

# Determinants of Type 2 Diabetes Mellitus among Passive Smokers

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## Abstract

Type 2 diabetes mellitus (T2DM) leads to complications of other diseases. The modifiable risk factors for T2DM are overweight, physical activity, hypertension, unhealthy diet, and smoking. This study aimed to analyze determinants of T2DM incidence in passive smokers among various factors. This study was conducted at Hospital X in Surabaya City, East Java Province, Indonesia, from September 2019 to April 2020. The variables were univariate, bivariate, and multivariate. Case samples were T2DM patients and passive smokers, while control samples were non-T2DM patients and passive smokers, with 52 respondents per group, of 104 total respondents. Variables statistically significant related to the incidence of T2DM in passive smokers were age >45 years, level of education (not attaining primary school), lack of physical activity, and hypertension. While, the variables having no relation were sex, occupation, sedentary lifestyles, income, and genetics. The multivariate analysis showed that age was a major factor contributing to the incidence of T2DM in passive smokers at Hospital X Surabaya. In brief, age is the most dominant risk factor for the incidence of T2DM in passive smokers.

**Keywords:** determinants, passive smoker, type 2 diabetes mellitus

## Introduction

Type 2 diabetes mellitus (T2DM) accounts for about 90% of all cases of diabetes. In T2DM, there is a decrease in insulin's ability to stimulate glucose uptake by peripheral tissues and inhibit glucose production by the liver, which is defined as insulin resistance.<sup>1</sup> The cause of insulin resistance is often due to obesity, lack of physical activity, and aging. Another cause leading to T2DM is pancreatic cell dysfunction. The cells will show a disturbance in the first phase of insulin secretion, where insulin secretion fails to compensate for insulin resistance. If not treated properly, pancreatic cells will be damaged. This will occur progressively and cause insulin deficiency, hence patients eventually require exogenous insulin. If pancreatic cells cannot produce insulin secretion immediately and quickly to compensate for insulin resistance, fasting hyperglycemia and diabetes will appear.<sup>2</sup> Diabetes mellitus can cause complications to other diseases, such as blindness, heart attack, stroke, kidney failure, and leg amputation.<sup>3</sup> According to the World Health Organization (WHO), arterial hypertension and T2DM are the two most common cardiovascular risk factors in

the global population.<sup>3</sup> Despite their single roles as independent cardiovascular risk factors, hypertension and T2DM often coexist in the same patient. This coexistence multiplies the patient's risk of experiencing major acute cardiovascular events and accelerates the development of chronic heart and kidney failure.<sup>4</sup> Diabetes mellitus and the complications can be managed and prevented, especially when detected early. It is even better to take precautions by making lifestyle changes, such as improving diet and physical exercise.

In recent years, men have been considered a risk factor for T2DM. The reason that men are more prone than women to the development of this disease is not known yet. The development of T2DM results from the interaction between environmental factors and a strong genetic component. Environmental risk factors that influence the development of T2DM include obesity, sedentary lifestyle, birth weight, and stress.<sup>5</sup> In addition, diabetes is a disease with a high socioeconomic pattern, favoring the beneficiary group, especially in developed countries. According to a systematic review on socioeconomic positions and incidence of diabetes, low education is most

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consistently associated with an increased risk of diabetes compared to other socioeconomic indicators. The knowledge and skills acquired through education determine the responsiveness to health information.<sup>6</sup>

Physical activity is one of the risk factors for diabetes mellitus. Physical activity is body movement produced by skeletal muscles that release energy. The physical activity consists of strenuous, moderate, and light activity. Lack of physical activity is estimated to be the main cause of around 21-25% of breast and colon cancers, 27% of diabetes, and about 30% of the global burden of ischemic heart disease.<sup>7</sup> In addition, smoking is also a risk factor for diabetes. This is in line with a cohort study by Wang, *et al.*, which found that being either an active or a passive smoker increases the likelihood of developing T2DM.<sup>8</sup>

