ORIGINAL ARTICLE

Determinants of diabetes comorbidities in Indonesia: a cohort study of non-communicable disease risk factor

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ABSTRACT

BACKGROUND

Type 2 diabetes mellitus (DM) is a non-communicable disease that constitutes a huge health burden, with the presence of comorbidities of DM adding to it. This study aimed to obtain the main determinants of the combined incidence of DM and its main comorbidities in adults.

METHODS

This was a further analysis of the Non-Communicable Disease Risk Factor Cohort Study 2011 – 2018 involving 3730 subjects. Data of diabetes-free respondents at baseline were followed up every 2 years for 6 years. Data collection was carried out through interviews and health examinations. All subjects were assayed for blood glucose and lipid parameters. Chi-square test and Cox regression were implemented for data analysis.

RESULTS

During 6 years of follow-up, DM incidence occurred in 567 (15.2%) subjects. The most common comorbidities were increased low density lipoprotein (LDL), central obesity, increased total cholesterol, obesity and hypertension. Most of the comorbidities occurred before the diagnosis of DM incidence. The determinants of the combined DM incidence–increased LDL are obesity, hypertension, and a family history of DM. The determinants of the combined DM incidence–central obesity are increased triglycerides, hypertension, male gender, and family history of DM. While the determinants of the combined DM incidence–hypertension are obesity and increased triglycerides.

CONCLUSION

This study demonstrated a high burden of diabetes incidence with comorbidities among adults. Knowledge of the magnitude of the diabetes comorbidity determinants emphasizes the role of non pharmacological intervention such as weight reduction and dietary modification.

Keywords: Diabetes mellitus incidence, comorbidity, NCDRF Cohort Study, Indonesia

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INTRODUCTION

Diabetes mellitus (DM) constitutes a global and national health problem. Throughout the world, DM occurs in 463 million individuals aged between 20 and 79 years. Around 79.4 percent of them live in low- and middle-income countries.[1] Indonesia occupies seventh rank among the countries, with the highest number of DM patients of 10.7 million.[1] According to the results of the Indonesian Basic Health Research (*Riset Kesehatan Dasar*, Riskesdas) the prevalence of DM based on blood sugar examination of persons aged ≥15 years was 6.9 % in 2013, increasing to 8.5 % in 2018.[2,3] The highest prevalence of DM was in persons aged 55 years and over, were of female gender, had low education, and resided in rural areas.[3]

Comorbidities of DM are one or more chronic conditions occurring in patients with DM or are other diagnosed diseases found concomitantly with DM.[4] All cases of chronic disease are considered to be comorbidities, even though occurring before or after the diagnosis of DM incidence.[5] Comorbidities may be found at the time of diagnosis or at the time of follow-up.[6] According to the results of several studies worldwide, hypertension is the main comorbidity in DM, with a proportion of around 34.9 – 71.0%.[7-9]

According to the Indonesian Society of Endocrinology *(Perkumpulan Endokrinologi Indonesia)*, in Indonesia the main comorbidities of DM can be in the form of hypertension, dyslipidemia, obesity and coagulation disorders.[10] Based on a cross-sectional study involving patients with DM who were participants of the Chronic Diseases Management Program (*Program Pengelolaan Penyakit Kronik*, PROLANIS) in a community health center (*Puskesmas*) in Jakarta, it was found that the proportion of patients with DM and the comorbidity of obesity attained 63.9%.[11]

Based on the results of a retrospective observational study, concordant as well as discordant comorbidities in patients with DM were proven to increase healthcare utilization and costs.[12] Comorbidities, particularly depression, also cause a decrease in the quality of life.[13] In addition, comorbidities increase the risk of complications, such as renal failure, and interfere with diabetic control.[14]

The presence of comorbidities in diabetes mellitus and its risk factors have been reported in various studies.[15-17] However, in contrast with a previous study on the influence of the principal comorbidities such as hypertension, obesity and dyslipidemia, our study investigated their association with the time of occurrence of DM incidence in adults. The present study aimed to find the determinants of DM incidence and its main comorbidities in adult subjects.

