



PREDIABETES AND THE CONTRIBUTING FACTORS: A STUDY IN SEMARANG, CENTRAL JAVA

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ABSTRACT

Background. Prediabetes is a condition when blood glucose levels are above normal, but do not yet meet the criteria for diabetes mellitus. Many people have already been diagnosed with prediabetes. However, there is little data that shows the prevalence and characteristics of people with prediabetes.

Objective. To identify the prevalence and demographic characteristics of adults with prediabetes in Semarang, Central Java, Indonesia.

Method. A cross-sectional study conducted in 21 Puskesmas (public health centers) in Semarang which were randomly selected from a total of 37 Puskesmas. Out of 123 respondents participating in this study, 105 respondents met the inclusion criteria of the study. Oral Glucose Test Tolerance (OGTT) was done after peripherally screening for random glucose level. Univariate analysis was performed to calculate the frequency and percentage of each variable.

Results. The result shows that the prevalence of adult respondents with prediabetes in this study accounted for 17.14%. This study also found that the respondents' mean age was 38.57 ± 14.84 . The majority of the respondents were women (66.7%). They have normal BMI, yet higher waist circumference (23.82 ± 4.48 ; 83.13 ± 11.34), respectively.

Conclusion. Prediabetes is prevalent among adults in Semarang. Thus, to control the incidence of uncontrolled DM, screening needs to be done to identify individuals with prediabetes in order to prevent it from developing into DM. In addition, the application of healthy lifestyle interventions among adults at risk of diabetes also needs to be improved.

Keywords: Blood Glucose, Glycemic Status, HbA1c, Normal Glucose Tolerance, Prediabetes

ABSTRAK

Latar Belakang. Prediabetes adalah kondisi di mana kadar glukosa darah di atas normal, tetapi belum memenuhi kriteria untuk didiagnosis sebagai *diabetes mellitus* (DM). Banyak individu yang telah terdiagnosis prediabetes. Namun demikian, data yang menunjukkan prevalensi dan karakteristik orang dengan prediabetes belum banyak ditemukan.

Tujuan. Untuk mengidentifikasi prevalensi dan karakteristik demografi individu dengan pradiabetes di Semarang, Jawa Tengah, Indonesia.

Metode. Penelitian ini merupakan studi *cross-sectional* di 21 Puskesmas yang ada di kota Semarang, yang telah dipilih secara acak dari 37 puskesmas yang ada. Dari 123 responden yang berpartisipasi dalam penelitian ini, terdapat 105 responden yang memenuhi kriteria inklusi. *Oral Glucose Tolerance Test* (OGTT) dilakukan pada setiap individu setelah skrining perifer kadar glukosa darah sewaktu. Analisis univariat dilakukan untuk menghitung frekuensi dan persentase masing-masing variabel.

Hasil. Penelitian ini menunjukkan bahwa prevalensi individu dewasa dengan pradiabetes di Semarang adalah 17,14%. Hasil penelitian ini juga menemukan bahwa usia rata-rata responden adalah $38,57 \pm 14,84$. Mayoritas responden adalah wanita (66,7%). Mereka memiliki BMI normal, tetapi lingkar pinggang lebih tinggi ($23,82 \pm 4,48$; $83,13 \pm 11,34$).

Simpulan. Prediabetes banyak ditemukan pada kalangan individu dewasa di Semarang. Dengan demikian, untuk mengendalikan insiden DM yang tidak terkontrol, skrining perlu dilakukan untuk mengidentifikasi individu dengan pradiabetes agar tidak berkembang menjadi DM. Selain itu, penerapan intervensi gaya hidup sehat di kalangan individu dewasa yang berisiko diabetes juga perlu ditingkatkan.

Kata kunci: Glukosa Darah, HbA1c, Prediabetes, Status Glikemik, Toleransi Glukosa Normal

BACKGROUND

Prediabetes is a condition in which blood glucose levels are above normal, but are yet to meet the standards required to be diagnosed as diabetes mellitus (DM) (Canadian Diabetes Association, 2013; National Center for Chronic Disease Prevention and Health Promotion, 2016). This condition may progress to DM if not treated properly.

