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# The Relationship Between Smoking Status And Diabetic Foot Severity

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## Abstract

**The Association Between Smoking Status and Severity Degree of Diabetic Foot**. Diabetes mellitus is a chronic metabolic disease which happens to be the 7$^{th}$ leading cause of death worldwide. In Indonesia, 6.9% of population aged ≥ 15 years old suffers from this disease. Diabetic foot is one of the complication of diabetes mellitus which has high mortality and morbidity level. Smoking is an addictive behavior that is really common in Indonesia. Components inside a cigarette, such as nicotine, can contribute in determining the prognosis of diabetic foot through various mechanism. This study aims to investigate the association between smoking status and the severity degree of diabetic foot. This study is an observational analytic study using a cross-sectional approach. Data collection was conducted on January 2019 until July 2019 in RSUK Pesanggrahan and Atma Jaya Hospital Jakarta. The research data was obtained through interviews with diabetic foot patients and medical record reading. Data was analyzed using the chi-square method. There were 40 patients eligible to be the subject of this study. The smoker status with the most distribution was moderate smoker (27.5%) and severity degree of diabetic foot with most distribution was Wagner 3 (25%). Bivariate analysis showed that there was a significant association between smoking status and severity degree of diabetic foot ($p < 0.001$). In conclusion, there is a significant association between smoking status and the severity degree of diabetic foot. Therefore, education regarding the importance of smoking cessation to diabetic foot patients should be done in order to improve the prognosis of diabetic foot patients.

**Keywords**: *Brinkman Index, diabetic foot, smoking status, Wagner*

## 1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disease which is the 7th leading cause of death in the world.[1] In Indonesia, 6.9% of the population aged ≥ 15 years suffer from DM.[2] The pathophysiology of DM causes sufferers to often experience complications that can affect various organs. One form of complication that most often causes DM sufferers to be hospitalized is *diabetic foot. Diabetic foot* greatly affects patient morbidity and mortality, causing around 90.000 amputations per year.[3]

Smoking is an addictive behavior that is often found everyday. Approximately 39% of Indonesia's population has a smoking habit and Indonesia is also the country with the third highest number of smokers in the world.[4] Smoking can aggravate *diabetic foot* through various mechanisms such as inflammation and increased oxidative stress. This can interfere with the wound healing process and increase the risk of amputation.[5.6]

The relationship between smoking and *diabetic foot* is still not fully understood. To date, there have not been many studies that specifically discuss the relationship between smoking status and severity of *diabetic foot,* therefore, researchers conducted a study to better understand the relationship between smoking status and the severity of *diabetic foot*.

## 2. Method

This research is an analytic observational study with a cross sectional study. The subjects of this study were *diabetic foot* patients at Pesanggrahan Hospital and Atma Jaya Hospital, Jakarta. Sampling was done by *consecutive sampling.*

Data were collected by means of interviews with subjects and also reading medical records. *Diabetic foot* data is taken based on Wagner's classification, namely *Wagner* 1 *to Wagner* 5, while smoking status data is taken based on the Brinkman Index, which is the result of the multiplication of smoking duration in years and the number of cigarettes smoked per day. The data obtained were non-smokers (Brinkman Index 0), light smokers (Brinkman Index 1-200), moderate smokers (Brinkman Index 201-600), and heavy smokers (Brinkman Index > 600).

The data obtained will be analyzed and processed using SPSS version 23.0. Univariate analysis was performed to see patient characteristics. Bivariate analysis using the *chi square test* was carried out to see the relationship between the independent variables and the dependent variable

## 3. Results

During the study period, there were 43 *diabetic foot* patients at RSUK Pesanggrahan and Atma Jaya Hospital. Of the 43 patients, there were 40 patients who met the study criteria and could become the subject of this study (3 patients could not be classified as smoking status based on the Brinkman Index).

Characteristics of the subjects can be seen in **Table 1.** Obtained subjects were 24-71 years old with a median age (min-max) of 57 (24-71). Most of the subjects (52.5%) were included in the pralant group (45-49 years). Male subjects (75%) were more than female subjects (25%). Most of the subjects (97.5%) were found to be married, while 2.5% of the subjects were unmarried. Subjects belonging to the *underweight* category were 2.5%, the normal category was 30%, the *overweight* category was 20%, and the obesity category was 47.5%. Subjects suffering from hypertension were 15% and subjects suffering from dyslipidemia were 7.5%. 70% of subjects were smokers, while 30% of subjects did not smoke.

