Jurnal Ners Volume 9 Nomor 3 Tahun 2025 Halaman 3719 - 3725
JURNAL NERS
Research & Learning in Nursing Science
http://journal.universitaspahlawan.ac.id/index.php/ners

TYPE 2 DIABETES MELLITUS AND PULMONARY FUNCTION IMPAIRMENT

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Abstract

Diabetes mellitus (DM) is a disease that can lead to complications in other organs, such as the lungs, which typically manifest after three years of DM onset. Mild symptoms often reduce public vigilance. Information and research on this topic are still rare. This study aims to determine the relationship between type 2 DM and pulmonary function disorders in individuals aged 40-65 years. This quantitative study employs a cross-sectional design. A total of 2,414 respondents were randomly selected. Cox regression analysis was used. The proportion of pulmonary function disorders in type 2 DM patients was 48.8%. A significant relationship was found, with a prevalence ratio of 1.99 (1.67-2.37; p=0.000) after controlling for age, sex, and smoking degree. Increasing awareness of pulmonary function testing in type 2 DM patients is an important consideration for preventing further complications.

Keywords: *Diabetes Mellitus; Pulmonary Function; Non-Communicable Diseases*

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INTRODUCTION

With the increase in social and economic status, lifestyle changes, and rising life expectancy, Indonesia is experiencing a shift in disease patterns from infectious to non-communicable diseases. In recent years, the trend of increasing prevalence of non-communicable diseases has become more evident, one of which is diabetes mellitus (DM). In Indonesia, Riskesdas data shows an increase in the prevalence of diabetes from 6.9% in 2013 to 8.5% in 2018.[1] Similarly, data from the International Diabetes Federation (2021) indicates that the estimated number of people with diabetes in Indonesia was around 19.5 million in 2021, projected to rise to 28.6 million by 2045.[2]

Type 2 DM is a significant health issue and requires special attention due to its short-term and long-term complications. These complications impact life expectancy, increase morbidity due to complications affecting other organs, and decrease the quality of life. Chronic diabetes complications can affect all organ systems, including the respiratory system.[3] Complications that can arise in the lungs of diabetes mellitus patients include pulmonary function impairment, reduced vital capacity, total lung capacity, decreased CO2 diffusion capacity, reduced CO2 transport factor, decreased maximum oxygen uptake, respiratory muscle decline, left ventricular abnormalities, pleural effusion, obstructive sleep apnea, infection, poor prognosis for community-acquired pneumonia, increased risk of aspiration pneumonia, mucormycosis infection, and tuberculosis.[4]

Pulmonary dysfunction is a condition where several lung functions are affected, leading to decreased pulmonary function. This decline can be observed through the examination of lung vital capacity.[5] Pulmonary dysfunction is categorized into two types: restrictive and obstructive pulmonary disorders. Some cases also show mixed pulmonary disorders, a combination of obstruction and restriction. Pulmonary function assessment can highlight issues in the ability to generate optimal ventilation. The results of this assessment are crucial for diagnosis, monitoring, and screening. The tool used is spirometry. Restrictive lung disorders are indicated by a forced vital capacity (FVC) value < 80%. Obstructive lung disorders are indicated by a forced expiratory volume in one second (FEV1) compared to FVC (FEV1/FVC) < 75%.[6 7]

The impact of DM on the lungs is not yet fully understood. Microangiopathy complications from DM can affect blood vessels in the alveoli. However, due to their significant reserve, microvascular loss can be tolerated without causing breathing difficulties. Consequently, the presence of diabetic microangiopathy in the lungs often goes unnoticed in clinical settings. The prevailing theory suggests that non-enzymatic protein glycosylation in lung tissue and the chest wall is responsible. This process reduces collagen's sensitivity to proteolysis, resulting in its accumulation in the lungs. Over time, this collagen buildup can lead to restrictive lung disorders, causing the lung parenchyma and chest wall to become stiff.[8]

