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# Study of serum Ykl-40 level and its relationship to BODE index in patients with chronic obstructive pulmonary disease

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## Abstract

**Background** Chronic obstructive pulmonary disease (COPD) is a significant global health concern characterized by growing rates of mortality and morbidity. The purpose of this work was to evaluate the serum YKL-40 level and its relationship to body mass index (BMI), obstruction of airflow, dyspnea, exercise capacity (BODE) index, and the extent of COPD.

**Methods** This prospective work was carried out on 70 adult male patients, allocated into three groups: group A—36 smokers with stable COPD with different degrees of severity; group B—19 smokers without COPD; and group C—15 healthy non-smokers as a control group.

**Results** The BODE index was 5.56 ± 2.52. Prebronchodilator forced expiratory volume in 1 s (FEV1) and FVC were substantially decreased in group A contrasted to group B and group C (*P* value < 0.001). Prebronchodilator forced expiratory volume in 1/forced vital capacity (FEV1/FVC) ratio was substantially decreased in group A contrasted to groups B and C and lower in group B than in group C (*P* value < 0.001).

Chest X-ray (CXR) signs of COPD and mMRC Dyspnea Scale were significantly higher in group A than in groups B and C (*P* value < 0.001). The 6-min walking test was substantially decreased in group A than in groups B and C and lower in group B than in group C (*P* value < 0.001 and 0.006 correspondingly). Serum YKL-40 was substantially greater in group A contrasted to group C (*P* value = 0.005). There was no correlation between serum YKL-40 and (BODE index, $O_2$ saturation, or smoking index) in group A. A substantial positive association existed among serum YKL-40 and [degree of severity and white blood cells (WBCs)] in group A. Serum YKL-40 cannot predict the severity of COPD (*P* = 0.227 and AUC = 0.584) at cut-off > 0.394 with 80.65% sensitivity, 41.03% specificity, 52.1% PPV, and 72.7% NPV.

**Conclusions** Serum YKL-40 level was substantially greater in the COPD group contrasted to healthy non-smokers, no substantial association existed between serumYKL-40 and BODE index, $O_2$ saturation, or smoking index. A substantial positive association existed between SerumYKL-40 and the degree of severity and WBCs.

**Keywords** Serum Ykl-40 level, BODE index, Chronic obstructive pulmonary disease

## Background

Chronic obstructive pulmonary disease (COPD) is a significant global health issue marked by the gradual deterioration of lung tissue, leading to a reduction in the performance of the lungs and increased rates of mortality and morbidity [1].

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The primary presentation of airflow obstruction in COPD is characterized by a decline in forced expiratory volume in 1 s (FEV1) [2]. Nevertheless, the American Thoracic Society (ATS) and the European Respiratory Society (ERS) argue that relying just on the measurement of FEV1 fails to adequately reflect the intricate clinical implications of COPD. Therefore, it is recommended to consider and analyze additional indicators alongside FEV1 [3].

In recent years, there have been significant advancements in the comprehension of the systemic aspects of COPD. As a result, a multidimensional categorization system has been developed to accurately assess the level of mortality risk in persons affected by COPD [4].

The body mass index (BMI), obstruction of airflow, dyspnea, and exercise capacity (BODE) index is a commonly employed approach for evaluating prognosis. This index combines several established indicators of mortality in individuals with COPD, including a decreased BMI, reduced FEV1, severity of dyspnea, and exercise capacity. The BODE index has been found to be correlated with a heightened risk of fatalities [5].

The BODE index incorporates both symptomatic manifestations and physiological data and is currently regarded as a superior indicator compared to FEV1 in terms of prognosticating mortality and assessing the severity of COPD [6]. Individuals with COPD have elevated levels of several mediators, such as chemokines, cytokines, growth factors, and reactive oxygen species. These mediators can be found in either the blood, the airways, or both compartments [7].

Recently, there has been a growing interest in YKL-40, also known as human cartilage glycoprotein-39 (HCgp-39) and chitinase-3-like-1 protein (CHI3L1), as a valuable biomarker for several disorders. There was an observed rise in systemic inflammation [8].

The aim of this work was to evaluate the serum YKL-40 level and its relationship to BODE index and the severity of COPD.

