The Pre-diabetic Epidemiological Study in Depok, West Java

Em Yunir*, Sarwono Waspadji*, Ekowati Rahajeng**

* Department of Internal Medicine, Faculty of Medicine, University of Indonesia – dr. Cipto Mangunkusumo Hospital. Jl. Diponegoro no. 71, Jakarta Pusat 10430, ** Research and Development Division, Department of Health, Republic of Indonesia.

Correspondence mail to: *dr_yunir@yahoo.com.*

ABSTRACT

Objective: to recognize the prevalence of impaired fasting glucose level (IFG) and impaired glucose tolerance (IGT) in general population of Depok Area, West Java.

Methods: the study was conducted in a population with age ≥ 25 years, in Depok Area, West Java, which was selected by using two stage random sampling. Data were collected by using the Step Wise Approach of WHO. Subjects without previous diabetes history were categorized as diabetes if their fasting blood glucose level ≥126 mg/dL, and or the 2-hour-after 75 gram glucose load ≥200 mg/dL. While pre-diabetes was defined as IFG when the fasting blood glucose ≥100 mg/dL to <126 mg/dL or IGT when the 2-hour-after 75 gram glucose load level ≥200 mg/dL (ADA 2003).

Results: of 1200 participants, there were 975 participants who fulfilled the invitation and there were 969 eligible participants to be evaluated.

Among the participants aged ≥ 25 years, there were 40 (4.13%) subjects with isolated IFG and 234 (24.25%) subjects with isolated IGT, 55 subjects (5.68%) with mixed IFG/IGT.

Conclusion: the prevalence of isolated impaired fasting blood glucose in population with age ≥25 years is 4.13%; while the prevalence of isolated impaired glucose tolerance is 24.25%. Mixed IFG/IGT is 5.68%. The total prevalence of pre-diabetic patients is 33.96%.

Key words: diabetes, impaired fasting glucose level, impaired glucose tolerance, pre-diabetes.

INTRODUCTION

Diabetes mellitus (DM) is one of chronic progressive diseases which consequently may cause various complications. Nowadays, DM has become pandemic in all over the world.[1] In addition to the high cost, it also frequently causes various organ damages which will lead to reduced quality of life.[2] In 2000, the prevalence of diabetes in America was 7.2 % and in the year of 2050, it is estimated that there will be an increase of diabetic patients to about 165%.[3] In Mexico-American population, the incidence of diabetes increases 3 folds in 2-8 years period.[4]

The natural history of illness of DM caused by insulin resistance and reduced insulin secretion in beta pancreatic cells will include the pre-diabetic phase.[5,6] Pre-diabetes is categorized into impaired fasting glucose (IFG) when the blood glucose level is 100 mg/dL – 125 mg/dL and impaired glucose tolerance (IGT) when the 2-hour-after 75 gram oral glucose load level (Oral Glucose Tolerance Test = OGTT) ranges between 140 - 199 mg/dL .[7,8]

Currently, it is estimated there are 300 millions of people who have pre-diabetes condition in all over the world.[9] In Indian population of Arizona, Oklahoma and North Dakota districts, the prevalence of pre-diabetes is 14.8 %, 15.1 %, and 22.8%, respectively.[10] Some studies demonstrate a significant difference of prevalence between IFG and IGT. In Australia, Mauritanius, and Scandinavia, the IFG ranges between 4.55-10.15 %; moreover, in Taiwan, it reaches 23.3 %.[11] The data of pre-diabetes in other countries such as Japan, Singapore, South Africa and India rangest between 8.02 and 15.85%. The pre-diabetes condition may increase the risk of diabetes, cardiovascular disease and death.[11,12]

By the progression of disease, 1/3 of IGT will become diabetes in 3-5 years period.[12] Another study in America of population with subjects aged over 20 years found IFG of 6.9%.[13] Data in Baltimore, US of population with subjects aged 17–91 years demonstrates 3.5% IFG, 40.3% IGT and 17.7% mixed IFG/IGT.[14] Another study conducted in Grancanian, Spain found prevalence of pre-diabetes as 26.4%, which consists of 14.6 % IFG, 6.5% IGT and 5.3% mixed IFG/IGT.