While, 28.11% of the population aged >10 years in East Java are classified as smokers with the intensity of smoking daily.<sup>9</sup> With the increasing number of smokers, the problem of passive smoking is also increasing; 85% of households in Indonesia are exposed to cigarette smoke, with an estimated eight smokers dying from active smoking and one passive smoker dying from exposure to other people's cigarette smoke.<sup>10</sup> In passive smokers, exposure to cigarette smoke can increase the risk of T2DM by several mechanisms almost the same as those in active smokers. This mechanism involves 5,000 chemicals, including 50 types of carcinogenic and toxic materials. Endothelial function disorders due to smoking cause changes in blood circulation, resulting in decreased blood flow to skeletal muscles, leading to insulin resistance.<sup>8</sup>

Cigarette smoke can increase blood sugar levels. The effect of nicotine stimulates the adrenal glands and can increase glucose levels.<sup>11</sup> Nicotine can also inhibit insulin secretion. The mechanism of nicotine in inhibiting insulin secretion is when nicotine attaches to the nicotinic acetylcholine receptor (nAChR) on pancreatic cells. Nicotine attached to these receptors causes an increase in oxidative stress (ROS) in cells, leading to changes in cell mitochondria's function and structure.<sup>12</sup> These changes will interfere with the adenosine triphosphate (ATP) formation process in secreting insulin, resulting in pancreatic cell apoptosis.<sup>13</sup> Pancreatic cell apoptosis is the death of cells in the pancreas, so that the function of insulin secretion in the pancreas decreases and insulin decreases in the body.<sup>14</sup>

Diabetes mellitus is a serious problem in Indonesia and the world. Based on the 2018 National Basic Health Research/*Riset Kesehatan Dasar (Riskesdas)*,<sup>9</sup> East Java is the fifth highest province for diabetes mellitus incidence in Indonesia, by 2.6%. This number has increased compared to the results of 2013 National Basic Health Research,<sup>10</sup> by 2.1%. Surabaya, the capital city of East Java Province, has the highest diabetes cases, by 3.4% in

the 2018 National Basic Health Research results.<sup>9</sup> In the continuous year, the number of the diabetics in Surabaya continues to increase. Likewise, with the prevalence of physical activity. Based on the 2018 National Basic Health Research results, 61.5% of the population had sufficient physical activity, and 33.5% had less physical activity in East Java Province.<sup>9</sup> This number illustrates an increase compared to the percentage of physical activity in the 2013 National Basic Health Research, by 26.1% of the population doing less physical activity.<sup>10</sup> The increasing number of smokers in Indonesia tends to increase the risk of developing T2DM. This study aimed to analyze the determinants of T2DM incidence in passive smokers among factors of age, sex, education, occupation, income, heredity, sedentary lifestyle, physical activity, and hypertension.

## Method

This study used an analytical observational study design with a case-control approach. This study was conducted in outpatient and inpatient polyclinic at Hospital X in Surabaya City, East Java Province, Indonesia. The population of this study consisted of a case population of T2DM and all passive smoker patients at Hospital X. At the same time, the control population in this study were all the non-T2DM and other smoking-related diseases at Hospital X who were passive smokers. The sample of this study was all patients classified as passive smokers at Hospital X. In this study, the sample was divided into two; case samples were patients with T2DM and passive smokers, and the control sample was the non-T2DM and patients of other smoking-related diseases but were passive smokers.

The sampling technique used was simple random sampling. The inclusion criteria for this study were patients diagnosed with T2DM or non-smokers with smoking-related diseases at Hospital X participating in the study. In addition, the second inclusion criterion was passive smokers with a family member or coworkers smoke at work every day. The total population obtained was 400 people consisting of 300 population cases of smoking-related diseases and 100 population control. According to the study criteria, the sample size was 159 T2DM patients who were passive smokers as the case population and 52 non-T2DM patients who were passive smokers as the control population. This amount was then adjusted by simple random sampling with a lottery method to 159 case populations to obtain 52 respondents per the number of control samples. The final sample for each group consisted of 52 respondents, and the total sample in this study was 104.

Data retrieval was through secondary data. The data collected were then inputted and cleaned, so that they could be analyzed. These variables were univariate, bi-

variate, and multivariate. Univariate analysis was done for each variable with the proportional results of each. Bivariate analysis was done with Chi-square, and the results showed a relationship between each independent variable and the dependent variable; if the p-value was less than 0.05, it was considered to have statistical significance. Multiple logistic regressions with backward determinant modeling showed multivariate results to find significant determinant factors.