As of 2014, there are 314 million people worldwide with prediabetes and the number is predicted to grow to 418 million by 2025 (Manaf, 2014; World Health Organization, 2006). The prevalence of prediabetes in Indonesia is very high, reaching 10% (Manaf, 2014). A Previous study stated that one-third of people diagnosed with prediabetes will develop diabetes (Fujiati, Damanik, Bachtiar, Nurdin, & Ward, 2017). Moreover, another study also stated that, at one year of follow-up, 3.7% of those with prediabetes had progressed to have diabetes and, by five years of follow-up, 17.1% had progressed to have diabetes (DeJesus et al., 2017). Thus, it is necessary to implement a prevention strategy both to prediabetes and its progress into DM (Soewondo & Pramono, 2011). Specifically, based on the Indonesian Health Profile 2014, it was also reported that the prevalence of DM and Impaired Glucose Tolerance (IGT) in Central Java reached 7.8% and 13.1%, respectively (Kementerian Kesehatan Republik Indonesia, 2014). However, as with the iceberg phenomenon, the prevalence of undiagnosed prediabetes may be much higher.

Currently, prediabetes has become a serious health problem worldwide. Prediabetes is a high-risk group for the development of DM, which, in turn, can lead to complex and multiple complications (Diabetes Care Program of Nova Scotia, 2009). These can be seen from the many incidents of micro and macro vascular damages caused by DM, such as cardiovascular disease, stroke, kidney failure, and others (Grundy, 2012; Roquer et al., 2014).

Financially, the cost of prediabetes that develops into diabetes is high. Health insurance companies have reported that

DM management costs reached more than 22.4 million USD in 2010 (Soewondo, 2014). In addition, the management of patients with uncomplicated DM requires 40 USD/patient/year, while patients with complications require a higher cost of 800 USD/patient/year. In another research, the total cost needed for patients with complications in Banyuasin Hospital in 2015 reached Rp91,979,434.47, not including laboratory cost, medicine and other materials (Rahman, 2019).

People with prediabetes that eventually develop into DM often experience a disruption in work productivity, such as not having a steady job, being absent from work, and being unable to work due to complications. Thus, comprehensive management of patients can optimize the quality of life.

Early detection of prediabetes with DM screening has shown good results whereby blood sugar levels can be controlled, especially if DM is diagnosed early (Soewondo, 2014). Several recommendations for prediabetes screening and diagnostics have already been published. However, differences regarding the criteria of impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) still occur. Many studies have also recommended HbA1c to screen for prediabetes (Olson et al., 2010; Tentolouris, Lathouris, Lontou, Tzemos, & Maynard, 2013).

The Ministry of Health of the Republic of Indonesia, together with professional organizations and social institutions, launched a national program to control DM in 2012 (Soewondo, 2014). However, based on the technical guidelines for program implementation, the formulation has not been specific as to the condition of prediabetes (Kementerian Kesehatan Republik Indonesia, 2013). Programs and policies on DM control have also been carried out by the Indonesian Diabetes Association (PERSADIA), Indonesian Diabetes Education Association (IDEA), and Indonesian Society of Endocrinology (PERKENI) by preparing educational modules for communities and people with diabetes. Government policies on health services that prioritize promotive and preventive

efforts in the continuity of chronic diseases, in this case DM, are needed. Thus, there is a need for real and operational policies to do so.

A previous study conducted in Magelang in 2015 showed that out of 195 medical records examined, 65.5% had not recorded blood sugar levels regularly (Rachmawati & Kusumaningrum, 2015). It was also known that fasting blood sugar and two-hour postprandial blood sugar levels were badly categorized (75.3% and 90.5%, respectively). It was also known that HbA1c examinations were not applied regularly.

In addition, the Basic National Health Survey from the Indonesian Health Department revealed that in 2011, the percentage of DMT2 in Semarang was 19.7% and increased to 20.6% in 2013 (Widoyono, Pramudyanto, Endang, & Pandu, 2014). From the data, an increasing incidence of DMT2 can be seen. With such an increase, it is likely that the number of uncontrolled glycemic status cases is expected to increase as well. Thus, to control the incidence of uncontrolled DM, screening needs to be done to identify individuals with prediabetes in order to prevent it from developing into DM. Therefore, a study is needed to identify the prevalence and demographic characteristics of adults with prediabetes.

METHOD

This study is a cross-sectional study from 21 public health centers that were randomly drawn from the 37 public health centers in Semarang. The population was individuals who visited those public health centers, aged ≥ 20 years, had never been diagnosed with DMT1 or DMT2 and were not pregnant.

Ethical approval was obtained from the Medical and Health Research Ethics Committee (MHREC) of Faculty of Medicine Gadjah Mada University - Dr. Sardjito General Hospital Ref.: KE/FK/719/EC/2016. An informed consent form was also signed by each respondent. Confidentiality of the data gathered from the participants' information and clinical data was guaranteed, and written consent from each respondent was gathered as a

personal permit to be included in the study.