Based on the natural history of disease, 25% pre-diabetes will become type-2 diabetes; 25% turn out to be normal and 50% remain as pre-diabetes state in 2-5 years period.[8] The IGT group has greater risk to develop diabetes in the future compare to the the IFG group.[15] In addition, IFG is one of strong predictor of developing the forthcoming IGT.[12] Based on the risk of cardiovascular disease, IGT has greater risk than IFG (1.58 vs.1.33).[4] IGT also has greater risk of death than IFG as demonstrated by the result of Diabetes Epidemiology Collaborative Analysis of Diagnostic Criteria in Euope (DECODE) study.[12] The study indicates that the risk of death in IGT will increase if there is co-morbidity with IFG. Increased risk of cardiovascular disease in IFG will occur when it is accompanied by IGT; IFG itself as the cause of increased risk of cardiovascular disease is still controversial. There is a study that shows that both glucose tolerance disorder will increase various risk factors of cardiovascular disease, either exclusively or mutually.[11] In the population with normal glucose level, 31% will develop diabetes in 4.4 years; while in IGT group, 44% will develop diabetes, 22% remain as IGT, and 44% will turn out to be normal.[16]

Life style changes through increased physical activity, diet modification or utilization of metformin, alpha glucosidase inhibitor and thiazolidinedion may delay or lower the risk of diabetes incidence in the future.[7,18,19,20,21] The aim of the present study is to recognize the prevalence of IGT and IFG, as well as its affecting factors in population of Depok Area, West Java.

METHODS

The epidemiological study in the population was conducted in Abadi Djaya District, Depok, West Java. Subjects aged over 25 years were selected through proportional multistage random sampling by using the list of family residency card (*Kartu Keluarga)* issued by the local government.

Data were collected by using the Step Wise Approach of WHO. Participants were invited in 12-14 hours of fasting state for the examination of fasting glucose level, lipid profile and insulin level. Then, the interview was conducted to obtain demographic data, and anthropometric measurements were performed, including measurement of weight, height, waist and hip circumference, as well as the blood pressure measurement. Subjects without previous diabetes history were categorized as diabetes if their fasting blood glucose $\geq$126 mg/dL, and or the 2-hour-after 75 gram glucose load (oral glucose tolerance test or OGTT) $\geq$ 200 mg/dL. In addition, pre-diabetes is defined as Impaired Fasting glucose (IFG) when the fasting blood glucose $\geq$100 mg/dL - <126 mg/dL or as Impaired Glucose Tolerance (IGT) when the 2-hour-OGTT glucose level was 140 -199 mg/dL (ADA 2004).[7] Furthermore, interview was performed to obtain demographic data and risk factors of cardiovascular disease.

Over weight is defined as body mass index (BMI) $\geq$ 22.9 kg/m^2, categorized as dyslipidemia when the HDL cholesterol level $\leq$ 40 mg/dL for male and $\leq$45 mg/dL for female, total cholesterol $\geq$150 mg/dL and triglycerides $\geq$150 mg/dL and LDL cholesterol level $\geq$100 mg/dL. (*Konsensus PERKENI 2006*).[17] Hypertension is defined as systolic or diastolic blood pressure $\geq$140 mmHg or 90 mmHg or currently using anti-hypertension drugs (Joint National Committee VII = JNC VII). Subjects without diabetes history were categorized as new cases of diabetes if the fasting blood glucose $\geq$126 mg/dL (ADA 2004)[7] and or the 2-hour-after 75 gram glucose load level $\geq$ 200 mg/dL.

RESULTS

Of 40,000 accessible populations that lived at the Abadi Jaya District, Depok, West Java, there were 1200 subjects who were selected as participants and 975 came to fulfill our invitation. Of 975 participants fulfilling the invitation for examination, there were 389 male subjects (39.9 %) and 586 female subjects (60.1%) with the limit of age 25 years to 84 years. Among them, there were 969 eligible subjects to be evaluated.

Table 1 shows the characteristics of participants. In the population with age $\geq$25 years, 502 subjects (51.80%) were categorized as normal glucose tolerance, 40 subjects (4.13%) were included as isolated impaired fasting glucose (Isolated IFG), 234 subjects (24.15%) with isolated impaired glucose tolerance (isolated IGT), 55 subjects (5.68%) were mixed IFG/IGT and 138 subjects (14.24%) with diabetes.

Total IFG, which consists of isolated IFG or mixed IFG/IGT, was found in 10.01% participants; while total IGT, which consisted of isolated IGT or mixed IFG/IGT, was found in 29.83% participants.

Table 1. Glucose Intolerance in Population with Subjects Aged ≥ 25 Years, in Depok, West Java