The study was conducted at Hospital X from September 2019 to April 2020. This study used secondary data from interviews with T2DM patients conducted in the second author's study group.<sup>15</sup> The lack of physical activity measurement questionnaire consisted of questions taken from the 2018 National Basic Health Research, a modification of the WHO Global Physical Activity Questionnaire (GPAC)—a part of the WHO STEPS instrument for measuring and monitoring risk factors for non-communicable diseases.<sup>9</sup>

## Results

From January to June 2019, the number of DM patients at Hospital X of Surabaya was 8,060, while T2DM patients were 7,875. The average one-month visit was 1,313 people, representing the number of DM patients in general. The study was conducted on T2DM patients who made outpatient visits at the Outpatients and Inpatients Internal Medicine Polyclinic at Hospital X at Surabaya.

Most of the respondents were at the age range above 45 years, as many as 58 people (44.2%). The sex distribution of respondents showed that the majority (80.8%) were females. The education level was classified as uneducated/attaining elementary school, junior high school, senior high school, and higher education, and most respondents attained high school level (31.7%). These data indicated that most of the respondents were classified as having a low level of education. It was also found that

**Table 1. Characteristics of Passive Smoker Patients at the Hospital X of Surabaya in 2019 (n = 104)**

Characteristic	Category	n	%
Age (year)	18–45	46	44.23
	≥46	58	55.77
Sex	Male	20	19.23
	Female	84	80.77
Education	Uneducated/Elementary school	31	29.81
	Junior high school	17	16.35
	High school	33	31.73
	Higher education	23	22.11
Occupation	Unemployed	48	46.15
	Employed	56	53.85
Physical activity	Not enough	19	18.30
	Enough	85	81.7
Sedentary lifestyle	≥6 hours	32	30.80
	<6 hours	72	69.20
Income	>Minimum wage	34	32.70
	<Minimum wage	70	67.30
Genetic	Yes	41	39.42
	No	63	60.58
Hypertension	Yes	30	28.85
	No	74	71.15

**Table 2. Results of Bivariate Analysis of Type 2 Diabetes Mellitus Incidence in Passive Smokers**

Variable	Category	Disease Incidence X				p-value	OR (95%CI)
		Yes		No			
		n	%	n	%		
Age (year)	8-45	4	7.7	43	82.7	<0.001	57.3 (16.4–199.6)
	≥46	48	92.3	9	17.3		
Sex	Male	14	26.9	6	11.5	0.082	2.825 (0.99–8.059)
	Female	38	73.1	46	88.5		
Education	Uneducated/Elementary school	26	50	5	9.6	<0.001	8.09 (2.268–28.853)
	Junior high school	5	9.6	12	23.1		
	High school	12	23.1	21	40.4		
	Higher education	9	17.3	14	26.9		
Occupation	Unemployed	26	50	22	42.3	0.555	1.364 (0.629–2.955)
	Employed	26	50	30	57.7		
Physical activity	Insufficient	14	26.9	5	9.6	0.042	3.463 (1.1145–10.477)
	Sufficient	38	73.1	47	90.4		
Sedentary lifestyles	≥6 hours	15	28.8	17	32.7	0.832	0.835 (0.362–1.922)
	<6 hours	37	71.2	35	67.3		
Income	>Minimum wage	35	67.30	35	67.30	1.000	1.000 (0.441–2.269)
	<Minimum wage	17	32.70	17	32.70		
Genetic	Yes	23	44.23	18	34.52	0.422	0.668 (0.303–1.472)
	No	29	55.77	34	65.38		
Hypertension	Yes	30	57.69	0	00.00	<0.001	0.423 (0.308–0.581)
	No	22	42.31	52	100.00		

