Original Article

Progression of Prediabetes to Type 2 Diabetes Mellitus in Thai Population

Apilak Wutthisathapornchai MD[1], Raweewan Lertwattanarak MD[2]

[1] Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

[2] Division of Endocrinology and Metabolism, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Background: Pre-diabetes (pre-DM) increases the risk of developing type 2 diabetes mellitus (T2DM). The incidence of progression from pre-DM to T2DM varies in different ethnic populations.

Objective: To examine the rate of progression from pre-DM to T2DM in a Thai population.

Materials and Methods: This was a cohort study involving participants with pre-DM, diagnosed according to the results of fasting plasma glucose (FPG) and plasma glucose levels two hours after a 75-g oral glucose tolerance test (OGTT) (2-h PG), including IFG+/IGT–, defined by an FPG of 100 to 125 mg/dL (IFG+) and a normal 2-h PG of less than 140 mg/dL (IGT–); IFG–/IGT+, defined by a normal FPG of less than 100 mg/dL (IFG–) and a 2-h PG of 140 to 199 mg/dL (IGT+), and IFG+/IGT+. Each participant was followed-up until diabetes developed or for three years. The incidence of progression to T2DM was calculated every year until the 3-year follow-up period.

Results: Three hundred twenty-five pre-DM participants were enrolled and classified into the following categories: IFG+/IGT– (22.5%), IFG–/IGT+ (44.3%), and IFG+/IGT+ (33.2%). During the 3-year follow-up period, 63 of 325 (19.4%) participants developed T2DM. The incidence of progression to T2DM was 3.1%, 5.7%, and 11.8% at 1, 2, and 3 years, respectively. The mean time to progression to T2DM was 25.5 months. When comparing between subgroups of pre-DM, the IFG–/IGT+ or IFG+/IGT+ subgroups had a higher chance of developing T2DM than the IFG+/IGT– subgroup ($p<0.05$). Some risk factors, which were a family history of T2DM in first-degree relatives, FPG of 110 mg/dL or more, and an HbA1C of 6.0% or greater were significantly associated with the progression of T2DM in univariate analysis ($p<0.05$). However moderate-intensity exercise and diabetes self-management education (DSME) attainment were the protective factors ($p<0.05$).

Conclusion: Almost one-fifth of the participants with pre-DM progressed to T2DM within three years. The annual incidence of DM development was 3.1%, 5.7%, and 11.8% at 1, 2, and 3 years, respectively. People with FPG of 110 mg/dL or more, and an HbA1C of 6.0% or higher, or IGT or combined IGT&IFG should be screened for DM more frequently, using FPG and HbA1C, perhaps every three to six months, especially in those with a family history of T2DM in first-degree relatives. Otherwise, lifestyle modification should be strongly emphasized to prevent development of T2DM in these people.

Keywords: Pre-diabetes, Glucose tolerance test, Diabetes mellitus

Received 27 December 2020 | Revised 21 February 2021 | Accepted 23 February 2021

J Med Assoc Thai 2021;104(5):772-80

Website: http://www.jmatonline.com

The incidence of newly diagnosed type 2 diabetes mellitus (T2DM) in adults has been increasing during the last decade. According to the World Health Organization (WHO) data, the global prevalence of diabetes mellitus (DM) increased from 108 million in 2009 to 422 million in 2014[1]. In Thailand, approximately 4.4 million people or 8.2% of the total population had diabetes in 2017[2]. Long-term macrovascular and microvascular complications of hyperglycemia in T2DM affect many major organs and eventually cause disability or death[3]. The death rate from diabetic complications in Thailand apparently increased from 8.8% in 2013 to 22.3% in 2016[4]. Therefore, the early detection and management of T2DM, including by providing diabetes self-management education (DSME), especially lifestyle modifications, are essential in the prevention and reduction of acute and chronic complications from DM.

Prediabetes is a condition characterized by an abnormal glucose metabolism, resulting in an increased blood glucose level higher than normal but not meeting the criteria for a diagnosis of diabetes. The American Diabetes Association (ADA)[5] has

Correspondence to:

Lertwattanarak R.

