Analysis of the total serum levels of IgE levels in patients with acute exacerbations chronic obstructive pulmonary disease

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Research Article

Keywords: acute exacerbations chronic obstructive pulmonary disease (AECOPD), total IgE(T-IgE), allergic phenotype

Posted Date: May 17th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1651108/v1

Abstract

Background

Currently, no studies have demonstrated the relationship between IgE and AECOPD. Also, the utility of total serum IgE levels as a biomarker to guide AECOPD treatments remains to be determined.In this study, the total serum levels of IgE in patients with acute exacerbation chronic obstructive pulmonary disease (AECOPD) were investigated and correlated with the clinical characteristics.

Methods

Our study retrospectively included AECOPD patients that were hospitalized at the Liaocheng People's Hospital from July 2018 to July 2019.we investigated the demographic variables, body mass index, smoking history, lung function, the frequency of acute exacerbation episodes in the past 12 months, the course of chronic obstructive pulmonary disease (COPD), medication history and complications. Routine blood tests, C-reactive protein levels and total IgE levels in the serum of patients were determined along with blood gas analysis. The length of hospital stay, mechanical ventilation during hospitalization, ICU admission, glucocorticoid administration, cumulative dose of glucocorticoid administration during hospitalization, duration of glucocorticoid administration, and the average dosage of glucocorticoid were also recorded.

Results

A total of 285 patients were included in the study that had a high proportion of males(74.1%). The proportion of patients with increased levels of T-IgE was 49.82%. According to the results of total IgE serum levels (> 60 kU/L as abnormal value), the patients were divided into high (n=142) and low high T-IgE groups (n=143). There was no significant difference in the dosage of glucocorticoid (including the number of patients receiving glucocorticoid, the average dosage of glucocorticoid, cumulative dosage and medication time) between the two groups. Patients in the high T-IgE group had shorter hospital stays and a lower probability of mechanical ventilation compared to the low T-IgE group. After adjustment for confounding factors, T-IgE was negatively correlated with the length of hospital stay. Univariate and multivariate Logistic regression analysis showed that low T-IgE was a statistically significant risk factor for mechanical ventilation and ICU admission in COPD patients.

Conclusion

Increased levels of t-IgE were found in many AECOPD patients suggesting that an allergic phenotype may be displayed in AECOPD. AECOPD patients with elevated t-IgE had shorter hospital stays and lower risks of mechanical ventilation and ICU admission. Our data show that t-IgE may have value as a biomarker in evaluating the condition of patients and guiding treatment decisions in AECOPD patients.

Background

Chronic obstructive pulmonary disease (COPD) is a common and frequently occurring lung disease that is a serious threat to human health. Studies have shown that the prevalence of COPD worldwide is 10.1%[1] and 13.7%[2] in the Chinese population over 40 years of age. Acute exacerbation chronic obstructive pulmonary disease (AECOPD) is a process of exacerbation of respiratory symptoms and acute onset of chronic disease in COPD patients. The typical manifestations of AECOPD are exacerbated dyspnea, aggravated cough, increased sputum volume and/or purulent sputum beyond daytime variation. Acute exacerbation is an essential event in the progression of COPD that seriously impacts patient quality of life and increases readmission rates and mortality[3, 4]. AECOPD is a heterogeneous condition and its diagnosis is nonspecific and dependent on subjective assessment by clinicians. The treatment of patients with different phenotypes of AECOPD is mainly based on clinician experience and lacks specific treatments[3]. Further research is required to identify clinical biomarkers in AECOPD patients that can indicate disease-specific phenotypes and inform treatment decisions in the clinic.

Allergic reactions have been proposed as common factors in asthma and COPD patients. Currently, the role of allergy in the pathogenesis of asthma has been generally recognized but its role in COPD has not been extensively studied[5]. Studies have suggested that the allergic phenotype is a particular subtype of COPD and that COPD patients with allergic symptoms have severe respiratory symptoms and frequent exacerbation history[6]. Immunoglobulin E (IgE) is an antibody that mediates allergic reactions and has important value in the diagnosis of various allergic diseases[7]. IgE-related allergic diseases have been shown to affect about 30% of the population worldwide[8]. A longitudinal study of COPD showed that total serum IgE levels are negatively correlated with FEV_1/FVC[9]. Another study showed that total serum IgE levels are associated with impaired lung function impairment and respiratory symptoms in patients with COPD (e.g., dyspnea)[10]. Currently, no studies have demonstrated the relationship between IgE and AECOPD. Also, the utility of total serum IgE levels as a biomarker to guide AECOPD treatments remains to be determined.