**Notes:** OR = Odds Ratio, CI = Confidence Interval, \*Variables that were significantly related, p-value<0.05

**Table 3. Multivariate Analysis of Variable Associated with Type 2 Diabetes Mellitus Incidence in Passive Smokers**

Variable	Category	$\beta$	p-value	OR	95% CI
Step 1 <sup>a</sup>	Age	3.992	0.001	54.143	4.866–602.418
	Sex	-3.035	0.013	0.048	0.004–0.521
	Physical activity	0.841	0.507	2.318	0.193–27.793
	Education	0.098	0.954	1.103	0.039–30.904
	Hypertension	22.747	0.997	~	~
	Constant	-27.384	0.996	<0.001	
Step 2 <sup>a</sup>	Age	4.010	<0.001	55.122	12.218–248.673
	Sex	-1.519	0.077	0.219	0.041–1.178
	Physical activity	1.482	0.123	4.404	0.668–29.029
	Education	0.680	0.506	1.974	0.266–14.631
	Constant	-7.800	0.001	<0.001	
Step 3 <sup>a</sup>	Age	4.301	<0.001	73.768	17.635–308.569
	Sex	-1.317	0.137	0.268	0.047–1.518
	Physical activity	1.465	0.108	4.327	0.724–25.882
Step 4 <sup>a</sup>	Age	4.189	<0.001	65.987	16.975–256.509
	Physical activity	1.694	0.058	5.442	0.943–31.389
	Constant	-9.014	<0.001	<0.001	
Step 5 <sup>b</sup>	Age	3.937	<0.001	51.250	9.360–280.613
	Physical activity	1.506	0.145	4.509	0.595–34.199
	Hypertension	21.503	0.997	~	~
	Constant	-29.018	0.997	<0.001	–

Notes: OR = Odds Ratio, CI = Confidence Interval.

<sup>a</sup>Variable(s) entered in step 1: Age, Physical activity, Education, Hypertension, Sex.

<sup>b</sup>Variable(s) entered in step 5: Hypertension.

**Table 4. Multivariate Final Model of Variable Associated with Type 2 Diabetes Mellitus Incidence in Passive Smokers**

Variable	$\beta$	p-value	OR	95% CI
Age (>45)	3.937	<0.001	51.250	9.360–280.613
Insufficient of physical activity	1.506	0.145	4.509	0.595–34.199

Notes: OR = Odds Ratio, CI = Confidence Interval.

most respondents were passive smokers on their way to work.

While, the income of the respondents was balanced between below and above the Surabaya minimum wage. Most respondents were passive smokers with sufficient physical activity and excessive sedentary behavior (69.20%). Most respondents had no records of diabetes in the family (60.58%) or a record of hypertension (71.15%) (Table 1).

Table 2 shows the distribution of study participants according to the incidence of T2DM in passive smokers. Bivariate analysis showed that age (p-value<0.001, OR = 57.3), uneducated/elementary school graduate (p-value<0.001, OR = 8.09), physical activity (p-value<0.042, OR = 3.463), and hypertension (p-value<0.001, OR = 0.423) variables were significantly correlated with the incidence of T2DM in passive smokers. It also showed that sex, junior high school, senior high school, higher education graduates, occupation, sedentary lifestyle, income, and genetics variables were not significantly correlated

with T2DM in passive smokers (p-value>0.05).

Based on Table 4, age, sex, and physical activity variables are significant with the incidence of T2DM with a p-value of <0.25. Multivariate analysis was applied to determine the dominant factors of T2DM incidence in passive smokers. The Backward Wald method was carried out on all independent variables that met the requirements included in the model. The insignificant variables were excluded gradually, starting from the variable with the highest p-value. In Table 4, the age variable (p-value<0.001) is a factor significantly related to T2DM incidence in passive smokers after being controlled with age, sex, education, hypertension, and physical activity. In the final stage of logistic regression, results obtained that age was the most important risk factor for T2DM incidence in passive smokers (OR = 51.520, 95% CI = 9.360–280.613).

**Discussion**

Most of respondents with T2DM and passive smokers



were more than 45 years old (54.8%) with a p-value < 0.001, meaning that there was a significant relationship between age in passive smoking and the incidence of T2DM, classified as elderly. Along with increasing age, diabetes mellitus and heart disease risk increase.<sup>16</sup> This result is in accordance with the report from the International Diabetes Federation in 2017 stated that along with increasing age, the prevalence of diabetes mellitus also gets higher.<sup>17</sup> This is because diabetes mellitus often appears after a person enters a vulnerable age, especially after the age of 45, and those who are overweight. Hence, the body is no longer sensitive to insulin. The aging process results in changes in the body's anatomical, physiological, and biochemical systems that can cause insulin resistance. This condition will get worse if it is accompanied by complications of other diseases, especially in the elderly group.<sup>18</sup> The body's metabolism slows down naturally as the human ages, which causes decreased physical activity. Low mobility will speed up the replacement of muscle mass with body fat. This condition can lead to obesity, which is one of the risk factors for T2DM.