Division of Endocrinology and Metabolism,Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Wanglang Road, Bangkoknoi, Bangkok 10700, Thailand.

Phone: +66-2-4197799, **Fax**: +66-2-4197792

Email: tuk102@yahoo.com

How to cite this article:

Wutthisathapornchai A, Lertwattanarak R. Progression of Prediabetes to Type 2 Diabetes Mellitus in Thai Population. J Med Assoc Thai 2021; 104:772-80.

doi.org/10.35755/jmedassocthai.2021.05.12099

classified prediabetes into three categories, impaired fasting glucose (IFG), defined by a fasting plasma glucose (FPG) level between 100 to 125 mg/dL, impaired glucose tolerance (IGT), defined by a 2-hour plasma glucose level after a 75-g oral glucose tolerance test (OGTT) of 140 to 199 mg/dL, and an HbA1C value of 5.7% to 6.4%. Several previous studies have shown that prediabetes is associated with an increased risk for the development of T2DM[6-13]. The China Da Qing Diabetes Prevention Study[6] showed that Chinese patients with prediabetes developed T2DM at an average rate of 11% per year and 93% of the participants in that study eventually progressed to diabetes after a 20-year follow-up. Moreover, participants with prediabetes had some complications of diabetes, such as proteinuria, transient ischemic attack or stroke, and ischemic heart disease, despite their plasma glucose level not meeting the diagnostic criteria for diabetes[7,8].

The rate of progression from prediabetes to T2DM has been reported in several ethnic populations[9-13]. The Inter99 Study in Denmark revealed that their Danish study population with prediabetes developed T2DM at the rate of 4% per year after a 5-year follow-up and the progression rate from IFG, IGT, and IFG plus IGT was 2.5%, 3.8%, and 9.3% per year, respectively[9]. The Hoorn Study in the Netherlands showed that the incidence of T2DM during a 6-year follow-up was 5.1%, 5.8%, and 11.2% per year in participants with category of IFG, IGT, and IFG plus IGT, respectively, compared with a rate of 0.7 per 100 person-years in those with normal glucose tolerance[11], and further that the cumulative incidence of diabetes developed from IFG, IGT, and IFG plus IGT was 33%, 33.8%, and 64.5%, respectively[11]. The progression rate in non-White prediabetes patients varied from 21.6% to 41.2% during a 5-year follow-up[14,15]. To the best of the authors' knowledge, there has been no study yet on the rate and risk factors for the progression from prediabetes to T2DM in Thailand. Consequently, the present study aimed to determine the annual rate of progression from each category of prediabetes, including IFG (IFG+/IGT–), IGT (IFG–/IGT+), and IFG plus IGT (IFG+/IGT+), to T2DM during a 3-year follow-up in a Thai population.

Material and Method

Participants

Between 1 January 2005 and 31 December 2019, participants aged 18 years and older with at least a one-time FPG level of 100 to 125 mg/dL and that had undergone a 75-g OGTT during their routine follow-up at the present study institution were enrolled. Participants who had the following conditions were excluded, OGTT results were normal or consistent with diabetes, gestational DM, and patients who took medication known to affect glucose metabolism, such as anti-diabetes drugs, glucocorticoids, protease inhibitors, and atypical antipsychotic drugs. Participants' electronic medical records were reviewed for their demographic and clinical data, including age, gender, body mass index (BMI), family history of diabetes in first-degree relatives, comorbidities such as hypertension and dyslipidemia, current medications, and biochemical results on the day of their OGTT. Hypertension and dyslipidemia were accounted for as underlying diseases if the participants had these diagnoses shown in their medical records or had been receiving anti-hypertensive or lipid-lowering agents. During a 3-year follow-up period, the participants' body weight, intensity of exercise, DSME attainment, and biochemical data, including FPG and HbA1C, were assessed every three to six months. Participants who were assessed at least once a year for the three consecutive years were defined as having "complete follow-up". The type and average duration of exercise were assessed to determine the intensity and adequacy of exercise. Adequate exercise was considered if a participant had at least undertaken moderate-intensity exercise defined by different types of exercise, including fast walking, running, swimming, bicycling, or aerobic exercise, and the exercise duration was 30 minutes or more per day and three days or more per week or 150 minutes or more per week. Every participant underwent a confirm OGTT for diagnosis of prediabetes before the study. The OGTT was performed according to the method described by the WHO Diabetes Study Group[16]. In brief, the test was performed in the morning after an overnight fast for at least eight hours. For the test, each participant drank 250 mL of glucose solution containing 75 grams of anhydrous glucose within five minutes. Venous blood samples were collected before (at 0 minute) and at 120 minutes after drinking the glucose solution. The blood samples were immediately processed for measurement of the plasma glucose levels. Prediabetes was diagnosed and classified into three categories based on the results of the fasting plasma glucose (FPG) and plasma glucose levels two hours after the OGTT (2-h PG) at recruitment, including IFG+/IGT–, defined by an FPG level of 100 to 125 mg/dL and a 2-hour plasma glucose level after the