Data showing the extent of pulmonary dysfunction in type 2 DM patients in Indonesia has not been found by researchers. Several studies on the lungs as a target organ for complications in DM patients have been conducted for a long time but have not provided conclusive results, making it an interesting issue to investigate further. Schuyler et al. (1976) were the first to conduct pulmonary function tests on 11 DM patients aged 21-28 years, including spirometry, carbon monoxide (CO) diffusion, lung elasticity, and airway resistance tests. Lung elasticity was reported to be decreased compared to the control group. Sandler et al. (1987) found similar results in DM patients aged 15-60 years, with decreased pulmonary blood flow and CO diffusion capacity. However, these studies cannot be used as references due to different age samples. Recent studies examining differences in lung function in diabetic patients still show inconsistent results.[9]

Pulmonary dysfunction has not received serious attention either as a direct or indirect result of type 2 DM compared to other body organs. Unfortunately, public awareness of pulmonary dysfunction is still relatively low. This may be because symptoms are often considered trivial, such as cough and shortness of breath. In fact, lung complications from chronic hyperglycemia can also increase morbidity in DM patients. Early detection of lung abnormalities in DM can provide important information about disease prognosis, especially the emergence of more severe advanced complications. Research reports on the impact of type 2 DM on the lungs in Indonesia are also rare. Therefore, researchers want to explore the relationship between pulmonary dysfunction and type 2 DM patients further.

METHOD

This research is an analysis of baseline data from the 2011-2012 Cohort Study on Non-Communicable Diseases (NCD) using a cross-

sectional study design. The baseline data were collected from five sub-districts within the city of Bogor: Kebon Kelapa, Babakan Pasar, Ciwaringin, Panarangan, and Babakan.

The population for this study consists of all adults aged 40-65 who have an identity card (KTP) and a permanent residence (owned by the household head or themselves) in Central Bogor district. The sample units in this study are all households selected through simple random sampling in chosen neighborhoods (RT), which were previously selected using proportional random sampling based on the number of RTs in each RW, sub-district, and district in one regency. All household members from the randomly selected households in the chosen RTs will be the subjects/samples for the cohort study on NCD risk factors in Central Bogor District, Bogor City. Exclusion criteria include suffering from other respiratory diseases caused by infection or other factors such as tuberculosis, lung cancer, etc., lacking complete data related to covariate variables, and being pregnant. The total number of respondents selected as the research sample was 2,414.

Data collection for the study was conducted through annual surveillance of NCD risk factors, which has been ongoing since 2011. Data collection for surveillance activities was carried out using questionnaires and the WHO Step Approach method. Data collected through the WHO Step Approach for surveillance of NCD risk factors meets medical standards.

The analysis used in this study is Cox Regression with the assumption of constant time. This analysis process was conducted to estimate the relationship between type 2 DM and pulmonary function impairment after controlling for several covariate/potential confounder factors. The model used is Hierarchically Backward Elimination. The measure of association is the Prevalence Ratio and precision with a 95% confidence interval range

RESULTS AND DISCUSSION

Results

Pulmonary function impairment in this study was determined by measuring the Forced Vital Capacity (FVC) percentage and the Forced Expiratory Volume in One Second (FEV1)/FVC ratio using a spirometer, while blood glucose levels were measured using fasting blood glucose and 2-hour post-load blood glucose tests. The prevalence rate of pulmonary function impairment overall was found to be 26.0% (24.3 – 27.8). When broken down by the type of pulmonary function impairment experienced by respondents, obstructive pulmonary function impairment had the largest proportion, at 14.2%, compared to other types of pulmonary function impairment. Meanwhile, the prevalence of type 2 diabetes mellitus in this study was 15.3% (13.8 – 16.7) (Table 1).

In Table 2, the physical activity variable showed no association with pulmonary function impairment ($p > 0.05$), whereas all other variables were statistically associated. Subsequently, all variables were included in the model as potential confounding variables analyzed using Cox regression analysis. From the analysis results, it was found that all suspected confounding variables did not show statistically significant changes in PR before and after testing, > 10% in each variable. Thus, the final model obtained is as shown in Table 3.