This study aimed to investigate the expression of total IgE levels in the serum of AECOPD patients and to evaluate clinical characteristics of the allergic phenotype. Furthermore,we also explored the use of total IgE as a biomarker in the treatment of AECOPD.

Methods

Study subjects

Our study retrospectively included AECOPD patients that were hospitalized at the Liaocheng People's Hospital from July 2018 to July 2019. The inclusion criteria for the study were (1) patients over 40 years old with risk factors for COPD including smoking (2) patients who had undergone pulmonary function tests at a stable stage (at least one month before admission) and meet the criteria of FEV1/FVC<0.7 after bronchodilator inhalation; (3) patients with acute symptoms on

admission such as acute exacerbation of respiratory symptoms beyond daytime variation that required medication adjustment.

The exclusion criteria for the study were (1) allergic rhinitis and other allergic diseases; (2) bronchial asthma, allergic bronchopulmonary aspergillosis, pneumonia, bronchiectasis, interstitial lung disease and other respiratory diseases; (3) acute left heart failure and other unstable heart diseases; (4) patients who died during discharge without doctor's advice or hospitalization; (5) patients without complete total IgE levels in serum and other related laboratory tests. All patient treatments during hospitalization including anti-infection treatments, systemic glucocorticoid administration, adjuvant treatments (e.g. oxygen therapy or mechanical ventilation) and discharge, were decided by the physician-in-charge and were not affected by our study.

Sample information

Clinical information included demographic variables, body mass index, smoking history, lung function (after inhalation of bronchodilator), the frequency of acute exacerbation episodes in the past 12 months, the course of COPD, medication history (regular glucocorticoid inhalation) and complications (ischemic cardiomyopathy, hypertension, cardiac insufficiency and diabetes). Routine blood tests, C-reactive protein, total serum IgE levels and blood gas analysis were conducted before treatment. The total serum IgE levels (ImmunoCap TM 100, Pharmacia Company, Sweden) were measured by the Liaocheng Key Laboratory of Respiratory Diseases. According to the reference values, total IgE levels in serum of > 60 kU/L are abnormal. Other tests were performed by the clinical laboratory of the Liaocheng People's hospital. The length of hospital stay, mechanical ventilation during hospitalization (including noninvasive and invasive mechanical ventilation), ICU admission, glucocorticoid administration, cumulative dose of glucocorticoid administration during hospitalization, days of glucocorticoid administration and average dosage glucocorticoid (cumulative dose/administration days) were recorded. The dose of glucocorticoid doses was converted to the dose of methylprednisolone.

Statistical analysis

The categorical variables were expressed as numbers and percentages, and the continuous variables were expressed as the mean ± standard deviation. A chi-square test was used to compare two sample rates. A Kolmogorov-Smirnov test was used to identify the data distribution which conformed to a normal distribution. A Two-sample t-test or Mann-Whitney test was used for two sample continuous variables with a normal and non-normal distribution. Binary Logistic regression and multiple linear regression analysis were used to evaluate the relationship between dependent and independent variables. All data were statistically analyzed using IBM SPSS 25.0 (IBM Corphan, Armonk, NY, USA).

Results

A total of 431 AECOPD patients were included in this study. Patients with complications including 37 cases of pneumonia, 2 cases of bronchial asthma, 3 cases of bronchiectasis, 4 cases of allergic bronchopulmonary aspergillosis and 13 cases of acute left heart failure were excluded from the analysis. 15 patients died during hospitalization, 68 cases did not have total IgE serum level tests and 4 cases were automatically discharged. Data from 285 patients were finally included in the analysis. Based on the total IgE serum levels (> 60 kU/L as the abnormal value), serum T-IgE data was not normally distributed (statistical K-S=0.286, p<0.01) and ln T-IgE values conformed to a normal distribution after logarithmic transformation (statistical K-S=0.040, p=0.200). The patients were divided into two groups specifically as a high T-IgE group (n=142) and a low T-IgE group (n=143). 49.82% of the patients had elevated T-IgE levels. The clinical characteristics of the two groups are summarized in Table 1.