METHODS

Research design

This study was a further analysis of the Cohort Study on NCD Risk Factors (*Studi Kohor Faktor Risiko PTM)*, hereafter designated NCDRF cohort study, that was conducted by the National Institute of Health Research and Development for the years 2011–2018 in Bogor city, West Java. Baseline data were collected in three stages, namely in the years 2011, 2012 and 2015, whereas periodic follow-up was performed every four months for a limited number of parameters (data on blood pressure and anthropometrics) and every two years for the complete set of parameters.[18]

Study subjects

The study population comprised the subjects of stages 1 and 2 of the NCDRF cohort study (2011 and 2012 baseline data), whereas the study sample consisted of subjects who were free of DM on initial observation. The inclusion criteria were subjects who participated fully in the baseline data collection (interviews and health examinations) and in the biennial follow-ups. Each of the groups of subjects had been followed-up for 6 years, where the subjects of stage 1 were followed up in the years 2013, 2015 and 2017,

while the subjects of stage 2 were followed up in the years 2014, 2016 and 2018. The exclusion criteria were subjects with incomplete data for the study variables of interest.

Measurements

DM incidence were defined as subjects who had ever been diagnosed with DM by health personnel, or who had a fasting blood glucose concentration of ≥126 mg/dL or a blood glucose concentration of ≥200 mg/dL two hours after loading with 75 g glucose in 250 mL drinking water. The definition of blood glucose concentration was according to the 2019 criteria of the Indonesian Society of Endocrinology (*Perkumpulan Endokrinologi Indonesia*, PERKENI).[10]

The comorbidities evaluated in this study were obesity, central obesity, hypertension, dyslipidemia, coronary heart disease, and stroke. The comorbidities could occur before, at the time of, or after the diagnosis of DM incidence and were determined from interviews, measurements, and ancillary examinations.

Obesity was defined as a body mass index (BMI) of ≥25 kg/m^2 based on the criteria of obesity in Asian populations according to the PERKENI 2019 guidelines for dyslipidemia management,[19] whereas central obesity was defined as an abdominal circumference of >90 cm for males or >80 cm for females based on the PERKENI 2019 criteria.[10] Hypertension was defined according to the JNC VIII criteria as a systolic blood pressure of ≥140 mmHg or diastolic blood pressure of ≥ 90 mmHg at rest.[20] Dyslipidemia was defined as abnormal lipid metabolism, marked by an increase or a reduction in the plasma lipid fraction. The main lipid fraction abnormalities were increased total cholesterol (≥200 mg/dL), LDL (≥100 mg/dL), increased triglycerides (≥150 mg/dL), or decreased HDL (<40 mg/dL for males and <50 mg/dL for females).[10,19] Coronary heart disease (CHD) was defined as ischemic heart disease or infarction on the resting or active/stressed electrocardiogram (EKG).[18] Stroke was defined as a history of stroke based on interviews and the finding of sequelae in the form of neurological deficits.[18]

The independent variables consisted of the sociodemographic characteristics (age, gender, marital status, highest level of education, and family history of DM). Age was in the form of continuous data, gender consisted of male and female, highest level of education consisted of low education (unschooled to finished elementary school), middle (finished junior and/or senior high school), and high (university graduate), marital status consisted of married, single, and divorced, and family history of DM was based on presence of family members who had been diagnosed with DM or had died as a result of DM. [18]

The behavioral risk factors investigated were smoking status, physical activity, and mental-emotional abnormality. Smoking status was defined as the smoking behavior in the last month, and was categorized into non-smoker, ex-smoker, and active smoker. Physical activity was defined as the intensity of daily activities of living and was calculated from the weight of the type of physical activity and its duration. Physical activity was categorized as adequate (≥600 MET per week) and poor (<600 MET per week).[21] Mental-emotional abnormality was defined as the psychological condition of an individual that has an influence on mood, thoughts, and behavior and was measured by answering 20 items in a self-reported questionnaire (SRQ) that described the condition in the last two weeks. [22]