oral glucose loading (2-h PG) of less than 140 mg/dL, IFG–/IGT+, defined by FPG of less than 100 mg/dL but a 2-h PG of 140 to 199 mg/dL, and IFG+/IGT+, defined as FPG level of 100 to 125 mg/dL and a 2-h PG of 140 to 199 mg/dL.

DSME attainment was defined as a participant having attended a DSME class conducted by the Siriraj Diabetes Center. The diagnosis of diabetes was based on one or more of the ADA criteria, 1) a FPG level of 126 mg/dL or more, 2) a 2-h PG level during 75-g OGTT of 200 mg/dL or more, 3) an HbA1C level of 6.5% or higher, and 4) a random plasma glucose of 200 mg/dL or more in a patient with classic symptoms of hyperglycemia. In the present study, values above the same diagnostic criterion on two different occasions or values above two different diagnostic criteria on the same or on two different occasions were required for establishing a diagnosis of DM. The present study was approved by the Siriraj Institutional Review Board (COA no. Si 007/2019).

Biochemical methods

All blood samples were collected after an overnight fast and immediately processed for plasma glucose, HbA1C, and other biochemical measurements in a laboratory that was accredited by the International Organization for Standardization (ISO 15189). Plasma glucose levels were measured by the hexokinase method using a Modular P800 automated analyzer (Roche/Hitachi, Indianapolis, IN, USA). HbA1C was measured by the turbidimetric inhibition immunoassay (TINIA) method (Roche/Cobas C153).

Sample size calculation

The sample size was calculated based on the China Da Qing Diabetes Prevention Study showing that the rate of progression from prediabetes to T2DM within the first three years of follow-up was approximately 30%[6]. Therefore, the present study required 323 participants to provide a precise estimate of the progression rate with a margin of error of 5% and a confidence level of 95% during the 3-year follow-up study.

Statistical analysis

Descriptive statistics were expressed herein as the mean ± standard deviation (SD) for continuous data or the number and percentage for categorical data. The rate of progression from prediabetes to T2DM was expressed as percent per year or number per 100 person-years. To determine the factors possibly associated with the progression from prediabetes to T2DM, the chi-square test or Fisher's exact test was used for comparing the categorical variables and the unpaired t-test or Mann-Whiney U test was used for comparing the continuous variables. Receiver operating characteristic (ROC) curves were performed to determine the FPG and HbA1C levels that had the highest accuracy in predicting the progression from prediabetes to T2DM. Variables with p-values of less than 0.10 according to the univariate analysis were potential predictors of developing T2DM and were subsequently included in the multivariable analysis and were evaluated using binary logistic regression analysis (backward stepwise). For all tests performed, a two-tailed p-value of less than 0.05 was considered to be statistically significant and the results are presented as odds ratio (OR) with 95% confidence interval (CI) for each variable. IBM SPSS Statistics, version 25.0 (IBM Corp., Armonk, NY, USA) was used for all the statistical analyses.