The average age of the patients was (70.75 ±8.56) years and there was no significant difference in age between the two groups (P>0.05). 74.1% of the patients were male and the proportion of males in the high T-IgE group was higher than that in the low T-IgE group (P<0.05). Compared to the low T-IgE group, the proportion of patients with glucocorticoid inhalation in the high t-IgE group increased, whilst the proportion of body mass index and complications (hypertension, diabetes and ischemic heart disease) was significantly lower (P<0.05). There was no significant difference in the proportion of smokers, the frequency of acute exacerbation episodes in the past 12 months, the course of COPD, pulmonary function parameters and the proportion of heart failure complication between the two groups (P>0.05). The laboratory parameters of the two groups are summarized in Table 2. The laboratory test results after admission showed that the pH value in the high T-IgE group was higher than the low T-IgE group (p<0.05). PaCO2 was lower in the high T-IgE group compared to the low T-IgE group (p<0.05). There were no significant differences in white blood cell count and the levels of neutrophils, eosinophils, CRP and PaO2 between the two groups (P>0.05).

32.3% of patients in the high T-IgE group and 34% of patients in the low T-IgE group received systemic glucocorticoid treatment. Clincal variables are symmarized in Table 3 .No significant differences were observed in the dosage of glucocorticoid during the treatment (including the number of patients treating with glucocorticoid, the average dosage of glucocorticoid, cumulative dosage and medication time) between the two groups (P>0.05).

Compared to patients in the low T-IgE group, patients in the high T-IgE group had shorter hospital stays (9.49 ±3.05 vs. 10.59 ±3.42, p<0.01) and lower probabilities of ICU admission (3.9% vs 10.2%, p<0.01) and mechanical ventilation (5.3% vs 14.4%, p<0.01). The data are summarized in Table 3. As the ln T-IgE data were normally distributed after logarithmic transformation, linear regression was applied to analyze the relationships between the ln T-IgE and related variables. We found that males (β=-0.147, 95% CI: -0.234to -0.060, p<0.01), hypertension (β=-0.970, 95% CI: -1.055 to -0.885, p<0.01), diabetes (β=-0.357, 95% CI: -0.474 to -0.239, p<0.01), PaCO2 (β=-0.003, 95% CI: -0.006 to -0.000, p<0.01) and the length of the hospital stay (β=-0.017, 95% CI: -0.029 to -0.006, p<0.01) were negatively correlated to the Ln values (T-IgE). The application of ICS was related to on the Ln (T-IgE) (β=0.409, 95%CI: 0.331 to 0.478, p<0.01). Body mass index, ischemic heart disease and PH values had no

significant effect on Ln (T-IgE) (Table.4). Univariate Logistic regression analysis showed that low T-IgE levels, ischemic heart disease, high BMI, high PaCO2 and low pH were risk factors for mechanical ventilation and ICU admission in COPD patients. Multivariate Logistic regression analysis showed that after correction for ischemic heart disease, BMI, PaCO2 and pH value, T-IgE was still a significant risk factor for mechanical ventilation and ICU admission in COPD patients (see Tables 5 and 6).

Discussion

Previous research into the allergic phenotype and COPD has mainly focused on the stable phase. Studies have emphasized the relationship between the allergic phenotype and the epidemiological characteristics of COPD patients, clinical symptoms and lung function. Jamieson *et al.* found that 25–30% of COPD patients manifest an allergic phenotype[6]. Another study that investigated t-IgE as an allergy biomarker showed that 47.3% of COPD patients had elevated serum levels of total IgE[10]. A recently published META analysis showed that about one-third of COPD patients have allergic symptoms[11].

The allergic symptoms in COPD patients have been shown to correlate with occupation, dust exposure and other factors. These are accompanied by obvious respiratory symptoms, poor lung function and frequent acute exacerbation[6, 10, 12–14]. These studies have suggested that the allergic phenotype may be important phenotypes in COPD but are limited to the stable stage of disease and did not assess COPD patients with acute exacerbation. AECOPD has a variety of clinical manifestations and pathophysiological characteristics that result and so the condition has been divided into various phenotypes based on heterogeneity. AECOPD patients display four subtypes; bacterial predominant, viral predominant, eosinophilic predominant and pauci-inflammatory subtypes[15]. Xx *et al.* classified AECOPD into four subtypes (subtype A-D) according to the severity of clinical symptoms and complications[16]. Gulati *et al.* classified patients into four subtypes (E1-E4) according to pathological and clinical characteristics[17]. The current classification of AECOPD phenotypes does not fully account for the clinical characteristics of AECOPD in acute exacerbation. In this study, we showed that many AECOPD patients have elevated total serum IgE levels and the allergic phenotype may be particularly important in the clinic.