From Table 3, the final model of the relationship between type 2 diabetes mellitus and pulmonary function impairment was obtained after controlling for age, gender, and smoking status. The prevalence ratio obtained was 1.99 (1.67-2.37), indicating that the occurrence of pulmonary function impairment in type 2 diabetes mellitus patients is 1.99 times higher compared to respondents who do not have type 2 diabetes mellitus.

Table 1. Frequency Distribution of Pulmonary Function Impairment and Type 2 Diabetes Mellitus

Variable	Total		SE	95%CI
	N	%		
Pulmonary Function Impairment	628	26,0	0,9	24,3 – 27,8
Normal	1.786	74,0	0,9	72,2 – 75,7
Based on the Type of Pulmonary Function Impairment				
1. Restriction	216	8,9	0,6	7,9 – 10,1
2. Obstruction	343	14,2	0,7	12,5 – 13,6
3. Restriction and Obstruction	69	2,9	0,3	2,2 – 3,5
4. Normal	1.786	74,0	0,9	72,2 – 75,6
Diabetes mellitus				
Diabetes mellitus	369	15,3	0,8	13,8 – 16,7
Normal	2.045	84,7	0,8	83,3 – 86,2
Total	2.414	100,0	-	-

Table 2. The Inclusion of Pulmonary Function Impairment into the Model as a Potential Variable with Other Variables

Variable	p-value	PR	95%CI	
			Lower	Upper
Diabetes melitus	0,000	1,99	1,67	2,37
Age	0,000	1,44	1,22	1,69
Gender	0,000	1,38	1,16	1,66
Degree of Smoking	0,000	1,37	1,17	1,61

Table 3. Final Model of the Relationship Between Type 2 Diabetes Mellitus and the Incidence of Pulmonary Function Impairment with Confounding Variables

Variable	Pulmonary Function Impairment		Normal		PR (95% CI)	p-value
	n	%	n	%		
Diabetes Melitus						
- Diabetes	180	48,8	189	51,2	2,22 (1,95 – 2,54)	0,000
- Normal	448	21,9	1.597	78,1		
Gender						
- Men	294	36,2	518	63,8	1,24 (1,17 – 1,31)	0,000
- Women	334	20,8	1.268	79,2		
Age						
- ≥ 50 years	392	32,1	831	67,9	1,62 (1,41 – 1,86)	0,000
- < 50 years	236	19,8	955	80,2		
Smoking Status						
- Active Smoker	213	33,0	432	67,0	1,41 (1,18 - 1,67)	0,000
- Former Smoker	107	35,1	198	64,9	1,49 (1,22 – 1,83)	0,000
- Passive Smoker	141	18,8	611	81,3	0,79 (0,65 – 0,97)	0,016
- Not smoking	167	23,5	545	76,5	1,00	-
Duration of Smoking						
- > 20 years	223	36,3	392	63,7	1,63 (1,42 – 1,86)	0,000
- 11 - 20 years	34	28,1	87	71,9	1,27 (0,94 – 1,71)	0,067
- < 10 years	371	22,1	1.307	77,9	1,00	-
Number of Cigarettes Smoked						
- > 24 cigarettes	28	51,9	26	48,1	2,17 (1,66 – 2,83)	0,000
- 11 – 24 cigarettes	97	38,2	157	61,8	1,59 (1,34 – 1,90)	0,000
- < 10 cigarettes	503	23,9	1603	76,1	1,00	-
Degree of Smoking						
- Heavy Smoker	31	60,8	20	39,2	2,74 (2,06 – 3,28)	0,000
- Moderate Smoker	111	38,1	180	61,9	1,71 (1,37 – 1,92)	0,000
- Light Smoker	486	23,5	1.586	76,5	1,00	-
Physical Activities						
- Light	221	27,5	583	72,5	0,87 (0,66 – 1,15)	0,202
- Moderate	387	24,7	1.116	75,3	0,78 (0,59 – 1,03)	0,060
- Heavy	40	31,5	87	68,5	1,00	-
Pollutant Status						
- Exposed	146	30,2	338	69,8	1,21 (1,03 – 1,42)	0,021
- Not Exposed	482	25,0	1.448	75,0		

