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# COMPARISON OF D-DIMER LEVELS IN SMOKES THAT SUFFER CHRONIC OBSTRUCTIVE PULMONARY DISEASE WITH SMOKES THAT DO NOT SUFFER CHRONIC OBSTRUCTIVE PULMONARY DISEASE

**Saut Adi H. Pane[1], Amira P. Tarigan[2] & Adi Koesoema Aman[1]**
[1]Departemen / SMF Patologi Klinik Fakultas Kedokteran Universitas Sumatera Utara / RSUP H. Adam Malik Medan
[2]Departemen / SMF Pulmonolgi Dan Respirologi Fakultas Kedokteran Universitas Sumatera Utara / RSUP H. Adam Malik Medan

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## Abstract
**Background:** Chronic obstructive pulmonary disease (COPD) is one of the main causes of morbidity and mortality worldwide. Because of the progressive decline in lung function, it seriously affects their quality of life and their ability to work. COPD is a chronic inflammatory disease characterized by hypercoagulation. A persistent inflammatory response can cause hypercoagulation, possibly through cytokine-induced endothelium activation or by monocyte induction to express tissue factors. D-dimers are a marker of ongoing fibrin formation and degradation.
**Methods:** Sampling was conducted during July 2019. Total population was 56 people (29 COPD patients and 27 non-COPD patients), the entire population was examined D-dimer, Spirometry and Brinkman index, then the results were compared in both populations. The study was conducted after obtaining ethical approval and informed consent.
**Results:** There was no difference in the Brinkman Index between the COPD and non-COPD groups with a value of p = 0.369 (p<0.05). There was a difference in FEV between the COPD and non-COPD groups with a value of p = 0,000 (p <0.05), where the COPD group had a lower FEV than the non-COPD group. There is a difference in D-Dimer levels between the COPD and non-COPD groups with a value of p = 0.003 (p <0.05). There is a difference in age between the COPD and non-COPD groups with a value of p = 0.001 (p <0.05), where the COPD group has a higher age than the non-COPD group
**Conclusions:** Increased D-Dimer levels, in stable COPD patients, can be used to assess a prognosis and as a treatment for determining treatment in hospital.

## Introduction

### Background
Chronic Obstructive Pulmonary Disease (COPD) is a disease condition that can be prevented and treated with characteristics in the form of limited breast flow that is not completely reversible (Arliny, 2015). Limitations of air flow are progressive and are associated with lung inflammatory reactions to particles or harmful gases, mainly caused by cigarette smoke. Chronic Obstructive Pulmonary Disease not only affects the condition of the lungs but also has important systemic consequences. A persistent inflammatory response can cause hypercoagulation, possibly through activation of endothelium induced by cytokines or by induction of monocytes to express tissue factors ((Zhang *et al*, 2016).

Chronic obstructive pulmonary disease is a major health problem with a high prevalence, morbidity and mortality. Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable lung disease that is characterized by respiratory symptoms and persistent airflow obstruction caused by significant exposure to harmful particles or gases (GOLD, 2019).

Based on the Burden of Obstructive Disease (BOLD) program it is estimated that the number of COPD was 384 million in 2010, with a global prevalence of 11.7% globally, with three million deaths annually. With the

increasing prevalence of smoking in developing countries, and the elderly population in high-income countries, the prevalence of COPD will increase in the next 30 years and in 2030 there are 4.5 million deaths each year from COPD associated with this condition (GOLD, 2019).

Granulocyte macrophage colony-stimulating factor (GM-CSF) activates leukocytes also prolongs the survival of these cellsin circulation and acts as a degranulation factor that increases tissue damage by granulocytes. Interleukin-1β is an acute cytokine reaction that increases the production of cytokines by many cells, stimulates hematopoesis, activates endothelial cells, which are pyrogenic and triggers acute phase responses. TNFα and IL-1 cytokines with IL-6.(Lichtman, 2000).

**Material and Methods:**
Sampling was conducted during July 2019. Total population was 56 people (29 COPD patients and 27 non-COPD patients), the entire population was examined D-dimer, Spirometry and Brinkman index, then the results were compared in both populations. The study was conducted after obtaining ethical approval and informed consent.

**Results:**
There was no difference in the Brinkman Index between the COPD and non-COPD groups with a value of p = 0.369 (p<0.05). There was a difference in FEV between the COPD and non-COPD groups with a value of p = 0,000 (p <0.05), where the COPD group had a lower FEV than the non-COPD group. There is a difference in D-Dimer levels between the COPD and non-COPD groups with a value of p = 0.003 (p <0.05). There is a difference in age between the COPD and non-COPD groups with a value of p = 0.001 (p <0.05), where the COPD group has a higher age than the non-COPD group.

***Table 1. Characteristics of Research Subjects***

| | Whole Subject (n=56) | COPD (n=29) | Non COPD (n=27) | *p value* |
|---|---|---|---|---|
| Gender, n(%) | | | | |
| Male | (100%) | (100%) | (100%) | |
| Age (years) | 59 ± 9.47 | 63.0 ± 10.06 | 54.9 ± 6.86 | <0.001* |
| FEV1 (%) | 86.3 ± 19.53 | 69.4 ± 12.79 | 103.1 ± 5.08 | <0.001* |
| Brinkman index | 351.6 ± 73.5 | 360.5 ± 78.7 | 342.8 ± 68.1 | 0.369 |

*) significant with the Mann Whitney test

There was a significant difference in the age of smokers who had COPD and those who did not (COP <0.05). Smokers who suffer from COPD are older (63.0 ± 10.06) compared to smokers who do not suffer from COPD (54.9 ± 6.86).