Systemic glucocorticoid treatment is an important therapy for AECOPD that can reduce the rates of treatment failure and rehospitalization in patients with non-respiratory failure[18]. Although the recommended dose of systemic glucocorticoid have been proposed in the GOLD guidelines, differences in the dose and course of treatment remain in the clinic[4, 19]. Our results showed that the dose of glucocorticoid in AECOPD treatment was independent of total serum Ig-E levels and They have no relationship each other.

The prolonged hospitalization of AECOPD patients is an important factor that contributes to increased medical expenses and personal burden. The early identification of COPD patients with acute exacerbation that causes long-term hospitalization can reduce the occurrence of adverse events and treatment costs. Current studies have found that age, disease severity, complications and acute respiratory acidosis are

important predictors of prolonged hospitalization in AECOPD patients[20, 21]. Our study suggested that total serum IgE levels can also predict hospitalization in AECOPD patients.

Mechanical ventilation is an important treatment for AECOPD patients with respiratory failure that can reduce mortality during hospitalization[19]. There is currently no accepted standard for AECOPD patients to be admitted to ICU administration that can importantly inform clinical decision-making. Moreover, there are no reliable biomarkers to guide clinicians in identifying patients for ICU admission[22]. Compared to the control group, patients with elevated IgE levels had a lower risk of mechanical ventilation and ICU admission. These data suggest that total serum IgE levels could be a useful biomarker to assess the severity of AECOPD and inform decisions for patients requiring mechanical ventilation treatment and ICU admission. Based on our data, it can be concluded that total serum IgE levels may play an important role in evaluating the condition of AECOPD patients and guide treatment decisions.

Currently, the underlying mechanism supporting our observations remain largely unknown. Previous studies have suggested that the expression of IgE is associated with pulmonary inflammation and airway remodeling in patients with stable COPD. Elevated IgE levels may aggravate lung inflammation and promote airway remodeling in COPD patients resulting in decreased lung function and severe respiratory symptoms[6, 10]. In AECOPD patients, we speculate that the observed changes may be due to the activation of Th2 cells and that IgE levels are increased by Th2 cells and other related factors such as IL-4, IL-5 and IL-13. Exogenous IgE could bind to the FceR I receptor on the surface of effector cells and exert biological effects including the initiation and maintenance of airway inflammation, and induced airway hyper responsiveness[23–25][23–24, 7]. Bronchodilators, glucocorticoids and other drugs used in treatment could alleviate the hyperresponsiveness of airways during the acute exacerbation phase and inhibit the related inflammatory response[26][25]. Consequently, the hospitalization time and the risk of mechanical ventilation in AECOPD patients could be reduced. However, bronchodilators and glucocorticoids do not directly affect the total IgE levels nor do they guide the dosage of glucocorticoids.

Previous studies of IgE and COPD have focused on stable COPD. This study aimed to investigate the relationship between total serum IgE levels and the phenotype of AECOPD. We demonstrated a significant role for IgE as a biomarker in the diagnosis, treatment and classification of AECOPD. However, our data are based on retrospective analysis from a small study small sample size. Due to the short follow-up time, the influence of seasonal factors on IgE and COPD could also not be excluded. In this study,by using strict exclusion and inclsion criteria, our population did not included asthmatics, but we did not exclue ACO populations. As the subtype of COPD, our team think this subtype should not be exclued, due to they have the clinical characterictics of COPD. There is no question that tabacco smoking is one of the main risk factors for COPD, but ambient air pollution occupational dust are important risk factors for COPD, and it is unevenly spread. Our data require further validation in a larger sized patient cohort with long-term follow-up.

Conclusions

Our study confirmed that AECOPD patients have elevated t-IgE levels and suggests that the allergic phenotype may be important in AECOPD. AECOPD patients with elevated t-IgE levels had shorter hospital stays and a lower risk of mechanical ventilation and ICU admission. These data suggest that t-IgE has potential value as a biomarker in evaluating the condition of AECOPD patients and guiding treatment.