## Methods

This prospective work was performed on 70 adult male individuals allocated into 3 groups: group A—($n=36$) smokers with stable COPD with different degrees of severity as defined by Global Initiative for chronic obstructive lung disease (GOLD) criteria [9]; group B—($n=19$) smokers without COPD; and group C—($n=15$) healthy non-smokers as a control group.

The study was conducted subsequent to obtaining permission from the Ethics Committee of Alexandria University Hospitals, Alexandria, Egypt. Each participant provided informed written permission.

Criteria for exclusion were previous episodes of acute exacerbation; being hospitalized within the past month; the use of systemic glucocorticoids, immune-suppressive agent, or any anti-inflammatory drugs in the last month; liver cirrhosis; chronic renal failure; collagen disease; cancer; infection; neuromuscular illness; obstructive sleep apnea; and decompensated heart failure.

All studied patients had been subjected to history taking; laboratory investigation [white blood cells (WBCs) and measurement of serum YKL 40]; chest examination; BMI; oxygen saturation by pulse oximetry (at rest); chest radiography CXR which was done to exclude other diagnosis and confirm signs related to COPD like signs of lung hyperinflation, "ribbon heart," and rapid tapering of the vascular markings; estimation of mMRC Dyspnea Scale [10]; 6-min walking (6MWT) test [11, 12]; and spirometry [13].

### Spirometry

The diagnosis of individuals with COPD was conducted in accordance with the GOLD criteria, which are established according to the symptoms, risk factors, and post-bronchodilator forced expiratory volume in 1/forced vital capacity (FEV1/FVC) ratio of less than 70% [13]. Spirometry was done for all patients to estimate FEV1, FVC, and FEV1/FVC ratios. Bronchodilator reversibility assessment was conducted on group A patients by giving them 400-µg short-acting beta2-agonist, then spirometry was repeated after 10–15 min. The patient should not use any bronchodilator for at least 48 h before the test. In general, a positive outcome of a bronchodilator challenge test is often characterized by a minimum rise of $\geq 12\%$ and $\geq 200$ mL as an absolute value when contrasted with the baseline measurements of either FEV1 or FVC. Patients with non-reversible airway obstruction were classified as COPD, then the severity of the obstruction was graded [13].

### Six-minute walking test

The 6MWT is a well-established assessment tool utilized for evaluating both exercise capacity as well as life quality in individuals with COPD. The 6MWT was conducted in accordance with the recommendations established by the ATS [14]. The participants have been provided with instructions to remain seated for a duration of a 20-min period before the commencement of the examination. The participants had been provided with an explanation that the objective of the task was to move at the highest feasible speed for a duration of 6 min along a level 30-m corridor within the hospital facility. The assessment of heart rate and saturation of oxygen was conducted using pulse oximetry prior to, throughout, and following the test. Additionally, the evaluation of dyspnea and

fatigue throughout the test was performed using the Borg Scale. Participants were instructed to discontinue walking in the event of chest pain, acute shortness of breath, severe cramping of the muscles, excessive sweating, unsteady gait, or a pale or ashen complexion. They were also encouraged to resume walking as soon as possible. The distance traversed within the duration of 6 min was recorded, and the percentage anticipated was determined based on the formulas developed by Enright PL and Sherrill DL, as well as the Indian reference equation [11, 12].

#### Serum YKL 40

All participants provided a venous blood specimen comprising about 5 ml, left for 30 min to be coagulated, and then centrifuged for 10 min. The serum was collected within an Eppendorf tube and kept in a refrigerator at − 20 °C till analysis by enzyme-linked immunosorbent assay.

The kit employs a double-antibody sandwich ELISA technique to quantify the concentration of Human Chitinase-3-like Protein 1 (YKL-40/CHI3L1) in various specimens. Incorporate YKL-40/CHI3L1 into the monoclonal antibody enzyme properly, which has been previously coated with Human YKL-40/CHI3L1 monoclonal antibody, for the purpose of incubating. Next, the YKL-40/CHI3L1 antibodies, which have been labeled with biotin, are introduced and coupled with Streptavidin-HRP to create immune complexes. Subsequently, an incubation period is initiated, followed by a washing step to eliminate any remaining unbound enzyme. Next, introduce Chromogen Solution A and B to the mixture, resulting in an obvious alteration in the liquid's color to blue. Subsequently, upon the addition of an acidic substance, the color of the solution ultimately transitions to yellow. The color chroma and the Human Substance (YKL-40/CHI3L1) concentration in the sample exhibited positive results [15].