Table 1 also shows that the FEV1 value of smokers who experienced COPD was much lower (69.4 ± 12.79%) compared to smokers who did not experience COPD (103.1 ± 5.08), which is a statistically significant difference.

***Table 2.Differences in D-Dimer Levels in the COPD and non-COPD groups***

| | D dimer (mg/dl) | p |
|---|---|---|

| | Mean ± SD | Median (Min - Maks) | value |
|---|---|---|---|
| COPD | 158.8 ± 126.5 | 116 (10 - 441) | |
| Non COPD | 78.0 ± 104.3 | 56 (10 - 535) | 0.003* |

*) significant with the Mann Whitney Test

Table 2 shows that there are differences significant (p <0.05) D-dimer levels among smokers who have COPD and those who did not have COPD. Smokers with COPD have levels The D-dimer is much higher, which is almost double compared to that with smokers who did not experience COPD (median value of 116 mg / ml vs56 mg / ml).

***Table 3. Relationship of Age, Forced Expiratory Volume Value, and Brink Index with D-dimer Levels in Smokers***

| | | D-dimer | Median (Min-Maks) | *p value* |
|---|---|---|---|---|
| Umur (Years) | <50 | 149.3 ± 148.5 | 65.5 (14 – 535) | 0.29[a] |
| | 50-59 | 70.8 ± 66.4 | 52 (23 – 286) | |
| | ≥ 60 | 129.6 ± 126.2 | 73 (10 – 441) | |
| FEV1 (%) | ≥ 100 | 80.3 ± 112.7 | 56 (10 – 535) | 0.04[a] |
| | 80-99 | 139.4 ± 99.4 | 101 (10 – 286) | |
| | 50-79 | 160.2 ± 145.3 | 82 (19- 441) | |
| | 30-49 | 172 ± 71.7 | 95.5 (48 – 209) | |
| Brinkman Index | Mild (0-299) | 105.5 ± 114.1 | 56 (14 – 361) | 0.18[b] |
| | Moderate (300-599) | 125.1 ± 126.1 | 71 (10 – 535) | |

[a]) uji Kruskal Wallis

[b]) uji Mann Whitney

Table 3 shows that there is a significant relationship between indigo FEV1 and D-dimer levels in smokers. It is seen that the lower the FEV1 value of a smoker, the higher the smoker's D-dimer levels, and this difference is statistically significant (p <0.05).

Table 3 also shows that there is no relationship between the age of smokers and the amount of cigarette consumption (Brinkman Index) with D-dimer levels in smokers.

## Discussion

The study involved 56 male smokersmeet the inclusion and exclusion criteria, which consists of 29 people who have COPD and 27 non-COPD people. In this study 100% were male because researchers did not find female smokers. Price and Wilson, 2012 also said that COPD attacks men twice as many as women, presumably because men are heavy smokers. The incidence of COPD has increased 450% since 1950 and is now the fourth most common cause of death. (Price and Wilson, 2012).

The age of the patients in this study varied with the youngest sample 42 years and the oldest 86 years with a mean of 59.00 ± 9.47 years. This age is older than research data in Cairo, Egypt in 2016 which showed an average of 56.18 ± 11.15 years. (HA Abdelhalim, 2017).
In this study showed differences in levels of D-Dimer in the COPD and non-COPD groups, 60 smokers were analyzed, consisting of 30 people who suffered from COPD and 30 non-COPD people. From the two groups, there were significant differences between the two groups with a value of p = 0.002. This shows that the COPD group has higher D-Dimer levels compared to non-COPD ones. D-dimers are the final product of cross-linked fibrin degeneration by plasmin's work activity in the fibrinolytic system. Since 1990, the D-dimer test has been used to examine thrombosis. Positive examination results indicate the presence of a thrombus, but can not indicate the location of the abnormality and rule out other potential etiologies (Rahajuningsih, 2007).

D-dimer is a marker of fibrin formation and ongoing degradation, D-dimer itself is the most commonly used clinical trial to detect the activation of the coagulation system. D-dimers are also acute phase reactants whose production stimulates high levels of cytokines such as IL-6 and IL-1. Finally, D-dimers and other fibrin degradation products can also influence the inflammatory and acute phase responses by promoting the activation of neutrophils and monocytes, which encourage the release of IL-6. So D-dimer can be used as a marker of inflammation for several diseases (Ismir, 2018).

Research by Liu et al, 2016 also found a significant relationship between levels of D-dimer and fibrinogen in patients with acute exacerbation of COPD with stable phase COPD and healthy control groups, where P <0.05 (Liu, 2016). COPD patients were associated with higher D-dimer levels than control subjects. This shows that the level of D-dimer is increased in patients with COPD which are exacerbated regardless of the presence of Deep vein thrombosis (DVT) or deep venous thromboembolism (Ismir, 2018).

This study is also similar to the study conducted by Hesham, 2016 found that D-Dimer levels were higher in patients with COPD compared with the control group with a value of p = 0.001. Systemic inflammation associated with COPD, specifically the inflammatory response in acute exacerbation of COPD, is the result of an endothelial coagulation system and protrombotic conditions that change the blood coagulation status. (HA Abdelhalim, 2017).

## Conclusion

In this study, a significant difference in D-Dimer levels was found in the COPD and non-COPD groups with p = 0.003. The COPD group had higher D-Dimer levels compared to the non-COPD group. Age differences were found between the COPD and non-COPD groups, where the COPD group had a higher age than the non-COPD group. The difference in FEV was found between the COPD and non-COPD groups, where the COPD group had a lower FEV than the non-COPD group. There is no difference in the Brinkman Index between the COPD and non-COPD groups.

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