Results

Three hundred forty-five participants were enrolled in the present study. Five Participants were excluded due to returning a normal result for their 75-g OGTT and 15 participants were excluded due to being treated with a glucose lowering agent. Therefore, 325 participants who had OGTT results and met the criteria of having completed follow-up during the 3-year study were included in the analyses. Of these, 73 participants (22.5%) had IFG+/GT–, 144 (44.3%) had IFG–/IGT+, and 108 (33.2%) had IFG+/IGT+ at baseline. The participants' demographic and clinical characteristics are shown in Table 1. The mean age was 57.6±11.2 years old and 197 participants (60.6%) were female. During the 3-year follow-up, 63 out of the 325 prediabetes participants (19.4%) developed T2DM. The participants who developed T2DM had statistically significant higher FPG and HbA1C levels at enrollment than those who did not. There was no significant difference in age, gender, body weight, height, BMI, and serum creatinine levels between those who developed T2DM and those who did not. The ROC curves showed that the FPG level of 110 mg/dL and HbA1C level of 6.0% had the highest accuracy in predicting the progression from prediabetes to T2DM (Figure 1). Univariate analysis demonstrated the statin therapy, a family history of T2DM in first-degree relatives, hypertension, and obesity were the factors significantly associated with the increased risk of progression from prediabetes

Table 1. Patients' characteristics and parameters

Baseline characteristics	Total (n=325); mean±SD	Non-DM (n=262); mean±SD	T2DM (n=63); mean±SD	p-value
Age (years)	57.6±11.2	57.5±11.4	58.1±10.7	0.68
Female; n (%)	197 (61)	161 (61)	36 (57)	0.53
Body weight (kg)	66.5±13.6	65.9±13.8	68.8±12.6	0.15
Height (cm)	160.6±8.7	160.7±8.8	160.4±8.4	0.95
BMI (kg/m^2)	25.7±4.4	25.4±4.2	26.7±4.2	0.06
Underlying disease; n (%)				
Hypertension	182 (56)	138 (53)	44 (70)	0.02*
Dyslipidemia	221 (68)	172 (66)	49 (78)	0.09
Obesity[a]	236 (73)	184 (70)	52 (83)	0.049*
Initial FPG (mg/dL)	100.1±8.9	99.5±8.7	102.4±9.2	0.02*
Initial HbA1C	5.9±0.4	5.8±0.4	6.1±0.3	0.001**
Initial Cr (mg/dL)	0.86±0.21	0.86±0.21	0.88±0.21	0.41

BMI=body mass index; Initial FPG=fasting plasma glucose at enrollment; Initial HbA1C=HbA1C at enrollment; Initial Cr=creatinine at enrollment; SD=standard deviation

[a] Obesity; BMI ≥23 kg/m^2

* p<0.05 and ** p<0.01. The statistical significance of sex and underlying disease were calculated using chi-square, others were using t-test.

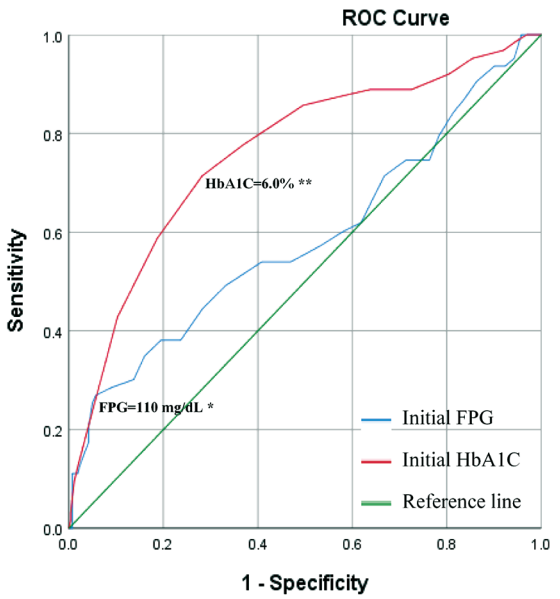

Figure 1. Receiver operating characteristic (ROC) curves between initial FPG or HbA1C level in order to identify optimal cut-off value for predicting the progression from prediabetes to T2DM. Area under the curve of both initial FPG (blue line) and initial HbA1C (red line) were statistically significant (* p<0.05 and ** p<0.01).