#### Statistical analysis

The statistical analysis was conducted using SPSS v27 (IBM©, Chicago, IL, USA). The normality of the data distribution was assessed using the Shapiro-Wilks test and histograms. The study offered quantitative parametric data in the form of mean and standard deviation (SD). These data were subjected to statistical analysis using the (ANOVA) test, followed by a post hoc test (Tukey) for further comparisons. The study utilized quantitative non-parametric variables, which was expressed as the median and interquartile range (IQR). Statistical analysis was performed using the Kruskal–Wallis test, followed by the Mann Whitney-test for comparing the different groups. The qualitative parameters were expressed in terms of frequencies and percentages (%) and were subjected to analysis using the chi-square test. A Spearman correlation analysis was conducted in order to assess the extent of correlation between the two parameters. A two-tailed $P$ value < 0.05 was considered statistically significant [16].

## Results

Regarding age, BMI, and history for ICU admission, they had been insignificantly various across the three groups. Smoking index and sputum were substantially greater in group A contrasted to group B and group C and they were significantly greater in group B contrasted to group C. History of previous hospital admission, wheezes, and CXR-positive signs were significantly higher in group A contrasted to both groups B and C and insignificantly different between group B contrasted to group C. $O_2$ saturation was substantially decreased in group A than in group C ($P$ value < 0.001) and was insignificantly different among group B, group A, and group C. Cough was significantly higher in group A contrasted to group C and group B than in group C ($P$ value < 0.001) and insignificantly different among group A and group B (Table 1).

mMRC Dyspnea Scale was substantially greater in group A contrasted to both groups B and C ($P$ value < 0.001) and insignificantly different among both groups B and C. The 6-min walking test was substantially decreased in group A contrasted to both groups B and C and lower in group B than group C ($P$ value < 0.001 and 0.006 respectively). Prebronchodilator FEV1, FVC, and FEV1/FVC ratio were substantially decreased in group A contrasted to both groups B and C ($P$ value < 0.001) and insignificantly different among group B and group C but prebronchodilator FEV1/FVC ratio was lower in group B contrasted to group C ($P$ value < 0.001) (Table 2).

FEV1/FVC ratio significantly increased in post-bronchodilator than prebronchodilator in group A ($P$ value < 0.05). The BODE index with mean value (± SD) of 5.56 (± 2.52). The degree of severity was 1 in 5 (13.89%) patients, 2 in 17 (47.22%) patients, 3 in 10 (27.78%) patients, and 4 in 4 (11.11%) patients (Table 3).

WBCs were insignificantly different among the three groups. Serum YKL-40 was substantially higher in group A contrasted to group C ($P$ value = 0.005) and insignificantly different among group B, group A, and group C (Table 4).

A substantial positive association existed among serumYKL-40 and the degree of severity and WBCs in group A (Table 5).

Serum YKL-40 cannot predict the severity of COPD ($P$ = 0.227 and AUC = 0.584) at cut-off > 0.394 with 80.65% sensitivity, 41.03% specificity, 52.1% PPV, and 72.7% NPV (Fig. 1).