Data collection procedures

Data collection in the NCDRF cohort study was conducted according to the WHO STEPS Approach for surveillance of NCD risk factors.[23] The STEPS instrument covers three different levels of "steps" of risk factor assessment, consisting of questionnaires on demographic information and behavioral measurements, physical measurements, and biochemical measurements. Collection of data on socio-demographics, behavior, and medical history was performed by trained enumerators in STEP

1, using a questionnaire that was specially developed for the Indonesian NCDRF cohort study. In STEP 2 the blood pressure was measured 2–3 times with an interval of 5 minutes between measurements, using an AND digital blood pressure monitor on the left upper arm with the subject in the sitting position. Anthropometric measures were determined by measuring height with a fiberglass stadiometer, weight with AND digital scales, and abdominal circumference using measuring tape. The determination of blood pressure and anthropometric measures was performed by trained health personnel from the Bogor Municipal Health Service. The neurological examinations to determine stroke sequelae was done by a team of neurologists. The EKG was recorded using electrocardiograph was provided with the Minnesota code, and the EKG results were read by a cardiologist and validated by two cardiology consultants. The laboratory examinations comprised fasting and 2-hour postprandial blood glucose, total cholesterol, triglycerides, low density lipoprotein (LDL), and high density lipoprotein (HDL) using enzymatic clinical chemistry methods and were performed in STEP 3 by a certified medical laboratory.

Statistical analysis

Descriptive analysis was used to for the subject characteristics at baseline and follow-up in the second, fourth and sixth years. Bivariate analysis using the chi-square test was done to determine the distribution of DM incidence based on the presence of comorbidities and the time of comorbidity onset. Multivariate analysis using the Cox regression test was done to evaluate the determinants that play a role in the combined incidence of DM with the main comorbidities. Variables with p values of <0.25 in the bivariate analysis were selected for further multivariate analysis. In the multivariate analysis, the variables that were statistically non-significant and were not confounders, were removed one by one from the model, so that the final model contained the adjusted hazard ratios of the independent variables that were determinants. A 95% confidence interval and a 5% level of significance was used to interpret statistical significance.

Research ethics

The NCDRF cohort study was submitted annually for review by and ethical approval from the Commission of Health Research Ethics of the National Institute of Health Research and Development. All requirements for the subjects' informed consent had been met and had been approved prior to data collection. The numbers of the ethical approvals were as follows: No.KE.01.08/EC/485/2011; No.KE.01.05/EC/394/2012; No.LB.02.01/5.2/KE.215/2013; No.LB-02.01/5.2/KE.143/2014; No.LB.02.01/5.2/KE.135/2015; No.LB.02.01/5.2/KE.042/2016; No.LB.02.01/2/KE.108/2017; and No. LB.02.01/2/KE.076/2018.

RESULTS

Flow of subject selection

The baseline samples in stages 1 and 2 comprised 5296 subjects. Of this number, 467 subjects had DM at baseline and were removed from the samples, so there were 4829 subjects without DM. There were 1099 subjects that did not meet the criteria, so that the final sample for analysis was 3730 subjects. The flow of subject selection is depicted in Figure 1.