DM characteristics of patients can be seen in **Table 2.** Based on the results of interviews and medical records, it was found that 75% of the subjects had a family history of DM, while 25% of the subjects had no family history of DM. The onset of DM from the subject was at most 5-10 years (47.5%). As many as 82.5% of the subjects suffered from

other complications from DM. Based on the type of complication, 82.5% of the subjects had neuropathy, 5% of the subjects had retinopathy, 2.5% of the subjects had nephropathy, and 52.5% of the subjects had PAD. Subjects who received DM treatment in the form of Oral Hypoglycemic Drugs (OHO) were 55%, while 45% of subjects received combination treatment (insulin and OHO). Based on the classification of the level of DM control by PERKENI, 85% of the subjects were patients with DM that had not been well controlled.

**Table 3.** Shows the smoking status distribution of the subjects based on the Brinkman Index. 30% of the subjects did not smoke, 22.5% were light smokers, 27.5% were moderate smokers, and 20% were heavy smokers.

**Table 4.** shows the distribution of the severity of *diabetic foot* according to the *Wagner* classification. 22.5% of the subjects belonged to *Wagner 1,* 15% of the subjects belonged to *Wagner 2,* 25% of the subjects belonged to *Wagner 3*, 20% of the subjects belonged to *Wagner 4,* and 17.5% of the subjects belonged to *Wagner 5*.The highest severity of *diabetic foot* in patients was *Wagner 3.*

**Table 5.** shows the relationship between smoking status and the severity of *diabetic foot.* Results of statistical data analysis using *chi square,* obtained *p value* <0.001, which means that there is a significant relationship between smoking status and the severity of *diabetic foot*.

**Table 1. Distribution of Subjects Based on Data Demographics**

| Characteristic of Subjects | Value |
|---|---|
| **Age (years). median (min-max)** | 57 (24-71) |
| **Age Group * (years). n(%)** | |
| <45 years | 4 (10) |
| 45-59 years (pralansia) | 21 (52.5) |
| 60-69 years (young elderly) | 12 (30) |
| ≥ 70 years (middle elderly)) | 3 (7.5) |
| **Gender. n (%)** | |
| Male | 30 (75) |
| Female | 10 (25) |
| **Marital Status. n(%)** | |
| Single | 1 (2.5) |
| Married | 39 (97.5) |
| **BMI ** (Kg/m$^2$). n (%)** | |
| Underweight (BMI < 18.5 kg/m$^2$) | 1 (2.5) |
| Normal (BMI 18.5 – 22.9 kg/m$^2$) | 12 (30) |
| Overweight (BMI23 – 24.9 kg/m$^2$) | 8 (20) |
| Obesity (BMI ≥ 25 kg/m$^2$) | 19 (47.5) |
| **Hypertension** | |
| Yes | 6 (15) |
| No | 34 (85) |
| **Dyslipidemia** | |
| Yes | 3 (7.5) |
| No | 37 (92.5) |
| **Smoker** | |
| Yes | 28 (70) |
| No | 12 (30) |

* Based on the 2014 Central Bureau of Statistics

** Asia Pacific IMT criteria based on *World Health Organization (WHO)*

**Table 2. Distribution of Subjects Based on the Characteristics of Diabetes Mellitus**

| Characteristics of subject | Value |
|---|---|
| **Family history of DM. n (%)** | |
| Yes | 30 (75) |
| Not | 10 (25) |
| **Onset of DM (years). median (min-max)** | 6.5 (1-27) |
| **DM onset (year). n (%)** | |
| <5 years | 14 (35) |
| 5-10 years | 19 (47.5) |
| > 10 years | 7 (17.5) |
| **DM complications. n (%)** | |
| Neuropathy | 33 (82.5) |
| Retinopathy | 2 (5) |
| Nephropathy | 1 (2.5) |
| PAD | 21 (52.5) |
| **DM Treatment Status. n (%)** | |
| Oral Hypoglycemic Drugs (OHO) | 22 (55) |
| Combination (OHO + Insulin) | 18 (45) |
| **Fasting Blood Glucose Level (mg / dL). median (min-max)** | 166.5 (69-456) |
| **DM management based on PERKENI (mg / dL). n (%)** | |
| Good (Fasting Blood Glucose 80-130 mg / dL) | 6 (15) |
| Not good | 3 (85) |