**Table 1** Patient's demographic data, $O_2$ saturation, symptoms, and CXR among the three groups

| | | Group A ($n=36$) | Group B ($n=19$) | Group C ($n=15$) | *P* value | Post hoc |
|---|---|---|---|---|---|---|
| **Age (years)** | | 49.89 ± 10.7 | 49.42 ± 12.63 | 44.27 ± 9.22 | 0.237 | |
| **Sex** | **Male** | 36 (100%) | 19 (100%) | 15 (100%) | --- | |
| **Smoking index severity** | | | | | | |
| **Nonsmoker** | | 0 (0%) | 0 (0%) | 15 (100%) | **< 0.001*** | **P1 = 0.029*** **P2 < 0.001*** **P3 < 0.001*** |
| **Smoker** | **Mild** | 3 (8.33%) | 4 (21.05%) | 0 (0%) | | |
| | **Moderate** | 10 (27.78%) | 9 (47.37%) | 0 (0%) | | |
| | **Severe** | 23 (63.89%) | 6 (31.58%) | 0 (0%) | | |
| **BMI (kg/m$^2$)** | | 24.68± 4.92 | 26.38± 7.79 | 27.81± 2.89 | 0.169 | |
| **History of previous hospital admission** | | 9 (25%) | 0 (0%) | 0 (0%) | **0.007*** | **P1 = 0.019*** **P2 = 0.033*** P3 = 1 |
| **History of ICU admission** | | 5 (13.89%) | 0 (0%) | 0 (0%) | 0.080 | |
| **$O_2$ saturation (%)** | | 96.75± 1.66 | 97.47± 1.07 | 98.53± 0.64 | **0.001*** | **P1 = 0.152** **P2 < 0.001*** **P3 = 0.068** |
| **Symptoms** | | | | | | |
| **Cough** | | 31 (86.11%) | 13 (68.42%) | 0 (0%) | < 0.001 | **P1 = 0.191** **P2 < 0.001*** **P3 < 0.001*** |
| **Sputum** | | 31 (86.11%) | 10 (52.63%) | 0 (0%) | < 0.001 | **P1 = 0.006*** **P2 < 0.001*** **P3 < 0.001*** |
| **Wheezes** | | 29 (80.56%) | 5 (26.32%) | 0 (0%) | < 0.001 | **P1 < 0.001*** **P2 < 0.001*** **P3 = 0.11** |
| **CXR** | | | | | | |
| **Presence of COPD abnormalities** | | 36 (100%) | 2 (10.53%) | 0 (0%) | **< 0.001*** | **P1 < 0.001*** **P2 < 0.001*** **P3 = 0.157** |
| **Normal** | | 0 (0%) | 17 (89.47%) | 15 (100%) | | |

Data are presented as mean ± SD or number (%). *BMI*, body mass index; *ICU*, intensive care unit; *P1*, *P* value between group A and group B; *P2*, *P* value between group A and group C; *P3*, *P* value between group B and group C; *CXR*, chest X-ray; *COPD*, chronic obstructive pulmonary disease; *FEV1*, forced expiratory volume in the first second; *FVC*, forced vital capacity; *WBCs*, white blood cells

* Significant *p* value as ≤ 0.05

**Table 2** mMRC Dyspnea Scale, the 6-min walking test, and prebronchodilator spirometry among the three groups

| | Group A ($n=36$) | Group B ($n=19$) | Group C ($n=15$) | *P* value | Post hoc |
|---|---|---|---|---|---|
| mMRC dyspnea Scale | 3 (1–4) | 0 (0–1) | 0 (0–0) | **< 0.001*** | **P1 < 0.001*** **P2 < 0.001*** **P3 = 0.088** |
| Six-min walking test (m) | 136.66 (116.24–184.96) | 450 (144.15–632.5) | 700 (660–755) | **< 0.001*** | **P1 < 0.001*** **P2 < 0.001*** **P3 = 0.006*** |
| FEV1% | 48.76± 19.42 | 78.51± 21.77 | 94.68± 4.42 | **< 0.001*** | **P1 < 0.001*** **P2 < 0.001*** **P3 = 0.103** |
| FVC % | 72.33± 20.49 | 84.17± 23.22 | 99.9± 7.81 | **< 0.001*** | **P1 < 0.001*** **P2 < 0.001*** **P3 = 0.158** |
| FEV1/FVC ratio | 52.41± 10.89 | 73.84± 18.3 | 96.8± 17.17 | **< 0.001*** | **P1 < 0.001*** **P2 < 0.001*** **P3 < 0.001*** |

Data are presented as median (IQR) or mean ± SD. *mMRC*, modified Medical Research Council; *FEV1*, forced expiratory volume in the first second; *FVC*, forced vital capacity

* Significant as *p* value ≤ 0.05

**Table 3** Spirometry pre- and post-bronchodilator and severity of COPD according to BODE index and degree of severity of the group A

| Spirometry | | | |
|---|---|---|---|
| | **Prebronchodilator** | **Postbronchodilator** | ***P* value** |
| **FEV1%** | 48.76± 19.42 | 55.3± 20.2 | **< 0.001*** |
| **FVC%** | 72.33± 20.49 | 78.61± 20.36 | **< 0.001*** |
| **FEV1/FVC ratio** | 52.41± 10.89 | 55.09± 10.66 | **0.002*** |
| **Severity of COPD** | | | |
| **BODE index** | | 5.5 (3—6.5) | |
| **Degree of severity** | **1** | 5 (13.89%) | |
| | **2** | 17 (47.22%) | |
| | **3** | 10 (27.78%) | |
| | **4** | 4 (11.11%) | |