Examination of blood samples for Oral Glucose Tolerance Tests (OGTT) was performed consecutively to 105 respondents in 21 public health centers in Semarang. Respondents with random blood glucose level ≤ 126 mg/dL were then scheduled to be examined invasively at Prodia Clinical Laboratories, Semarang. Invasive examination included fasting glucose tolerance test and two hours after glucose loading level.

Non-invasive screening was also conducted by filling out forms that included medical history and risk factors for DM. The questions included age, weight and height, abdominal circumference, family health history and gender.

Prediabetes was classified according to the American Diabetes Association 2017 criteria (American Diabetes Association, 2017), divided into three categories: (1) Impaired Fasting Glucose (IFG), (2) Impaired Glucose Tolerance (IGT), and (3) IFG and IGT. IFG was determined when the fasting plasma glucose (FPG) obtained is within the range of 100 - 125mg/dL, whereas the IGT of two hours after glucose loading level (2-h PG) is within the range of 140 - 199mg/dL.

The general demographic characteristics data were analyzed to describe the frequency distribution and percentage of each variable. Some data were also analyzed using mean (standard deviation; SD). The results obtained were displayed in the form of a frequency distribution table including the percentage of each demographic characteristic and glycemic status of the respondents. In order to identify the correlation between demographic characteristics and glycemic status, all *p values* were considered to be two tailed with a *p value* of less than 0.05 which represents the statistical significance.

RESULT AND DISCUSSION

Demographic Characteristics of the Respondents in Semarang

A total of 123 respondents volunteered to participate in this study. However, only 105 respondents met the inclusion criteria. Age, gender, physical

performance, health status history, family health history, and glycemic status of the respondents are shown in the table below.

The respondents' demographic characteristics are summarized in Table 1. The sample was predominately women (66.7%). However, it was reported that previous studies have generally analyzed males with diabetes (Aldossari et al., 2018; Brož, Brabec, Lukáč, Žďárská, &

Kvapil, 2017). The mean age was 38.57 ± 14.84 (SD) years. The respondents had normal BMI, but higher waist circumference (23.82 ± 4.48 ; 83.13 ± 11.34 , respectively). They also were more likely to be physically active on a daily basis. Most respondents had FPG < 110mg/dL (96.2%) with mean 87.13 ± 15.99 , and 2-h PG < 140mg/dL (81%) with mean 117.79 ± 42.85 .

Table 1. Demographic characteristics of the respondents in Semarang (n =105)

Characteristics	F	%
Age (years), mean ± SD	38.57 ± 14.84	
Gender		
Male	35	33.3
Female	70	66.7
BMI (kg/m²), mean ± SD	23.82 ± 4.48	
Waist Circumference (cm), mean ± SD	83.13 ± 11.34	
Physical Activity (Daily)	58	55.2
Vegetable and Fruit Consumption (Daily)	51	48.6
History of Hypertension (Yes)	19	18,1
History of Increased Blood Glucose Level (Yes)	3	2.9
History of Family Members with Diabetes Mellitus		
Mother	10	9.5
Father	11	10.5
Brother	2	1.9
Sister	3	2.9
Others	9	8.6
Have a baby with Birth Weight ≥ 4.1kg	4	5.97
Fasting Plasma Glucose (mg/dL), mean ± SD	87.13 ± 15.99	
< 110mg/dL	101	96.2
110 – 125mg/dL	2	1.9
≥ 126mg/dL	2	1.9
2-h PG (mg/dL), mean ± SD	117.79 ± 42.85	
< 140mg/dL	85	81
140 – 199mg/dL	16	15.2
≥ 200mg/dL	4	3.8

BMI = body mass index; SD = standard deviation; 2-h PG = 2-hour plasma glucose

This study also found that the majority of the respondents (almost 90%) had no history of diabetes in the family. This condition was also found in a previous study, that most people with prediabetes have no history of diabetes in the family (Abhishek, Mudey, & V, 2015; Madhu, Sandeep, Mishra, & Aslam, 2018). However, many previous studies are consistent in that family history of diabetes is a significant risk factor to develop

prediabetes.

Although genetic factors, such as family history of diabetes, will increase the risk of prediabetes, people with no history of diabetes may have prediabetes if they have other stronger factors, such as obesity, central obesity, and hypertension. In Ecuador, prediabetes and diabetes are allegedly considered as metabolic disorders strongly associated with increasing BMI. Obese individuals were

4.8 times more likely to be classified as having prediabetes than individuals with normal weight (Orces & Lorenzo, 2017). A previous study also proved that a persistent, heritable abnormality is present in cells originating from mesenchymal tissue of an extra pancreatic site of donors with overt diabetes or the predisposition to this disease (Goldstein, Moerman, Soeldner, Gleason, & Barnett, 1979).