**Table 3. Subject Distribution Based on Smoking Status**

| Smoking Status (Index of Brinkman) | Frequency n (%) |
|---|---|
| No Smoking (0) | 12 (30%) |
| Light smoker (1-200) | 9 (22.5) |
| Medium smoker (201 – 600) | 11 (27.5) |
| Heavy smoker ( > 600 ) | 8 (20) |

**Table 4. Distribution of Subjects by Degree of Diabetic Foot Severity**

| Degree of severity Diabetic foot | Frequency n (%) |
|---|---|
| *Wagner 1* | 9 (22.5 %) |
| *Wagner 2* | 6 (15%) |
| *Wagner 3* | 10 (25%) |
| *Wagner 4* | 8 (20%) |
| *Wagner 5* | 7 (17.5) |

**Table 5. The Relationship Between Smoking Status and Diabetic Foot Severity**

| Smoking Status | *Degree of severity Diabetic foot (Wagner)* | | | | | P value |
|---|---|---|---|---|---|---|
| | 1 N (%) | 2 N (%) | 3 N (%) | 4 N(%) | 5 N(%) | |
| No smoking | 3 (25) | 2 (16.7) | 2 (16.7) | 3 (25) | 2 (16.7) | 0.000 |
| Light smoker | 6 (66.7) | 3 (33.3) | 0 (0) | 0 (0) | 0 (0) | |
| Moderate smoker | 0 (0) | 1 (9.1) | 8 (72.7) | 2 (18.2) | 0 (0) | |
| Heavy smoker | 0 (0) | 0 (0) | 0 (0) | 3 (3.75) | 5 (62.5) | |

## 4. Discussion

### Subject Demographic Characteristics

From the collected subjects, the age range was between 24-71 years with the most age group being pralants (45-59 years), namely 52.5%. Research by Fitria *et al.,* In Banda Aceh City states that the majority of people with *diabetic foot* are in the age range of 56-65 years and are followed by an age range of 46-55 years.[7] Systemic functional decline with increasing age increases the risk of complications from DM such as neuropathy, PAD, and the vulnerability of a DM sufferer. This can be attributed to the increasing prevalence of *diabetic foot* with increasing age[8]

More subjects were male (75%) than female (25%). Research by Al-Rubeaan et al., Shows that there are more male DM subjects who experience ulcers, gangrene, and amputations.[9] In addition, a cohort study by Begun *et al.,* Showed that *diabetic foot* patients were more male (56.2%).[10] The meta-analysis by Zhang *et al.,* Also showed that male patients with *diabetic foot* had a greater risk of amputation than women.[11] This could be associated with more disregard for men's health than women as well as male activity. usually relatively heavier and riskier than women[12]

Most of the subjects (47.5%) were in the obese category ($\geq$ 25 kg/m$^2$). Based on a study by Al-Rubeaan *et al*., BMI of *overweight* and obesity categories are risk factors for *diabetic foot*.[9] This is because in obese individuals, there is an increase in pro-inflammatory cytokines, hormones, glycerol, and other factors that play a role in resistance. insulin. This mechanism can increase the risk of a person with DM developing complications[13]

### Characteristics of Subject DM

Most of the subjects (75%) had a family history of DM. The results are similar to the study by Ahmed *et al.,* A family history of DM is one of the risks of *diabetic foot*.[14] In addition, a study by Kogani *et al*., Said that a family history of DM increases the risk of a diabetic foot sufferer having to undergo amputation.[15] This can be caused by the presence of a *single nucleoide polymorphism (SNP)* passed down by parents. In DM patients, several SNPs were found that stimulated the overexpression of inflammatory mediators such as IL-6 and TNF α.[16]

The most onset of diabetes mellitus of the study subjects was between 5-10 years (47.5%). Based on research by Tarigan et al.,[17] and Zoungas et al.,[18] states that the onset of DM is a significant risk factor for diabetes complications, one of which is *diabetic foot*. This is because the longer a person has diabetes, the greater their risk of developing macrovascular and microvascular complications.