Abbreviations

AECOPD, acute exacerbations chronic obstructive pulmonary disease;T-IgE: serum total IgE; BMI, body mass index; FEV1 , forced expiratory volume in one second; FVC, forced vital capacity; CCQ, Clinical COPD Questionnaire; mMRC, modified Medical research Council; CAT, COPD assessment test; ICS, inhaled corticosteroid;CRP, C-reactive protein; PaCO2 , arterial carbon dioxide partial pressure; PaO2 , arterial oxygen partial pressure.

Declarations

Acknowledgements

The authors thank all patients for their participation.We thank Zhen Li, Jun Qi, Lili Li, and Tingting Jiang Tian Xiufen for assistance in patient recruitment. We thank Juan Zheng for performing the serum total IgE measurements, and we thank all technicians of the laboratory for Clinical Chemistry (the Liaocheng People's hospital) for assistance with sample preparation, measurements, and data collection. We thank Wang Yan, Peige Zhao and Lindong Yuan for their expert support in the planning of this study protocol.

Authors' contributions

Conceptualization and funding acquisition: Peige Zhao,Yan Wang. Data curation: Lindong Yuan. Investigation: Lili Li. Methodology: Zhen Li. Project administration: Lindong Yuan, Peige Zhao and ZiyunYang. Resources: Tingting Jiang. Software: Qin shan. Supervision: Jun Qi, Xiufen Tian. Validation: Juan Zheng. Writing – original draft, review & editing: Lindong Yuan, Peige Zhao,Yan Wang.

Competing interests

The authors declare that they have no competing interests.

Funding

This study was supported by the Intramural Research Program of the Liaocheng People’s Hospital.

Availability of data and materials

The datasets generated during and/or analyzed during the current study are not

publicly available, but are available from the corresponding author on reasonable

request.

Consent for publication

Participant's written consent for publication of pseudonymized data is included in the study consent form.

Competing interests

The authors declare that they have no competing interests.

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Tables

Table.1 Baseline characteristics of high T-IgE and low T-IgE in patients

Variables	Total patients(n=285)	high T-IgE(n=142)	low T-IgE(n=143)	*P*-value
Age(years)	70.75±8.56	70.11±8.63	71.38±8.47	0.212[#]
Male	211(74.1%)	117(41.1%)	94(33.0%)	**0.001[&]**
BMI(kg/m 2)	22.20±4.57	21.57±4.29	22.83±4.77	**0.019[#]**
Smoking status				0.087[&]
Current Smokers	80(28.1 %)	45(15.8%)	35(12.3%)	
Ex-smokers	118(41.4%)	62(21.8%)	56(19.6%)	
No-smokers	87(30.5%)	35(12.3%)	52(18.2%)	
Duration of COPD(years)	9.62±7.00	8.99±10.79	10.24±11.34	0.194*
Number of exacerbation in the past 12 months	1.37±1.00	1.37±1.78	1.37±1.05	0.696*
Spirometric Value(post-bronchodilator)				
FEV1(L)	0.87±0.23	0.86±0.25	0.88±0.22	0.586[#]
FVC(L)	1.96±1.26	1.89±0.39	2.04±1.73	0.335[#]
FEV1/FVC ratio(%)	0.46±0.08	0.46±0.08	0.46±0.09	0.627[#]
ICS use	150(52.6%)	89(31.2%)	61(21.4%)	**0.001[&]**
Co-morbidity				
Hypertension	96(33.7%)	4(1.4%)	92(32.3%)	**≤0.001[&]**
Diabetes mellitus	35(12.3%)	7(2.5%)	28(9.8%)	**≤0.001[&]**
Heart failure	21(7.4%)	7(2.5%)	14(4.9%)	0.116[&]
Ischaemic heart disease	107(37.5%)	44(15.4%)	63(22.1%)	**0.023[&]**

Note: Data are expressed as mean±SD n (%).([#]) *P* values were calculated by Student's t-test;(*) *P* values were calculated by the Mann-Whitney test;([&]) *P* values were calculated by the chi-square test.

Abbreviations: BMI, body mass index; FEV1 , forced expiratory volume in one second; FVC, forced vital capacity; CCQ, Clinical COPD Questionnaire; mMRC, modified Medical research Council; CAT, COPD assessment test; ICS, inhaled corticosteroid.