Data are presented as mean ± S Dor median (IQR). *FEV1*, forced expiratory volume in the first second; *FVC*, forced vital capacity; *COPD*, chronic obstructive pulmonary disease; *BODE*, body mass index, airflow obstruction, dyspnea, and exercise capacity

* Significant as *p* value ≤ 0.05

## Discussion

The present study revealed that serum YKL-40 level was substantially higher in the COPD group than healthy non-smokers. A substantial positive association existed among serum YKL-40 and degree of severity and WBCs. Serum YKL-40 could not predict the severity of COPD. No statistically substantial association existed among serum YKL-40 and BODE index in stable COPD individuals.

In the present study, smoking index was significantly higher in the COPD group than in smokers without COPD group and healthy non-smokers group ($P$ value = 0.029 and < 0.001 respectively) and smokers without COPD group contrasted to healthy non-smokers' group ($P$ value < 0.001). In concordance with our findings, Majewski et al. [8] did cohort research involving a total of 70 participants, comprising 40 COPD individuals and a control group that included 20 healthy smokers with at least a history of 10 pack-years smoke, and 10 healthy nonsmokers They discovered that those with COPD had a larger mean exposure to smoking when compared to healthy smokers ($P < 0.05$).

In the present study, CXR positive signs were substantially greater in the COPD group contrasted to smokers without COPD group and healthy non-smokers' group ($P$ value < 0.001) and insignificantly different among smokers without COPD group and healthy non-smokers group. The presence of COPD abnormalities was in all patients with stable COPD with different degrees of severity, in 2 (10.53%) patients in smokers without COPD group, and not in all patients in control group.

In agreement with our study, Yamada et al. [17] observed that COPD abnormalities in chest radiography were substantially greater in the COPD group contrasted to the non-smoker healthy volunteers' group.

In the present study, the mMRC Dyspnea Scale was substantially greater in the COPD group contrasted to smokers without COPD group and healthy non-smokers' group ($P$ value < 0.001) and insignificantly different among smokers without COPD group and healthy non-smokers group. In agreement with our study, Majewski et al. [8] revealed that the mMRC dyspnea scale was substantially greater among individuals with COPD contrasted to healthy nonsmokers' group and healthy smokers' group and insignificantly different among healthy nonsmokers' group and healthy smokers' group. Similarly, Xiong et al. [18] found that the mMRC Dyspnea Score was substantially greater in the COPD group contrasted to the control group.

In the present study, 6MWT was substantially decreased in the COPD group contrasted to smokers without COPD group and healthy non-smokers group and decreased in smokers without COPD group contrasted to healthy nonsmokers' group ($P$ value < 0.001 and 0.006 correspondingly). In agreement with our study, Majewski et al. [8] found that 6MWT was substantially decreased among individuals with COPD contrasted to healthy nonsmokers' group and healthy smokers' group ($P$ value < 0.001). Similarly, Xiong et al. [18] demonstrated that 6MWT was substantially lower in the COPD group contrasted to the control group.

In the present study, prebronchodilator FEV1 and FVC were substantially decreased in the COPD group contrasted to smokers without COPD group and healthy non-smokers' group ($P$ value < 0.001) and insignificantly different among smokers without COPD group

**Table 4** WBCs and serum YKL-40 among the three groups

| | **Group A (*n* = 36)** | **Group B (*n* = 19)** | **Group C (*n* = 15)** | ***P* value** | **Post hoc** |
|---|---|---|---|---|---|
| WBCs (cells/dL) | 6395.14± 1830.01 | 6963.16± 1729.55 | 6160± 1759.38 | 0.384 | |
| Serum YKL-40 (µg/L) | 0.542 (0.4–0.652) | 0.367 (0.335–0.579) | 0.589 (0.444–0.68) | **0.020*** | P1 = 0.257<br>**P2 = 0.005***<br>P3 = 0.121 |

Data are presented as mean ± S Dor median (IQR). *WBCs*, white blood cells. *Significant as *p* value ≤ 0.05