Subject characteristics

The subject characteristics are presented in Table 1. Initially there were 3730 subjects, then the attendance rates (response rates) decreased to 91.59%, 86.06% and 82.5%, respectively, during the follow-ups in the second, fourth and sixth years. The cumulative incidence of DM was 567 subjects (15.2%) in the six years of follow-up. According to socio-demographic characteristics, the mean age of the subjects at baseline was 43.7 ± 10 years, the majority were females, married, and had a medium educational level. The most frequent types of comorbidities found at baseline as well as at biennial follow-ups were obesity, central obesity and increased
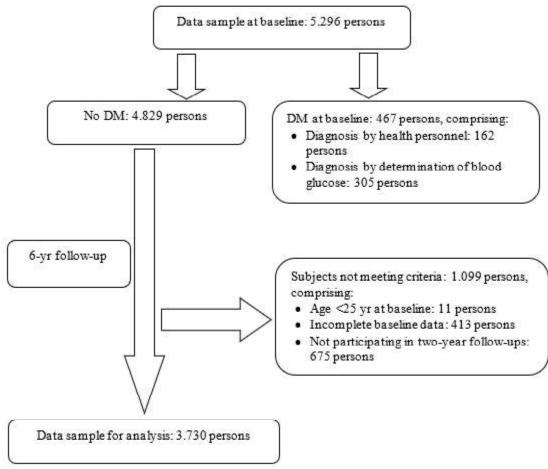
Figure 1. Flow of sample selection in cohort study

LDL. Based on the number of comorbidities, from the start of the data collection only less than 5 percent of subjects were free from comorbidities, more than half of the subjects had 1-3 comorbidities and almost 40 % of subjects had 4-6 comorbidities. During follow-up the proportion of subjects with 4-6 comorbidities increased to 51.4 % in the sixth year of follow-up.

For the subjects with DM incidence, bivariate analysis was performed to determine the proportion of comorbidities occurring at each follow-up, as presented in Table 2. It was found that LDL increased in nearly all subjects. Obesity, central obesity and increased total cholesterol occurred in around 80% of subjects. Hypertension, low LDL and increased triglycerides occurred in 57-78% of subjects, while comorbidities in the form of CHD and stroke occurred in a minority of subjects.

Based on the time of appearance of the comorbidities, in Table 2 are presented the proportions of occurrences of each of the comorbidities that are categorized as before, during, or after diagnosis of DM incidence. Particularly for the follow-up results in the sixth year, the proportions of occurrence of comorbidities after diagnosis of DM incidence could not be filled in because the available data were only up to the sixth year of follow-up. It was found that for obesity, central obesity, and hypertension, the largest proportion occurred before the diagnosis of DM incidence. The largest proportion of the increased total cholesterol, increased LDL and low HDL concentration occurred before diagnosis of DM incidence. Meanwhile, the largest proportion of increased triglyceride concentrations occurred at the time of diagnosis of DM incidence. The comorbidity CHD occurred most frequently at the time of

Table 1. Distribution of subject characteristics by follow-up period

Subject characteristic	Follow-up			
	Baseline n=3730	Year 2 n=3416	Year 4 n=3210	Year 6 n=3077
Incidence of DM (n)	-	157	129	281
Age (yr)	43.7 ± 10.0	45.7 ± 9.9	47.6 ± 9.8	49.6 ± 9.9
Gender				
Female	68.5	70	70.7	71.1
Male	31.5	30	29.3	28.9
Marital status				
Married	85.1	85.1	83.9	80.8
Single	5.8	5.3	4.2	3.5
Divorced	9.1	9.6	11.9	15.7
Educational level				
High	6.4	6.3	6.5	5.8
Middle	57.6	57.8	57.9	58.8
Low	36	35.9	35.6	35.4
Comorbidities				
Obesity	45.5	50.7	51.8	55.3
Central obesity	41.1	49.3	58.1	62.2
Hypertension	29.4	29.7	28.5	37.5
Increased total cholesterol	27.4	45.1	50.2	61.2
Increased triglycerides	16.5	18.8	19.9	25.5
Increased LDL	82.3	81.9	81.7	82.9
Low HDL	39.4	38.7	38.8	35.1
CHD	16	18.6	18.9	20.1
Stroke	1.8	2.8	3.3	3.8
Number of comorbidities				
None	3.9	4.3	4.6	3.3
1-3	53.1	51.3	48.8	41.6
4-6	39.9	41.9	44.7	51.4
7-9	2.7	2.5	1.8	3.7

Data presented as n (%), except for age (mean ± SD)

diagnosis of DM incidence,, whereas stroke had different patterns at each follow-up.