Table. 2 Laboratory variables of the patients(n=285)

Variables	Total patients(n=285)	high T-IgE(n=142)	low T-IgE(n=143)	*P*-value
T-IgE(kU/L)	140.33±167.58	257.04±170.10	24.43±16.98	**≤0.001**[&]
Ln(T-IgE)	1.78±0.63	2.32±0.28	1.25±0.38	**≤0.001**[#]
leucocyte count(10^9L)	8.90±4.33	8.97±3.72	8.83±4.88	0.784[#]
neutrophil count(10^9L)	7.32±6.34	7.57±7.05	7.06±5.55	0.499[#]
Eosinophilic count(10^9L)	0.14±0.62	0.12±0.24	0.17±0.84	0.484[#]
CRP(mg/dL)	36.02±43.95	39.49±52.77	32.57±30.01	0.667[&]
pH	7.40±0.07	7.41±0.06	7.39±0.07	**0.008**[#]
PaO_2(mmHg)	78.59±26.11	77.55±25.57	79.62±26.69	0.506[#]
paCO2 (mmHg)	50.91±16.54	48.96±14.61	52.84±18.11	**0.048**[#]

Note: Data are expressed as mean±SD.([#]) *P* values were calculated by Student's t-test; ([&])*P* values were calculated by the Mann-Whitneytest; .

Abbreviations: T-IgE: serum total IgE;CRP, C-reactive protein; PaCO2 , arterial carbon dioxide partial pressure; PaO2 , arterial oxygen partial pressure;

Table. 3 Clinical variables of the patients(n=285)

Variables	high T-IgE(n=142)	low T-IgE(n=143)	*P*-value
NO of using Systemic Corticosteroids of patients	92(32.3%)	97(34.0%)	0.587[&]
Average daily does of Systemic Corticosteroids, (mg)	26.84±27.54	30.11±35.54	0.539*
Average cumulative does of Systemic Corticosteroids,(mg)	203.32±234.88	180.06±179.50	0.699*
Length of Systemic Corticosteroids using,(days)	5.83±5.20	5.24±4.80	0.428*
Length of Hospital stay,(days)	9.49±3.05	10.59±3.42	**0.004***
ICU Admission	11(3.9%)	29(10.2%)	**0.002**[&]
Mechanical Ventilation	15(5.3%)	41(14.4%)	**≤0.001**[&]

Note: Data are expressed as n(%)or median (1st quartile; 3rd quartile). (*)*P* values were calculated by the Mann-Whitney test;(&) *P* values were calculated by the chi-square test.

Table. 4 multivariable linear regression analysis of Ln(T-IgE) and variables (n=285)

Variables	β	Std.Error	95%CI	*p*-value
Male	-0.147	0.044	-0.234 to -0.060	0.001
BMI(kg/m ^{2})	-0.008	0.004	-0.016 to 0.000	0.060
ICS use	0.409	0.039	0.331 to 0.478	≤0.001
Hypertension	-0.970	0.043	-1.055 to -0.885	≤0.001
Diabetes mellitus)	-0.357	0.060	-0.474to -0.239	≤0.001
Ischaemic heart disease	-0.002	0.041	-0.083 to 0.082	0.962
pH	-0.061	0.352	-0.755 to 0.632	0.862
paCO2 (mmHg)	-0.003	0.001	-0.006 to -0.000	0.032
Length of Hospital stay,(days)	-0.017	0.006	-0.029 to -0.006	**0.003**

Note: CI, confidence interval;

Abbreviations: BMI, body mass index; ICS, inhaled corticosteroid;T-IgE: serum total IgE; PaCO2 , arterial carbon dioxide partial pressure; PaO2 , arterial oxygen partial pressure.

Table 5.Results of univariale and multivariate analysis of correlation between baseline characteristics,laboratory test results and Mechanical Ventilation events