**Table 5** Correlation between serum YKL-40 and BODE index and degree of severity of the group A

| SerumYKL-40 (ng/L) | | |
|---|---|---|
| **BODE index** | ***P* value** | 0.246 |
| | ***r*** | 0.198 |
| **Degree of severity** | ***P* value** | **0.018*** |
| | **r** | 0.190 |
| **$O_2$ Saturation (%)** | ***P* value** | 0.889 |
| | ***r*** | 0.139 |
| **Smoking index** | ***P* value** | 0.065 |
| | ***r*** | −0.015 |
| **WBCs (cells/dL)** | ***P* value** | **0.004*** |
| | ***r*** | 0.400 |

*r*, Spearman coefficient; *WBCs*, white blood cells; *BODE*, body mass index, airflow obstruction, dyspnea, and exercise capacity

*Significant as *p* value ≤ 0.05

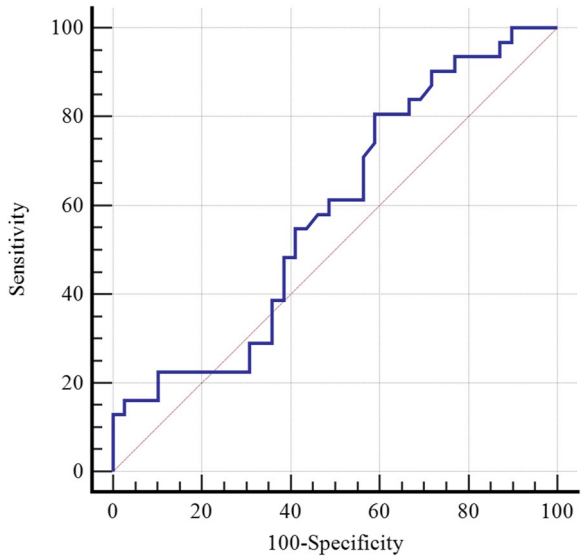


**Fig. 1** Serum YKL-40 in the prediction of severity of COPD

and healthy non-smokers' group. Our results were in line with Azab et al. [19] who showed that FEV1% was significantly decreased among individuals with COPD contrasted to the control group. Also, Majewski et al. [8] observed that FEV1% was substantially statistically decreased among individuals with COPD contrasted to the healthy nonsmokers' group and healthy smokers' group (*P* value < 0.001) and insignificantly different among healthy never-smokers group and healthy smokers group.

In the present study, prebronchodilator FEV1/FVC ratios were substantially decreased in the COPD group contrasted to smokers without COPD group and healthy non-smokers' group and decreased in smokers' group without COPD contrasted to healthy non-smokers' group (*P* value < 0.001). In line with our work, Majewski et al. [8] observed that FEV1/FVC ratio was substantially statistically decreased among individuals with COPD contrasted to the healthy never-smokers' group and the healthy smokers' group (*P* value < 0.001). Supporting our results, Letuve et al. [20] revealed that pre-$\beta_2$agonist FEV1/FVC (%) was substantially decreased among the COPD group contrasted to the healthy nonsmokers' group and currently heavy smokers lacking COPD group (*P* value < 0.0001).

In the present study, the FEV1/FVC ratio significantly increased in postbronchodilator than prebronchodilator in the COPD group (*P* value < 0.05). Supporting our results, Letuve et al. [20] found that the FEV1/FVC ratio increased in postbronchodilator than prebronchodilator in the COPD group.

In the present study, the BODE index in the COPD group ranged from 0 to 10 with mean value (± SD) of 5.56 (± 2.52). The degree of severity was 1 in 5 (13.89%) patients, 2 in 17 (47.22%) patients, 3 in 10 (27.78%) patients, and 4 in 4 (11.11%) patients. In agreement with our study, Majewski et al. [8] enrolled 40 COPD subjects and a control group. They observed that the BODE index in the COPD group ranged from 0 to 6 with a mean value of 1. Similarly, Xiong et al. [18] recruited a total of 409 patients (COPD group ($n = 368$) and control group ($n = 296$)). They found that the mean value (± SD) of BODE index (point) was 5.6 ± 2.7 in the COPD group.

In the present study, WBCs were insignificantly different among the three groups. Similarly, Xiong et al. [18] found that WBCs were insignificantly different among the COPD group and the controls.