Discussion

The findings of this study align with several previous studies. However, information on research related to the relationship between type 2 diabetes mellitus and pulmonary function impairment, specifically to determine the risk or association, has not been extensively conducted by other researchers, nor have similar studies been found by the researchers themselves. In this context, alignment refers to research results indicating a decrease in the average presentation of FVC and FEV1/FVC in individuals with type 2 diabetes compared to normal individuals.

Similar studies have shown that the mean FVC value is higher in the controlled diabetes group compared to the uncontrolled diabetes group, with means of 90.6 ± 7.5% predicted versus 82.5 ± 10.7% predicted, respectively, with a t-test result (P = 0.001), indicating a significant difference in the decrease of FVC percentage in controlled and uncontrolled diabetes [10]. Other studies have found that individuals with type 2 diabetes significantly reduce FVC and FEV1 with p-values of 0.01 and 0.04, respectively. Similarly, a study by Tri Setiana (2014) found that research subjects with hyperglycemia had lower FEV1 and FVC compared to normal subjects, with 16.7% experiencing obstructive pulmonary function impairment and 22.67% experiencing restrictive impairment.

Findings from The Copenhagen City Heart Study showed a significant decrease in FEV1 values in individuals with diabetes compared to the control group, with a reduction of 25 ml. This decrease is closely related to the severity of hyperglycemia, duration of diabetes, intensity of antidiabetic treatment, and smoking habits. Notably, the impact of diabetes and high blood sugar levels on lung function is particularly evident in smokers, suggesting a reciprocal relationship between these factors.[11]

The relationship between decreased lung function and diabetes has been discussed for many years. Although this relationship is not yet fully understood and remains an interesting issue for research, the characteristics of diabetes-related pulmonary complications are not entirely clear. Pulmonary function impairment in individuals with diabetes mellitus is believed to be due to chemical changes associated with the tissue constituents of the lungs, primarily collagen and elastin, and microangiopathy caused by non-enzymatic glycosylation of proteins induced by chronic hyperglycemia.[8]

The prevailing theory is non-enzymatic glycosylation of proteins in lung tissue and the chest wall. Non-enzymatic glycosylation is a process where glucose chemically attaches to free amino acids without the aid of enzymes. The degree of glycosylation corresponds to glucose levels. The result of glycosylation, which includes collagen and other long-term proteins in the interstitial tissue and blood vessel walls, will chemically convert to advanced glycosylation end products (AGEs) that accumulate in blood vessels. AGEs have pathogenic chemical and biological properties affecting the cellular matrix and target cells in diabetes complications. The formation of AGEs in proteins like collagen causes cross-linking between polypeptides and non-glycosylated plasma and interstitial proteins.[12] This makes collagen less sensitive to proteolysis, leading to its accumulation in lung tissue. Over time, restrictive lung impairment can occur due to increased collagen buildup, causing stiffness in lung parenchyma and the chest wall. This process also damages the elastin fibers in the airway walls. Elastin is a protein that maintains the elasticity of the airway and lung walls. Damage to elastin affects the extracellular matrix of lung parenchyma, resulting in increased collagen fibers as a consequence of pulmonary connective tissue remodeling and loss of lung elasticity. This leads to reduced lung compliance and recoil capacity.

In this study, age, gender, and smoking status were included in the final analysis model as confounding factors in the relationship between type 2 diabetes and pulmonary function impairment. Age affects lung elasticity similarly to other body tissues. Although the relationship between age and lung volume cannot be detected, aging significantly changes lung volume. This aligns with the concept of lung elasticity. Lung function increases with age, reaching an optimal point between 22-30 years old. After this point, there is a decline; after reaching the young adult stage, lung diffusion, ventilation, oxygen uptake, and all lung parameters decrease with age. Physiologically, as age increases, the function of body organs naturally declines, including pulmonary function, specifically lung vital capacity.[12] This condition worsens with exposure to dusty environments or other factors such as smoking habits and low physical activity. On average, at the age of 30-40 years, individuals experience a decline in lung function, and as age increases, the impairment becomes more significant. The older an individual gets, the higher the likelihood of respiratory disorders. Energy needs increase until they decline after age 40 due to decreased physical strength.