Risk Factors	Normal	Isolated IFG	Isolated IGT	Mixed IFG/IGT	DM
N	502 (51.80%)	40 (4.13%)	234 (24.15%)	55 (5.68%)	138 (14.24%)
Age (years)	43.90 ± 0.49	52.38 ± 1.77	48.77 ± 0.70	53.38 ± 1.40	54.04 ± 0.75
Sex					
• Male	40.80	40.00	33.80	47.30	44.90
• Female	59.20	60.00	66.20	52.70	55.10
Smoking (%)	62.90	63.20	69.30	80.00	76.90
Alcohol (%)	15.50	15.00	10.30	7.30	15.20
Education					
• < High School	36.50	42.50	46.30	49.10	47.10
• ≥ High School	63.50	57.50	53.70	50.90	52.90
BMI (kg/m^2)	25.68 ± 0.69	25.44 ± 0.84	25.19 ± 0.28	26.80 ± 0.71	26.63 ± 0.92
Waist circumference (cm)	81.24 ± 0.50	84.92 ± 1.52	83.11 ± 0.68	87.73 ± 1.51	87.67 ± 0.91
Hip circumference (cm)	95.13 ± 0.34	97.15 ± 1.43	100.01 ± 3.49	100.98 ± 1.57	99.91 ± 3.12
HDL cholesterol (mg/dL)	54.96 ± 0.51	53.77 ± 2.26	55.71 ± 2.44	52.51 ± 1.14	53.14 ± 1.06
LDL cholesterol (mg/dL)	129.75 ±1 .72	124.26 ± 6.13	139.00 ± 0.73	131.73 ± 6.48	142.25 ± 3.74
Triglycerides (mg/dL)	125.82 ± 3.86	161.23 ± 14.33	130.15 ± 5.36	172.89 ± 12.70	169.47 ± 7.61
Fasting glucose (mg/dL)	85.72 ± 0.36	107.52 ± 1.03	86.1 ± 0.49	106.13 ± 0.84	150.66 ± 5.98
2 h PP glucose (mg/dL)	111.29 ± 0.79	114.95 ± 2.90	160.57 ± 1.05	165.93 ± 2.19	284.01 ± 9.54
Fasting insulin (pmol/L)	8.26 ± 0.26	15.98 ± 2.17	8.19 ± 0.49	10.75 ± 1.12	10.79 ± 0.83
Systolic BP (mmHg)	129.76 ± 1.04	134.13 ± 3.17	136.56 ± 1.59	144.52 ± 3.55	150.03 ± 2.60
Diastolic BP (mmHg)	83.59 ± 0.68	85.53 ± 1.69	87.71 ± 87.0	91.83 ± 1.71	93.85 ± 3.27

In addition, the total prevalence of pre-diabetes, which consisted of isolated IFG, isolated IGT and mixed IFG/IGT reached 33.96%.

Subjects with IFG, IGT and diabetes have older mean age than normal subjects; moreover, in individual with isolated IFG or mixed IFG/IGT also has older mean age than pure IGT (52.38 and 53.38 vs. 48.77 years). There are increase mean age in normal subjects to isolated IGT, isolated IFG, mixed IFG/IGT, and diabetes, i.e. 43.90 vs. 48.77 vs. 52.38 vs. 53.38 vs. 54.04 years. Isolated IGT, isolated IFG, or mixed and diabetes are more frequently found in female subjects (66.2 %, 60 %, 52.7 and 55 %).

Both IGT and IFG have complication risk factors of cardiovascular diseases, but IFG has greater cardiovascular risk factors than IGT, since regarding risk factors, individual with IFG has greater IMT and waist circumference, lower HDL cholesterol level (53.77 vs. 55.71 mg/dl), higher triglycerides level (161.23 vs. 130.15 mg/dl), greater increase of insulin level than the IGT.

Moreover, in subjects with IGT compared to IFG, they have younger mean age (48.71 vs. 52.38) years, more frequent smoking habits and have higher systolic and diastolic blood pressure (36.56 vs. 134.13 mmHg and 87.71 vs. 85.53 mmHg). In subjects with mixed IFG/IGT, the cardiometabolic risk factors are greater regarding the mean age, more frequent smokers, i.e. up to 80%, lower cholesterol HDL, and higher triglycerides level.

Table 2 above shows the characteristics of pre-diabetes based on age group. Most isolated IFG are found at the age over more 50 years; while the highest isolated IFG prevalence is found in 50 – 60 years age group. In participants aged less than 40 years, 45.6% has been categorized as pre-diabetes. High prevalence of pre-diabetes is found in 50 – 60 years age group, i.e. 100% of participants have been categorized as pre-diabetes. There number of participants with pre-diabetes increases with age.

Most of pre-diabetes were found in subjects with body mass index of 25 - <30 kg/m2, i.e. 37.5% IFG, 41.2% IGT and 43.7% mixed IFG/IGT. Furthermore, in subjects with normal body mass index, i.e. 18.5 - < 23 kg/m2, there have also been glucose intolerance of 15% isolated IFG, 25.8% isolated IGT and 23.6% mixed IFG and IGT. The characteristics of BMI in pre-diabetes group, both IFG and IGT, are apparently similar to the diabetes group. The greater the BMI, the greater numbers of patients with glucose metabolism disorder.