The principal comorbidities that were evaluated in multivariate analysis were the three types of comorbidities having the highest proportion in bivariate analysis, namely increased LDL, central obesity, and hypertension. The independent variables that were entered into the initial model were age, gender, educational level, marital status, family history of DM, smoking status, physical activity, mental-emotional abnormalities, obesity, increased triglycerides, and hypertension. All independent variables were taken from the baseline data. Variables that were identical to the types of comorbidities under current analysis were not included. Central obesity was not entered simultaneously into the initial model because it had a lower crude hazard ratio (HR) than obesity, while from among the parameters of dyslipidemia only the triglyceride concentration was taken because it had the largest crude HR as compared with the other parameters.

The results of the multivariate analysis can be seen in Table 3. The determinants in the combined DM incidence and increased LDL were obesity, hypertension, and family history of DM. The determinants in the combined DM incidence and central obesity were increased triglycerides, hypertension, male gender and family history of DM, whereas the determinants in the combined DM incidence and hypertension were obesity and increased triglycerides.

Table 2. Type and time of appearance of comorbidities related to incident DM

Comorbidities	Time of appearance of comorbidities	Incidence of DM in year 2 (n=157)		Incidence of DM in year 4 (n=129)		Incidence of DM in year 6 (n=281)	
		n	%	n	%	n	%
Obesity	None	26	1.7	23	1.6	59	4.6
	Before diagnosis	128	6.1	106	4.7	221	9.1
	At time of diagnosis	2	6.1	0	0	1	4.8
	After diagnosis	1	2.7	0	0	-	-
Central obesity	None	13	1	15	1.4	39	4
	Before diagnosis	141	6	112	4.3	240	8.8
	At time of diagnosis	2	3.7	2	5.7	2	7.7
	After diagnosis	60	1	0	0	-	-
Hypertension	None	37	1.9	34	2	60	4.3
	Before diagnosis	113	7	93	4.8	211	9.2
	At time of diagnosis	4	5.5	1	2.7	10	20.8
	After diagnosis	3	3.5	1	2.1	-	-
Increased total cholesterol	None	16	1.5	19	1.8	48	4.6
	Before diagnosis	107	5.8	90	4.2	209	8.7
	At time of diagnosis	16	5.3	13	5.6	24	8.1
	After diagnosis	18	3.4	7	2.4	-	-
Increased triglycerides	None	60	2.5	54	2.2	120	5
	Before diagnosis	58	9.4	46	5.2	131	12.1
	At time of diagnosis	29	10.6	14	7.1	30	12.4
	After diagnosis	10	2.3	15	6.2	-	-
Increased LDL	None	6	2.2	5	1.9	12	4.5
	Before diagnosis	145	4.7	117	3.6	262	7.8
	At time of diagnosis	5	2.5	5	5.1	7	7.5
	After diagnosis	1	0.5	2	2.2	-	-
Low HDL	None	44	2.9	38	2.5	94	6.2
	Before diagnosis	81	5.5	73	4	172	8.7
	At time of diagnosis	23	6.1	6	4.5	15	6.2
	After diagnosis	9	2.4	12	5	-	-
CHD	None	147	4.1	119	3.3	262	7.4
	Before diagnosis	0	0	6	7.3	10	8.1
	At time of diagnosis	5	6.1	3	7.1	9	19.1
	After diagnosis	5	5.6	1	2.1	-	-
Stroke	None	138	3.8	114	3.2	274	7.6
	Before diagnosis	8	15.4	10	12.5	4	4
	At time of diagnosis	5	17.9	1	5.3	3	8.8
	After diagnosis	6	11.3	4	11.8	-	-