Most T2DM patients in this study had no education or graduated from elementary school (50%) (Table 2). The data processing results also showed that the education level of uneducated/graduated from elementary school was related to the incidence of T2DM (p-value < 0.001). While, respondents with junior high and senior high education levels had a p-value of > 0.05, hence there were no significant relationship between the junior high school, senior high school, and higher education levels than those uneducated/graduated from elementary school. This result followed previous study by Sacerdote, *et al.*, stating that people with a low level of education were 1.77 times at risk of suffering from DM than those with higher education.<sup>19</sup> Although elementary and junior high school education levels were included in the type of primary education, both have differences in the level of competence and knowledge taught. The level of education is believed to be an important factor for someone to understand the management of blood sugar control, overcome symptoms that arise with appropriate treatment, and prevent complications generally related to knowledge. The high-educated patients are believed to have better knowledge of diabetes and its effects on health than the low educated hence the patients will respond positively and try to recover.<sup>20</sup>

This study also revealed that physical activity was associated with the incidence of T2DM in passive smokers (p-value = 0.042). This showed a significant relationship between physical activity of passive smoking and the incidence of T2DM. In the physical activity variable, the OR value was 3.4, showing that people with less physical activity had a 3.4 times greater risk of T2DM than people with sufficient physical activity. These data found that

most of the respondents were passive smokers who did sufficient physical activity. These results were the same as Sipayung, Siregar, and Nurmaini's study which showed that 82.8% of 120 respondents did sufficient physical activity.<sup>21</sup>

When human rest, glucose absorption by body tissues requires insulin. While, in active muscles, the increasing need of glucose is not followed by the increase of insulin levels. This is due to an increase in sensitivity insulin receptor when a person is physically active causing active muscles.<sup>22</sup> The condition of insulin resistance makes glucose cannot enter the cells. However, when a person does a physical activity, the muscles are contracting. This condition makes the entrance of glucose easier. That is why, when a person does a physical activity, there will be a decrease in insulin resistance and it ultimately reduces blood sugar levels.<sup>22</sup> Based on the study by Himmah, *et al.*, it was found that physical activity was an influential variable in T2DM.<sup>23</sup> Patients with high physical activity experienced the most significant decrease in sugar levels of 53.6 mg/dL. The blood sugar level decrease in patients with moderate physical activity was 6.73 mg/dL. In comparison, the decrease in blood sugar levels in patients having low physical activity was 4.3 mg/dL.<sup>23</sup>

The result of this study found that hypertension had no significant relationship (p-value < 0.001, OR = 0.423) with the T2DM in passive smokers. It may occur because the case group mostly had a record of hypertension (57.69%). These results were the same as the study by Nainggolan, *et al.*, stating that hypertension was significantly associated with the incidence of T2DM (p-value < 0.001). Respondents with no hypertension had a protective value of 0.423 times compared to those with hypertension for diabetes. Hypertension is a factor that causes DM disease.<sup>24</sup> Hypertension and DM are closely related health problems that need to be handled carefully. High blood pressure causes the distribution of sugar blood in the cells not to run optimally, so that accumulation of sugar and cholesterol in the blood occurs. The point is that if blood pressure is good, blood sugar will also be good. Insulin acts as a substance controlling blood pressure and water levels in the body, so insulin levels are enough to maintain blood pressure.<sup>25</sup>

While, the sex variable did not significantly correlate with the incidence of T2DM in passive smokers. However, Table 1 shows that the majority of respondents are 84 (80.8%) female passive smokers. The results in the field showed that more women were affected by T2DM than men. In addition, the p-value = 0.082 is almost close to significant, indicating a possible relationship between the sex of passive smokers and the incidence of T2DM. This result is also in accordance with two previous studies. Nordström, *et al.*, stated that the prevalence of T2DM in men was higher than in women.<sup>5</sup>