DISCUSSION

The prevalence of isolated IGT is greater than isolated IFG (24.15% vs. 4.13%). In fact, the data are different from the data reported in America, which in a national survey, the prevalence of isolated IFG is found as 25% and isolated IGT 14% and mixed IFG/IGT 17%.[11] However, WHO report indicates that the prevalence of IGT is greater than IFG. It has not been clear, whether this condition is affected by race or ethnic background. Nevertheless, IGT is more

Table 2. The Characteristics of Pre-diabetes Based on Age

Age Group (years)	Classification of Glucose Intolerance				
	Isolated IFG (%)	Isolated IGT (%)	IFG and IGT (%)	Total prediabetes (%)	Diabetes (%)
<30	7.5	4.7	3.6	15.8	8.3
30 - < 40	7.5	14.7	7.6	29.8	17.3
40 - < 50	17.5	33.8	20.0	71.3	28.9
50 - < 60	42.5	29.5	38.0	100	30.2
60 - < 70	25.0	6.7	29.1	60.8	13.8
> 70	0	0.9	1.8	2.7	1.2

frequently found than IFG, especially in white and non-hispanic black people.[13]

Nonetheless, in general, the prevalence of pre-diabetes is as great as the prevalence in the present study 33.96 vs. 34.6%.

Table 3. The Characteristics of Pre-diabetes Based on Body Mass Index (BMI)

Body Mass Index (kg/m²)	Blood Glucose Intolerance			
	Isolated IFG (%)	Isolated IGT (%)	IFG and IGT (%)	Diabetes (%)
< 18.5	12.5	4.7	1.8	2.9
18.5 - < 23	15.0	25.8	23.6	24.6
23 - < 25	15.0	15.5	14.5	14.5
25 - < 30	37.5	41.2	43.7	42.8
> 30	20	12.9	16.4	15.2

The present study also reveals that both IFG and IGT is more frequently found in female, i.e. more than 50%; in contrast to the Mauritanius population, which isolated IGT is more frequently found in female and IFG is more frequently found in male subjects.[26]

Subjects with pre-diabetes have a great risk to develop diabetes in the future. Pre-diabetes with blood glucose level > 155 mg/dl by 1-hour-OGTT has incidence rate of 7.4%, and this number increases up to 14.3% when it is accompanied by metabolic syndrome.[27]

In the present study, most of pre-diabetes are found in 50 -60 years age group with body mass index more than 25 kg/m²

The background of high prevalence of isolated IFG and isolated IGT is still very varied. In fact, factors affecting the development of pre-diabetes are the same as factors affecting the development of diabetes, including: genetics, age, overweight, reduced physical activity, and metabolic syndrome. One of the studies which was conducted in subjects aged more than 52 years found the prevalence of isolated IFG as 25%, isolated IGT 14% and mixed IFG and IGT 17%.[12] The study also showed that in the age group with age over 52 years, there were high prevalence of IFG up to 67.5%, while isolated IGT only 17%. Actually, glucose metabo-

lism disorder is not only found in adults, but also found in children population. In a study with children population aged 12-19 years in the US, there are prevalence of IFG of 13.1% and IGT of 3.4%.[25] This might be associated with life style changes into the sedentary life style, which causes increased insulin resistance and reduce insluin secretion in pancreatic beta cells.[8,24]

High pre-diabetes rate currently has become serious concern of some diabetes organization in the world. It is recently argued, whether this group should get non-pharmacological treatment first or they may have immediate pharmacological treatment as provided for the diabetes group.[18,19,20,24,25]

There are different pathogenesis between IFG and IGT, which such condition may differ the forthcoming risk. Impaired insulin secretion and insulin resistance is the basic mechanism for the development of glucose metabolism disorder. In IFG, there are reduced basal insulin secretion, reduced phase 1 insulin secretion and reduced insulin sensitivity (insulin resistance) in hepatorenal system. Therefore, it will cause increase fasting blood glucose level. In contrast, the mechanism underlying IGT includes insulin resistance in muscle and fat (peripheral) tissues, impaired phase 1 and phase 2 insulin secretion which causes increased glucose level after glucose load or after meal.[23,24,28,29]

Thus, the mixed IFG/IGT group will have greater cardiometabolic risk factor compared to the isolated IGT or IFG.

CONCLUSION

The epidemiological study in population at suburban Depok area found 33.96% prevalence of pre-diabetes, with the natural history of disease about one third of them will develop diabetes in 3-5 years period. Such condition will increase the number of Indonesian diabetic patients in the future. Although there are differences which underlie the development of IFG and IGT, the both conditions will be the risk factors of increased morbidity and mortality in the community. Active intervention is necessary so that the rate of

increased number of diabetic patient that develop from pre-diabetes state can be delayed or reduced.

Further studies are needed to evaluate the role of insulin resistance and impaired insulin secretion in the population; thus, it can be identified what factors that have the role on the development of diabetes and some interventions can be performed in order to delay the development of diabetes in the future.

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