reported having long-term use of ICS due to the difficulty in collecting medical histories in the initiation of the pandemic. Further detailed information on comorbidities, prior medication and many bias factors should be taken into account to figure out the benefits or harms of ICS in COVID-19.

Different phenotypes of COPD and asthma based on the complex pathophysiology might also be partly involved in COVID-19; however, the hypotheses need to be further clarified. Kimura *et al*<sup>26</sup> found that type 2 inflammatory cytokines (IL-4, IL-5, IL-13) were negatively associated with ACE2 expression while positively associated with TMPRSS2 expression in an ex vivo study. Ferastraoaru et  $al^{27}$ 's work indicated that a Th2 asthma phenotype was a predictor of reduced COVID-19 morbidity and mortality, while Kermani *et al*<sup>28</sup> reported greater morbidity and mortality outcome in neutrophilic severe asthma. A previous report has highlighted that eosinophilic inflammation was also a common and stable phenotype in COPD and blood eosinophil counts could predict response to ICS treatment.<sup>29</sup> Watson et al did not find any gene expression differences in ACE2 in blood eosinophilic COPD, further indicating that these patients might not have a different vulnerability to SARS-CoV-2 infection.<sup>30</sup> Therefore, how different inflammation types of COPD and asthma might impact the progress of severe COVID-19 needs further investigation.

Our study also had some other limitations. First, due to the retrospective study design, the accuracy of all laboratory results was dependent on medical records. Observation bias might also exist in this study due to the limited sample size. Second, there could be a selection bias in the multivariate regression model when analysing the risk factors.

### CONCLUSION

Our study reveals that eosinopaenia and elevated LDH on admission are potential predictors of disease severity in adults with COVID-19 with underlying chronic airway diseases. Moreover, eosinophil counts could indicate disease progression of COVID-19, thus revealing treatment efficacy. These predictors

## Main messages

- Patients with chronic airway diseases are less likely to suffer from COVID-19.
- Eosinopaenia and elevated lactate dehydrogenase (LDH) can predict disease severity in patients with COVID-19 with underlying chronic airway diseases.
- Dynamic changes of eosinophil counts and LDH might indicate disease prognosis and treatment effectiveness.

### **Current research questions**

- Are other molecules related to chronic airway inflammation also involved in the development of COVID-19?
- Can the drugs targeting eosinophils be applied in COVID-19 treatment?
- ► How do patients with COVID-19 with chronic airway diseases manage themselves?

may help clinicians identify severe COVID-19 in patients with chronic bronchitis, COPD and asthma.

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### ORCID iD

Guohua Zhen http://orcid.org/0000-0001-5582-7900

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## **Original research**

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