The relationship between gender and lung function is strong because men require more oxygen than women.[14] Men have more energy compared to women, and their lung vital capacity is also larger, whereas women have about 20-25% smaller vital capacity.[15] However, the relationship between gender and pulmonary function impairment is influenced by other factors, such as smoking habits. Female smokers experience more severe lung function impairment compared to male smokers.[16] This exacerbates the impact of lung function in diabetes mellitus patients. Additionally, women with diabetes mellitus are at higher risk for severe lung function impairment due to hormonal factors, such as premenstrual syndrome and post-menopause, which cause body fat distribution to accumulate more easily due to these hormonal processes.[17]

The smoking degree factor in this study considers the duration and number of cigarettes smoked. Cigarette smoke stimulates mucus secretion, and nicotine paralyzes cilia, hindering airway cleaning functions. Consequently, mucus secretion accumulates, leading to coughing, excessive phlegm, and shortness of breath.[18] The effect of smoking habits on lung capacity shows that the more cigarettes smoked per day, the more restrictive the pulmonary function impairment. Lung function status is influenced by the number of cigarettes smoked by workers. The more cigarettes smoked, the more abnormal the lung function becomes, and vice versa.[19] Cigarettes contain several compounds harmful to lung health. These compounds can deposit in the lungs and cause physiological changes.[20] Smoking habits affect lung capacity, worsened by high dust levels, increasing the likelihood of pulmonary function impairment in workers.[21] The number of cigarettes smoked daily also affects lung function. The more cigarettes smoked, the more deposits accumulate in the lungs, narrowing the airways for inhalation and exhalation.[22] Additionally, long-term exposure to toxins in cigarettes accumulates in the body, disrupting oxygen and carbon dioxide exchange in the alveoli and, in severe cases, causing alveolar damage.

Research shows a dose-response relationship between smoking habits and low levels of FEV1/FVC and FVC 25-75%, with smoking 10 cigarettes per day being associated with a reduction in FVC 25-75% compared to non-smokers. The decrease in lung function in normal, non-smoking adults is around 20-30 ml/year, while for smokers, it is about 30-40 ml/year. There is a clear relationship between the number of cigarettes smoked annually and the duration of smoking with lung function. According to the Indonesian Ministry of Health, the annual decline in forced expiratory volume is 28.7 ml for non-smokers, 38.4 ml for former smokers, and 41.7 ml for active smokers. The impact of cigarette smoke can be greater than that of dust, with the latter contributing to only about one-third of the harmful effects of smoking.[24]

CONCLUSIONS

There is a relationship between type 2 diabetes mellitus (DM) and pulmonary function impairment, with an association prevalence ratio of 1.99 (1.67-2.37). This means that the occurrence of pulmonary function impairment in type 2 DM patients is 1.99 times higher compared to respondents without type 2 DM after controlling for age, gender, and smoking degree variables.

The high prevalence of pulmonary function impairment in type 2 DM patients warrants special attention. This study's results demonstrate a strong relationship between type 2 DM and pulmonary function impairment. Therefore, pulmonary function tests for type 2 DM patients are highly recommended, either through elderly health service programs (Posbindu) or other health

service centers, as a preventive measure. Public awareness regarding pulmonary function impairment, especially among type 2 DM patients, should be heightened, encouraging early check-ups before or after experiencing signs and symptoms of pulmonary function impairment.

Additionally, it is crucial for the community to start implementing the CERDIK behavior (Regular health checks, Avoid cigarette smoke, Active physical activities, Healthy and balanced diet, Adequate rest, and Stress management) to independently and sustainably control other NCD risk factors.

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