Most of the study subjects (82.5%) experienced other complications from DM. Complications include neuropathy, retinopathy, nephropathy, and also vascular complications. According to a publication by Amin and Doupis, the risk of a person with neuropathy developing *diabetic foot* increases sevenfold. In addition, vascular complications can also lead to progression of infection, increased tissue degeneration, and an inadequate supply of oxygen, nutrients, and antibiotics. This can lead to *diabetic foot* and affect the progression of *diabetic foot*[19]

There are 2 types of DM treatment from research subjects, namely consumption of OHO and a combination of OHO and insulin. 55% of subjects received OHO type treatment. Research by Pasquel *et al.,* Said that there was no significant difference in blood sugar levels and complications experienced by elderly people with diabetes who were treated with OHO and / or insulin.[20]

Based on the Consensus for the Management and Prevention of Type 2 Diabetes Mellitus by PERKENI, the definition of DM is well controlled if fasting blood sugar is in the range 80-130 mg / dL.[21] Most of the study subjects (85%) were classified as DM with poor management. Based on a systematic study by Hasan *et al.,* Control of fasting blood glucose levels can reduce the risk of amputation in *diabetic foot.*[22]

**Subject Distribution Based on Smoking Status**

Based on the data collected, 28 out of 40 (70%) smoked. The smoking status of most of the smoking subjects was moderate smokers (*Brinkman* Index 201-600), namely 27.5%. Nearly 80% of smokers in Indonesia started smoking when they were before 19 years of age. The average number of cigarettes consumed by Indonesians per day is approximately 12 cigarettes.[23] The longer a person smokes and the more cigarettes are consumed per day, the determination of smoking status based on the *Brinkman Index* will be heavier.

**Distribution of Subjects by Degree of Diabetic Foot Severity**

The severity of *diabetic foot* is measured using the *Meggitt-Wagner* classification because the *Meggitt-Wagner* classification is the most frequently used classification and is the criterion that develops other classification systems for *diabetic foot*.[24] In this study, the largest proportion was in the *Wagner* 3 group, which was 25%. Based on a study on 196 subjects by Ahmad *et al.,* The largest proportion of the severity of diabetic foot subjects was also *Wagner* 3 (42.9%).[25] The similarity in the distribution of *diabetic foot* subjects in both studies can be caused by several factors such as the onset of DM and the management of DM disease. In the study by Ahmad *et al.,* The onset of diabetes in 91.3% of the subjects was more than 5 years old and 47.4% did not receive treatment for DM. A longer onset of DM is a risk factor for complications from DM17,18 and good management of DM can reduce the risk of developing *diabetic foot*.[22]

**The Relationship Between Smoking Status And Diabetic Foot Severity**

Based on the results of the analysis using *the chi-square*, the obtained *p value* <0.05. This shows that smoking status is significantly related to the severity of *diabetic foot*. This is in line with a study conducted by Pal *et al*., That smoking is a risk factor for the occurrence of *diabetic foot* with a more severe degree and increases the risk of amputation.[6] Based on a meta-analysis study by *Liu et al*., Smoking increases the risk of amputation in DM patients compared to DM patients who do not smoke.[26] Another meta-analysis study by Fu et al., Stated that the *diabetic foot* group who smoked had a worse prognosis for recovery. than the non-smoking group. This results in a higher mortality rate in patients *diabetic foot*.[27]

The study by Fransiscus said that there was an association between smoking and gangrene in DM sufferers.[28] Another case with a study conducted by Shabira *et al.,* Which said that there was no relationship between smoking degrees and *diabetic foot*. These different results can be caused by other factors that influence the occurrence of *diabetic foot* such as trauma, use of footwear, systemic comorbid diseases, and foot care.[29]

The relationship between smoking status and the severity of *diabetic foot* is not fully understood, but the relationship between the two is related to several mechanisms. The first mechanism is through the production of free radicals and oxidants from cigarettes. Free radicals and oxidants can cause oxidative stress on the nervous system and blood vessels. Excessive production of AGE can cause activation of proinflammatory cytokines which can cause mitochondrial dysfunction, DNA damage, inflammation, and apoptosis in cells. . In addition, smoking can interfere with the synthesis of NO so that the vasodilation mechanism is inhibited. This can cause reduced blood flow to various places, one of which is the leg. In addition, the production of carboxyhemoglobin (carbon monoxide from cigarettes and body hemoglobin) can reduce oxygen transport to the limbs which results in disruption of the healing process. Another related mechanism is that smoking can interfere with various wound healing mechanisms in diabetic foot. ROS can cause interference with angiogenesis in wound healing. Besides being able to activate proinflammatory cytokines, ROS can interfere with the phagocytosis function of neutrophils due to suppression of caspase-3 activity. This can cause the body's defenses against

pathogens to be disturbed so that it can affect the occurrence of diabetic foot and its degree of severity.[27,29,30]

## 5. Conclusion

Based on this study, it can be concluded that there is a relationship between smoking status and the severity of *diabetic foot.*

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