The 2017 International Diabetes Federation report also stated that the prevalence of T2DM in the world in males was more significant than in females.<sup>17</sup>

The data processing results also showed that some variables were not associated with the occurrence of T2DM, such as the occupation of passive smokers (p-value = 0.431), the excessive sedentary behavior ( $\geq 6$  hours) in passive smokers (p-value = 0.832), the income of passive smokers (p-value = 1.000), and the genetics of passive smoker (p-value = 0.422). While, age is a major factor contributing to T2DM incidence in passive smokers at Hospital X Surabaya in 2019. Respondents older than 45 years old and passive smokers had a 51.52 times higher risk of developing T2DM compared to those under 45 years old and were passive smokers (OR = 51.52, 95% CI = 9.360–280.613). American Diabetes Association stated that the risk of T2DM increases with age. The underlying higher risk of T2DM in older individuals is increased body fat composition which accumulates in the abdomen, leading to central obesity. Central obesity further triggers insulin resistance in the initial process of T2DM.<sup>26</sup> The WHO also stated that after a person reaches the age of 40, blood glucose levels rise 1–2 mg% per year during fasting and rise approximately 5.6–13 mg% at couple hours after eating. Regarding that statement, it is not surprising if the age factor is a major factor in the increasing prevalence of diabetes mellitus especially T2DM and impaired glucose tolerance.<sup>27</sup>

Based on previous study by Wei, *et al.*, passive smoking is also one of the T2DM risks.<sup>28</sup> The study by Pan, *et al.*, also stated that both active and passive smoking are associated with significantly increased risks of T2DM. The risk of diabetes is increased in new quitters but decreases substantially as the time since quitting increases.<sup>29</sup> Therefore, interventions to prevent exposure to secondhand smoke remain an urgent priority.<sup>30</sup>

There are some limitations in this study, which include the absence of data regarding the length of smoke exposure by the passive smokers' coworkers, so the influence of the length of the smoke exposure variable on the respondent's age cannot be seen whether it is associated with the incidence of T2DM or not. Since the method of the present study use a case-control design, there is a high potential for recall bias to happen.

## Conclusion

Age is the most dominant risk factor for the incidence of T2DM in passive smokers. People under the age of more than 45 have 57 times the risk of developing T2DM than those in 18-45 years. The aging process results in changes in the body's anatomical, physiological, and biochemical systems that can cause insulin resistance. This condition will get worse if it is accompanied by complications of other diseases, especially in the elderly group.

## Recommendation

According to this study's results, the following suggestions are given by the authors for the Government of Surabaya City to reduce the incidence of T2DM. First, the government is expected to improve the health promotion and education programs about the effects of smoking, especially related to passive smokers who are affected by cigarette smoke and aged above more than 45 years or among the elderly. Second, increasing and activating the efforts to establish nonsmoking Areas in various public places and facilities. Lastly, providing sports facilities or jogging tracks in every area, such as parks or green open spaces, so that people, especially passive smokers, can be motivated to do physical activity.

## Abbreviations

T2DM: Type 2 Diabetes Mellitus; WHO: World Health Organization; nAChR: Nicotinic Acetylcholine Receptor; ROS: Oxidative Stress; ATP: Adenosine triphosphate; *Riskesmas*: Riset Kesehatan Dasar; GPAC: Global Physical Activity Questionnaire; DM: Diabetes Mellitus; OR: Odds Ratio, CI: Confidence Interval.

## Ethics Approval and Consent to Participate

This research was approved by the ethics committee of RSUD dr. Soetomo Surabaya with letter number 0727/KEPK/X/2018 and has received research permission from Hospital X in Surabaya. All subjects in the study also agreed to be respondents.

## Competing Interest

The author declares that there is no significant competing financial, professional, or personal interest that might have affected the performance or presentation of the work described in this manuscript.

## Availability of Data and Materials

All datasets generated and analyzed are available in the article.

## Authors' Contribution

SM designed the study and wrote the protocol, and all authors did the study. SM supervised all the steps in the review process, and all authors interpreted the findings. ART and RDN drafted the manuscript, SM supervised the writing, and KDA, SW, and RDN provided feedback.

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