Table 3. Determinants of combined incidence of DM and main comorbidity

DM–comorbidity	Determinant	Adjusted*		p value
		HR	95% CI	
DM–Increased LDL	Obesity	2.37	1.95 – 2.87	<0.001
	Hypertension	1.51	1.25 – 1.83	<0.001
	Family history of DM	1.47	1.17 – 1.84	<0,001
DM–Central obesity	Increased triglycerides	2.32	1.89 – 2.84	<0.001
	Male gender	2.23	1.74 – 2.85	<0.001
	Hypertension	1.77	1.45 – 2.16	<0.001
	Family history of DM	1.65	1.31 – 2.08	<0.001
DM– Hypertension	Obesity	3.19	2.46 – 4.15	<0.001
	Increased triglycerides	1.78	1.39 – 2.27	<0.001

*controlled for age at baseline

Obesity increased the risk of occurrence of the combined DM incidence–hypertension and DM incidence–increased LDL, with HR values of 3.19 (95% CI: 2.45–4.15) and 2.37 (95% CI: 1.95–2.87), respectively, in comparison with the non-obesiity groups. Males had a risk of 2.23 (HR=2.23; 95% CI: 1.74–2.85) for the combined DM incidence–central obesity when compared with females. For the lipid profiles, although increased triglycerides were not the main comorbidity in the incidence of DM, they posed an important risk for the occurrence of the combined DM incidence–central obesity as well as that of DM incidence–hypertension.

DISCUSSION

Type 2 DM is one of the principal NCDs in Indonesia. The presence of the comorbidity factor in patients with DM increases the risk of future complications, interferes with diabetic control, and reduces the patient's quality of life.[1,13,14]

In the present study, only less than 5% of subjects did not have comorbidities from the start of the study up to the 6-year follow-up, signifying that nearly all subjects had comorbidities. This proportion is higher than that of other studies. For example in Croatia, according to Lang and Markovic, in subjects with DM in the healthcare service, a total of 77.7% had comorbidities, with mean comorbidity of 1.6 ± 1.28.[24] In the Netherlands, a cohort study found that according to the Continuous Morbidity Registration data, there were almost 85% of patients with comorbidities at initial diagnosis of DM. Around one-fourth of subjects without comorbidities at initial diagnosis of DM will suffer from at least one comorbidity in one year of follow-up.[5]

Based on the type of comorbidities, it was found that increased LDL occurred in nearly all of the subjects. Obesity, central obesity and increased total cholesterol occurred in around 80% of subjects, whereas hypertension occurred in more than 70% of subjects. This finding associated with hypertension was similar to other study results, but for dyslipidemia and obesity the

results were different. According to Ekoru et al.,[9] the proportion of hypertension was 71%, but that of dyslipidemia was only 34% and that of obesity 27%. In other studies, hypertension was generally the main comorbidity in patients with DM. In Korea, from the results of further analysis of patients' medical records at Keimyung University, Dongsan, it was also found that the most common comorbidity was hypertension at 34.9%, followed by gastritis at 15.6% and senile cataract at 15.4%.[7] Hypertension as the most frequent comorbidity was also found in the most recent studies, such as the study in England by Nowakowska et al.,[6] the study on women of reproductive age in the US by Britton,[8] and the study in sub-Saharan Africa by Ekoru.[9] The finding associated with the high proportion of dyslipidemia merits special attention, in view of the fact that dyslipidemia is the primary risk for CHD and may play a role before the appearance of the other main risk factors. In patients with DM, dyslipidemia results in a higher risk of coronary abnormalities.[20]

The finding of CHD as comorbidity of DM in the present study differs from the results of previous studies. Only 6.4–7.8% of subjects with DM incidence had CHD as comorbidity. In contrast, based on the results of a study in Italy, from further analysis of several healthcare databases it was found that CHD was one of the most frequent comorbidities of DM with a proportion of 21.7%.[4] The results of the study in Croatia also state that the most frequent comorbidities as complications of DM were polyneuropathy, CHD, retinopathy, nephropathy, non-healing wounds, and amputations.[24]