In the present study, serum YKL-40 was substantially greater in the COPD group contrasted to the healthy non-smokers' group (*P* value = 0.005) and insignificantly different among smokers without COPD group and COPD group and healthy non-smokers' group. In agreement with our study, Zohrer et al. [21] found that the concentration of serum YKL-40 exhibited a statistically significant increase in males with COPD who were smokers, as in contrast to males who smoke lacking COPD ($p < 0.05$) and males who have never smoked and are in good condition ($p < 0.01$). Our findings are consistent with the observations made by Azab et al. [19], who reported a statistically substantial rise in blood YKL-40 levels in individuals who had COPD contrasted with the control group.

In the current work, there was no association among serum YKL-40 and BODE index, $O_2$ saturation, or smoking index in the COPD group. In accordance with our study, Majewski et al. [8] observed that no

association existed among serum YKL-40 and BODE index and smoking index in the COPD group. In disagreement with our findings, Azab et al. [19] found that a negative but non-significant association existed among $SaO_2$ and the serum YKL-40 level among individuals with COPD. This difference may be because of different sample sizes.

In the current work, a substantial positive association existed among serum YKL-40 and degree of severity and WBCs in the COPD group. In accordance with our study, Peng et al. [1] demonstrated that a substantial positive correlation existed between serumYKL-40 and WBCs in COPD patients. Supporting our results, Majewski et al. [8] observed that a substantial positive association existed among serumYKL-40 and neutrophils % in the COPD group. Similarly, Akboga et al. [22] carried out prospective cross-sectional work on 177 individuals with metabolic syndrome. They found that serum YKL-40 level was positively associated with WBC count ($r=0.251$, $p=0.001$).

In the present study, serumYKL-40 could not predict the severity of COPD ($P=0.227$ and AUC = 0.584) at cut-off > 0.394 with 80.65% sensitivity, 41.03% specificity, 52.1% PPV, and 72.7% NPV. In disagreement with our results, in a study conducted by Gumus et al. [23], it was observed that there exists a positive correlation between elevated blood YKL-40 levels and the severity of COPD. Their findings suggest that the measurement of serum YKL-40 levels may serve as a potential biomarker for the presence of hypoxemia and the deterioration of pulmonary function. This difference may be because of different sample sizes.

Limitations: single-center study, small sample size, observed impact of smoking cigarettes on the expression of chitinases presents a noteworthy factor that may pose a possible limitation to the investigation. Various comorbidities, which are frequently observed in individuals with COPD, are significant variables that may potentially impact the outcomes obtained.

## Conclusion

Serum YKL-40 was substantially greater in the COPD group compared to healthy non-smokers. There was no correlation between serum YKL-40 and BODE index, $O_2$ saturation, or smoking index in the COPD group. A significant positive association existed among serum YKL-40 and degree of severity and WBCs in the COPD group. SerumYKL-40 cannot predict the severity of COPD ($P=0.227$ and AUC = 0.584) at cut-off > 0.394 with 80.65% sensitivity, 41.03% specificity, 52.1% PPV, and 72.7% NPV.

### Abbreviations

| | |
|---|---|
| COPD | Chronic obstructive pulmonary disease |
| BODE | Body mass index, obstruction of airflow, dyspnea, and exercise capacity |
| BMI | Body mass index |
| WBCs | White blood cells |
| FEV1 | Forced expiratory volume in 1 s |
| ATS | American Thoracic Society |
| ERS | European Respiratory Society |
| HCgp-39 | Human cartilage glycoprotein-39 |
| CHI3L1 | Chitinase-3-like-1 protein. |
| GOLD | Global Initiative for chronic obstructive lung disease |
| 6MWT | 6-Minute walking |
| SD | Standard deviation |
| IQR | Interquartile range |

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None to declare.

### Authors' contributions

Study concept and design: A.E.F. and E.E.M.; analysis and interpretation of data: A.A.E. and H.A.E.; drafting of the manuscript: A.E.F.; critical revision of the manuscript for important intellectual content: A.E.F., E.E.M., and A.S.E.; statistical analysis: H.A.E.

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None to declare.

### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Declarations

### Ethics approval and consent to participate

The study was conducted after approval from the Ethics Committee of Alexandria University Hospitals, Alexandria, Egypt. Each participant provided informed written permission.

### Consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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