to T2DM with ORs of 2.24 (95% Cl 1.20 to 4.21), 2.14 (95% Cl 1.22 to 3.76), 2.08 (95% Cl 1.15 to 3.75), and 2.00 (95% Cl 0.99 to 4.04), respectively, as shown in Table 2. The FPG levels of 105 to 115 mg/dL and HbA1C levels of 5.8%, 6.0%, and 6.3% were all significantly associated with an increased risk of progression from prediabetes to T2DM. The FPG level of 115 mg/dL and HbA1C level of 6.3% demonstrated the highest ORs of 6.43 (95% CI 1.97 to 20.98) and 6.53 (95% CI 3.45 to 12.36), respectively. Whereas, moderate to high intensity exercise and the attainment of DSME were the protective factors against the progression to T2DM, with ORs of 0.13 (95% CI 0.06 to 0.30) and 0.11 (95% CI 0.05 to 0.24), respectively. Multivariable analyses showed that a family history of T2DM in first-degree relatives, FPG of 110 mg/dL or more, and HbA1C of 6.0% or more, but not hypertension, obesity, or statin therapy were the independent predictors significantly associated with the progression of prediabetes to T2DM. Overall, 10 out of 325 (3.1%), 18 out of 315 (5.7%), and 35 out of 297 (11.8%) prediabetes participants progressed to T2DM during the first, second, and third years of the follow-up, respectively, with an average incidence of 6.42% per year and a mean time of progression to T2DM of 25.5 months, as shown in Figure 2. Regarding the subgroups of prediabetes classified according to the result of the 75-g OGTT at enrollment, 32 of 108 participants (29.6%) in the IFG+/IGT+ subgroup, 26 of 144 participants (18.1%) in the IFG–/IGT+ subgroup, and 5 of 73 participants (6.8%) in the IFG+/IGT– subgroup progressed to T2DM. The progression rate from the IFG–/IGT+ and IFG+/IGT+ subgroups to T2DM were significantly higher than in the IFG+/IGT– subgroup (p<0.05) as shown in

Table 2. Factors related with progression to T2DM

Factors	T2DM (n=63)	Non-DM (n=262)	Univariate analysis		Multivariable analysis	
			Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Male	27	101	1.2 (0.68 to 2.09)	0.53		
Smoking[a]	3	17	0.72 (0.20 to 2.54)	0.78		
Alcohol intake	7	27	1.09 (0.45 to 2.63)	0.85		
Family history of DM[b]	30	78	2.14 (1.22 to 3.76)	0.01*	2.30 (1.11 to 4.75)	0.03*
Hypertension	44	138	2.08 (1.15 to 3.75)	0.01*	2.06 (0.99 to 4.29)	0.054
Dyslipidemia	49	172	1.83 (0.96 to 3.50)	0.06		
Obesity	52	184	2.00 (0.99 to 4.04)	0.049*	1.37 (0.56 to 3.37)	0.49
β-blocker	7	29	1.00 (0.42 to 2.41)	0.99		
Thiazide	1	6	0.69 (0.08 to 5.82)	1.00		
Statin	48	154	2.24 (1.20 to 4.21)	0.01*	1.80 (0.82 to 3.95)	0.15
Herbal	1	3	1.39 (0.14 to 13.61)	0.77		
Moderate-intensity exercise	7	128	0.13 (0.06 to 0.30)	<0.001**	0.19 (0.07 to 0.49)	0.001**
DSME attainment	7	142	0.11 (0.05 to 0.24)	<0.001**	0.19 (0.08 to 0.47)	<0.001**
FPG ≥110 mg/dL	17	15	6.09 (2.84 to 13.04)	<0.001**	5.11 (1.89 to 13.81)	0.001**
HbA1C ≥6.0%	49	97	5.95 (3.12 to 11.34)	<0.001**	4.14 (1.78 to 9.62)	0.001**

T2DM=type 2 diabetes mellitus; DSME=diabetes self-management education; FPG=fasting plasma glucose; OR=odds ratio; CI=confidence interval