Based on the results of the multivariate analysis, the determinants of the combined DM incidence–increased LDL were obesity, hypertension, and family history of DM. The determinants of the combined DM incidence–central obesity were increased triglycerides, hypertension, male gender, and family history of DM, whereas the determinants of the combined DM incidence–hypertension were obesity and increased triglycerides. Regarding the combined

DM incidence–increased LDL as well as the combined DM incidence–hypertension, the findings agreed with those of previous other studies that found increased BMI as one of the determinants. However, for the determinants of the combined DM incidence–central obesitythe present study found that the group of males had the higher risks, which is contrary to the other studies.[9]

In the present study it was found that obesity increased the risk of combined DM incidence–hypertension. Obesity as determinant of hypertension in patients with DM is in line with the guidelines on the care of the comorbidities of DM by the American Diabetes Association.[25] In persons with diabetes there is a tendency of increased BMI as compared with healthy persons. The results of the NHANES longitudinal study in the US state that in the 20 years of study, among subjects with undiagnosed DM there was an increase in BMI from 31.5 kg/m^2 to 34.3 kg/m^2, whereas in subjects with diagnosed DM there was an increase in BMI from 28.1 kg/m^2 to 32.6 kg/m^2.[26]

The presence of comorbidities of DM impacts on the occurrence of complications, such as cardiovascular disease. The accumulation of metabolic and cardiovascular risk factors in patients with DM may aggravate the condition and impede the attainment of therapeutic targets, which increases the risk of cardiovascular morbidity and mortality.[6] This is in line with the results of a systematic review conducted by Einarson et al., [27] indicating that the proportion of patients with DM and CHD was higher in the obese than in the non-obese and that there was a positive correlation between increased BMI and increased prevalence of heart disease in individuals with DM. Patients with DM have dysfunction of the blood vessel walls that may be triggered by environmental factors, such as sedentary life style, metabolic factors (chronic hyperglycemia, obesity) that is associated with increased regulation of reactive oxygen specie (ROS), chronic inflammation, and hypercoagulation, leading to atherosclerosis and cardiovascular disease.[6]

Based on the findings of the present study, a more comprehensive treatment of DM is necessary in patients with DM, i.e. regular taking of medications and having an increasingly healthy life style so that the treatment reaches its targets and reduces the risk factors of comorbidity. To this end, the follow-up of patients with DM at the community level should be increased through the NCD integrated health post *(posbindu PTM)* and household visits in the Healthy Indonesia through Family Approach Program (*Program Indonesia Sehat melalui Pendekatan Keluarga,* PIS-PK).

One of the limitations of the present study is the use of community-level data, so that there may be differences in results with those of other studies that use data from healthcare facilities. Another limitation is the short follow-up period (only 6 years), and the dearth of data on other comorbidities, i.e. the complications of DM, the study of which is still in the planning stage. By knowing the extent of the problem of the comorbidities of DM and their determinants, it is hoped that public health interventions may be instituted to prevent the occurrence of these comorbidities of DM.

It is necessary to conduct further cohort studies to determine the influence of comorbidities and the risk factors of the complications of DM, with the involvement of a larger number of associated determinants and longer observation periods.

CONCLUSIONS

In the six years of follow-up, the incidence of DM was 567 (15.2%) subjects. The most frequent comorbidities were increased LDL, central obesity, increased total cholesterol, obesity and hypertension. These findings again highlight the importance of implementing an integrated approach for managing all these conditions since they are responsible for a substantial proportion of the burden of DM.

CONFLICT OF INTEREST

None declared

CONTRIBUTORS

DK was the main contributor who was responsible for the initial design and data analysis. ER and NK were supporting contributors in directing the data analysis and final manuscript. ES and FD were supporting contributors in putting of the substance of the manuscript and its revision. All authors have read and approved the final version. ✚

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