Based on the information from the table, it can also be seen that there were more respondents (1.90%) with fathers having a history of DM compared to other family members. An earlier study stated that individuals with a family history of DM have a higher risk of DM than individuals without family history of DM (Chandra & Restuastuti, 2007).

Prevalence of Prediabetes in Semarang

The diagnosis criteria of glycemic status were divided on the basis of prediabetes criteria, as summarized in Table 2.

Table 2. Diagnosis criteria of glycemic status (n = 105)

Diagnosis criteria	f	%
Normal Glucose Tolerance (NGT)	83	79.05
Prediabetes	18	17.14
Undiagnosed Diabetes mellitus (DM)	4	3.81
Total	105	100

Prediabetes rate in this study is 17.14%. Compared to the previous national population survey (Soewondo & Pramono, 2011), the prevalence of prediabetes for adults in Semarang is higher than that in Indonesia. The same result was also found in the newest study that reported high prevalence of

prediabetes (21% as per WHO criteria and 39.5% as per ADA criteria) (Madhu et al., 2018). Another study also stated that, over a 6-year follow up, 27.3% children and 27.3% adults developed prediabetes/diabetes (Wang et al., 2018). However, the prevalence is lower than that in England (Mainous, Tanner, Baker, Zayas, & Harle, 2014).

Prediabetes has also become prevalent and leads to become diabetes mellitus when it is not treated effectively. Thus, in order to prevent the incidence of uncontrolled DM, screening needs to be done to identify individuals with prediabetes so as to not develop into DM. In addition, the implementation of healthy lifestyle interventions among adults at risk of diabetes also needs to be improved.

Demographic Characteristics of Respondents with Prediabetes in Semarang

Detecting prediabetes may be crucial to reduce the global T2D epidemic and is defined either by the presence of isolated impaired fasting glucose (i-IFG) or isolated impaired glucose tolerance (i-IGT), or both IFG and IGT. IFG is determined from an FPG, and occurs as a result of poor glucose regulation, resulting in raised blood glucose even after an overnight fast. Whereas in individual, IGT often related to defect in muscle insulin resistance (Goyal, Nguyen, & Jialal, 2020).

Based on the categorization of fasting GTT and 2-hour GTT, there are 18 respondents who belong in the category of prediabetes. The number is divided into three categories, three respondents (16.67%) in the category of IFG, 12 respondents (66.67%) in the category of IGT, and three respondents (16.67%) in the category of both IFG and IGT.

Table 3. Characteristics of Prediabetes in Semarang (n=18)

Characteristics	Category	IFG		IGT		IFG and IGT		p value
		f	%	f	%	f	%	
Age (years) , mean ± SD		3	16.67	12	66.67	3	16.67	0.743
		47 ± 16.09		43.25 ± 14.51		43 ± 17.44		
Sex (Female)	Male	1	5.56	4	22.22	2	11.11	0.432
	Female	2	11.11	8	44.44	1	5.56	
BMI (kg/m²) , mean ± SD		32.59 ± 7.15		25.33 ± 3.86		26.71 ± 5.56		1.000
	Underweight	1	5.56	1	5.56	0	0.00	

Characteristics	Category	IFG		IGT		IFG and IGT		p value
		f	%	f	%	f	%	
	Normal range	0	0.00	4	22.22	1	5.56	
	Overweight	2	11.11	7	38.89	2	11.11	
Waist circumference (cm), mean ± SD	Central obesity	1	5.56	4	22.22	2	11.11	0.793
	Normal range	0	0.00	7	38.89	1	5.56	
Fasting Plasma Glucose (mg/dL), mean ± SD		97.67 ± 7.57		84.75 ± 8.28		104.67 ± 8.8		
	< 110mg/dL	1	5.56	12	66.67	0	0.00	0.392
	110 – 125mg/dL	2	11.11	0	0.00	3	16.67	
	≥ 126mg/dL	0	0.00	0	0.00	0	0.00	
2-h PG (mg/dL), mean ± SD		133 ± 22.65		166.42 ± 20.85		153.67 ± 7.51		
	< 140mg/dL	2	11.11	0	0.00	0	0.00	0.046
	140 – 199mg/dL	1	5.56	11	61.11	3	16.67	
	≥ 200mg/dL	0	0.00	1	5.56	0	0.00	