Variables	Univariale analysis			Multivariate analysis		
	OR	95%CI	*P* vale	OR	95%CI	*P* vale
T-IgE	0.995	0.992-0.998	**0.001**	0.996	0.993-0.999	**0.005**
Sex						
male	1					
female	1.625	0.865-3.053	0.132			
Smoking status						
Never smoker	1					
Current smoker	0.610	0.282-1.318	0.208			
Former smoker	0.720	0.367-1.415	0.341			
Drug						
No	1					
ICS	0.560	0.309-1.013	0.055			
Co-morbidities						
Ischemic heart disease	3.005	1.649-5.477	≤0.001	2.872	1.500-5.499	**0.001**
Cardiac insufficiency	0.409	0.092-1.812	0.239			
Hypertension	1.603	0.882-2.914	0.122			
Diabetes mellitus	1.774	0.797-3.984	0.160			
Age	1.019	0.984-1.055	0.294			
BMI	1.065	1.000-1.134	**0.050**	1.035	0.968-1.106	0.317
Disease duration(year)	0.988	0.960-1.017	0.416			
Acute exacerbations of COPD	0.845	0.637-1.119	0.240			
FEV1(L)	1.400	0.421-4.656	0.584			
FVC(L)	0.831	0.420-1.644	0.595			
FEV1/FVC(%)	8.425	0.334-212.723	0.196			
WBC($\times 10^9$/L)	1.026	0.962-1.093	0.493			
Neutrophil($\times 10^9$/L)	0.984	0.928-1.043	0.580			

Eosinophil($\times 10^9$/L)	1.353	0.831-2.204	0.225			
CRP	1.003	0.997-1.009	0.340			
PH	0.015	0.000-0.720	**0.034**	1.529	0.008-299.844	0.875
PO_2	1.006	0.995-1.017	0.266			
PCO_2	1.019	1.002-1.036	**0.024**	1.019	0.998-1.040	0.075

Note: OR, Odds ratio;CI, confidence interval;

Abbreviations: BMI, body mass index; FEV1 , forced expiratory volume in one second; FVC, forced vital capacity; CCQ, Clinical COPD Questionnaire; mMRC, modified Medical research Council; CAT, COPD assessment test; ICS, inhaled corticosteroid;T-IgE: serum total IgE;CRP, C-reactive protein; PaCO2 , arterial carbon dioxide partial pressure; PaO2 , arterial oxygen partial pressure.

Table 6.Results of univariale and multivariate analysis of correlation between baseline characteristics,laboratory test results and ICU Admission

Variables	Univariale analysis			Multivariate analysis		
	OR	95%CI	P vale	OR	95%CI	P vale
T-IgE	0.994	0.990-0.998	**0.003**	0.995	0.992-0.999	**0.016**
Sex						
male	1					
female	0.913	0.431-1.934	0.811			
Smoking status						
Never smoker	1					
Current smoker	0.951	0.428-2.109	0.901			
Former smoker	0.947	0.418-2.146	0.896			
Drug						
No	1					
ICS	1.811	0.917-3.577	0.087			
Co-morbidities						
Ischemic heart disease	3.313	1.657-6.625	**0.001**	3.253	1.518-6.970	**0.02**
Cardiac insufficiency	0.288	0.038-2.212	0.232			
Hypertension	1.524	0.771-3.013	0.225			
Diabetes mellitus	2.019	0.844-4.827	0.114			
Age	1.033	0.992-1.076	0.120			
BMI	1.101	1.025-1.183	**0.008**	1.072	0.994-1.157	0.071
Disease duration(year)	0.975	0.940-1.012	0.182			
Acute exacerbations of COPD	0.770	0.548-1.082	0.132			
FEV1(L)	1.088	0.264-4.418	0.907			
FVC(L)	0.897	0.505-1.592	0.710			
FEV1/FVC(%)	1.788	0.037-86.553	0.769			
WBC($\times 10^9$/L)	1.035	0.965-1.110	0.340			
Neutrophil($\times 10^9$/L)	0.976	0.904-1.053	0.525			

Eosinophil($\times 10^9$/L)	1.467	0.842-2.555	0.176			
CRP	1.004	0.998-1.011	0.190			
PH	0.014	0.000-0.907	**0.045**	11.809	0.031-445.012	0.416
PO_2	1.003	0.990-1.015	0.658			
PCO_2	1.025	1.007-1.043	**0.007**	1.030	1.006-1.053	**0.012**

Note: OR, Odds ratio;CI, confidence interval;

Abbreviations: BMI, body mass index; FEV1 , forced expiratory volume in one second; FVC, forced vital capacity; CCQ, Clinical COPD Questionnaire; mMRC, modified Medical research Council; CAT, COPD assessment test; ICS, inhaled corticosteroid;T-IgE: serum total IgE;CRP, C-reactive protein; PaCO2 , arterial carbon dioxide partial pressure; PaO2 , arterial oxygen partial pressure.