BMI = body mass index; SD = standard deviation; 2-h PG = 2-hour plasma glucose

The mean value of IFG in the prediabetes category in each type is 97.67 ± 7.57mg/dL, 84.75 ± 8.28mg/dL, and 104.67 ± 8.8mg/dL respectively. Overall, the mean scores on this fit the agreed category (American Diabetes Association, 2015; Garber et al., 2008; Lipska et al., 2013). Similarly, for the mean value of 2-hour GTT, each type is 133 ± 22.65mg/dL, 166.42 ± 20.85mg/dL, and 153.67 ± 7.51mg/dL respectively. The previous results of the study about normal fasting plasma glucose showed that GDP levels of 90-94mg/dl increase the risk of type 2 diabetes by 49% and fasting blood glucose levels of 95-99mg/dl by 2.33-fold compared to that of 85mg/dl (Nichols, Hillier, & Brown, 2008). Under normal conditions, in prediabetes as well as diabetes, the blood glucose levels after the loading of glucose or after meals are usually higher than fasting blood glucose levels.

The result also showed that most respondents are in the prediabetes category of TGT type with an average age of 43.25 ± 14.51 years. This is in accordance with the previous research which stated that most prediabetes patients are in the age range of 38-47 years (Soewondo & Pramono, 2011). Similarly, this study, along with previous studies conducted in Asia in general (Shimodaira, Okaniwa, Hanyu, &

Nakayama, 2015) found that increased levels of fasting GTT and 2-hour GTT are often associated with the aging process. The aging process causes glucose intolerance due to decreased function of pancreatic beta cells, and decreased insulin sensitivity due to increased abdominal fat, decreased physical activity, hormonal changes, and increased oxidative stress and inflammation. Age is known as one of the risk factors for developing diabetes (Grech & Chaney, 2014). Thus, with the detection of prediabetes conditions in these individuals, it becomes increasingly important to do a test before a person is 45 years old.

Prediabetes is more common in women (44.44%) in IGT types. One reason for the dominance of women in prediabetes is that, in this research, they accounted for the majority of the participants. Pathophysiology of prediabetes is caused by insulin resistance in skeletal and adipose tissue often found in women. The Results of Basic Health Research conducted by the Indonesian Health Ministry in 2007 and 2013 showed the highest proportion of IGT in women, whereas IFG was highest in men (Ministry of Health, 2008, 2013). Soewondo and Pramono (2011), in their research, stated that there was not much different frequency of IGT in Indonesia

among females (61.6%).

From the Asian cohort study, it was proven that prevalence of prediabetes was higher than the Caucasian counterpart (Yip, Sequeira, Plank, & Poppitt, 2017). Another study stated that predictors of progression to prediabetes are advancing age, family history of diabetes, 2-h plasma glucose, glycated hemoglobin (HbA1C), low HDL cholesterol, and physical activity (Anjana et al., 2015). This finding should be considered in order to recommend modifiable intervention as the strategy to manage risk factors.

As with the previous studies, this research found that most of the respondents in Semarang have obesity (61.11%) and central obesity (38.89%). However, the BMI and waist circumference were not approaching the statistical significance ($p = 1.000$ and $p = 0.793$, respectively). Soewondo and Pramono (2011) said that 59.1% patients with central obesity have IGT. Additionally, another article stated that most of those with prediabetes have BMI ≥ 25 kg/m²; obesity and central obesity lead to insulin resistance and cause hyperglycemia (Yunir, Waspadji, & Rahajeng, 2009).

Based on this study, the proportion of people with prediabetes is 4.01 times higher than the proportion of diabetes. This condition can be found in several other studies, such as Soewondo and Pramono who reported the prevalence of prediabetes in Indonesia as twice higher compared to the prevalence of diabetes (Soewondo & Pramono, 2011). However, compared to their study, the proportion of prediabetes in this study is lower.

There is still limited studies that examine the glycemic status of patients in Semarang. Another study that analyzed the glycemic index stated that the progression of glycemic status varies (Kusumaningrum & Muin, 2019). Our findings suggest that 2-hour post-prandial glucose value should be associated with prediabetes state. This study has several limitations that should be considered when interpreting results, namely the small sample size and lack of diversity because the study was conducted in a certain area.

CONCLUSION

Prediabetes is prevalent among adults in Semarang. Thus, to control the incidence of uncontrolled DM, screening needs to be done to identify individuals with prediabetes in order to prevent it from developing into DM.

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