[a] Only first-degree relative family member of DM; [b] Currently smoking only

* p<0.05 and ** p<0.01

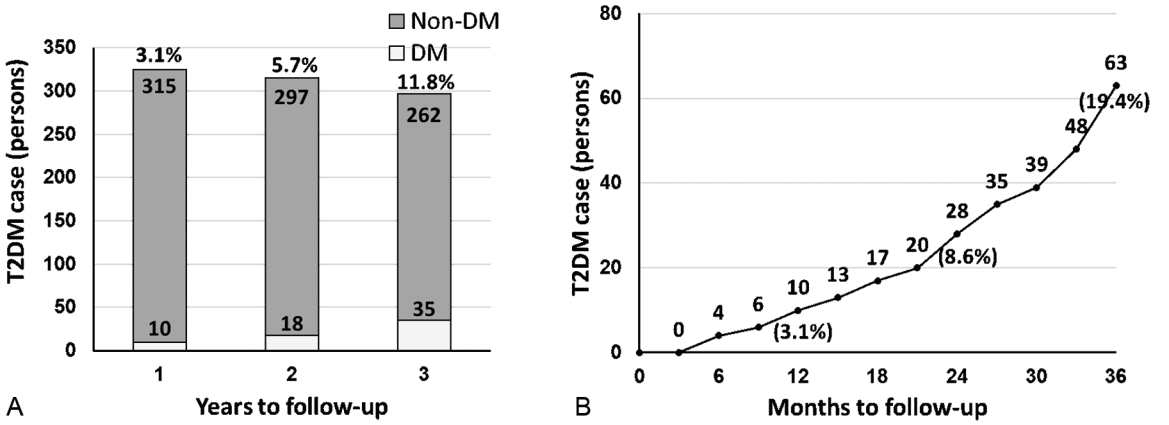

Figure 2. Rate of progression from prediabetes to T2DM during 3 years of follow-up in 325 Thai prediabetes patients. A: The bar shows the number of newly diagnosed T2DM cases and the percentage each year (light color) and non-DM cases (dark color). B: The black line represents the cumulative cases progressing from prediabetes to T2DM and the percentage demonstrates the cumulative diabetic progression rate.

Figure 3.

Discussion

The present study aimed to examine the rate of progression from prediabetes to T2DM in a Thai population, and the result showed that 19.4% of prediabetes participants progressed to diabetes within three years. The present study finding was lower than the 30% reported during the first three years follow-up in the China Da Qing Diabetes Prevention Study[6]. The cumulative incidence of progression from prediabetes to T2DM in other non-White populations vary from 9% in a Japanese population[17], 10.4% in a Korean population[18], and 39% in a Mauritian population[14] during 5-years follow-up. The different incidence among these

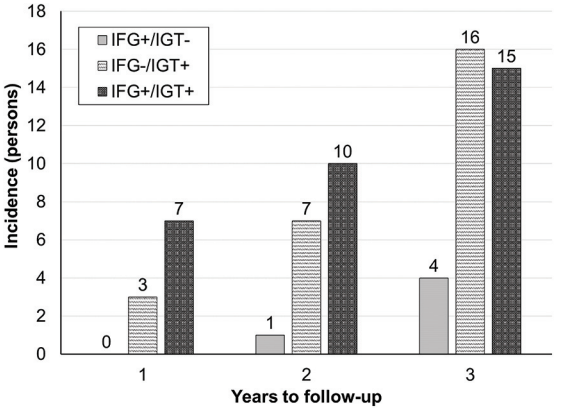

Figure 3. Incidence of T2DM based on prediabetes subgroups (IFG+/IGT–, IFG–/IGT+, and IFG+/IGT+). The progression rates for the IFG–/IGT+ and IFG+/IGT+ subgroups to T2DM were significantly higher than for the IFG+/IGT– subgroup (p<0.05).

studies might be due to the different susceptibility to develop T2DM in different populations and follow-up duration, the different methods and criteria used in the diagnosis of prediabetes and diabetes among the studies[6,14,17-18], as shown in Table 3. In particular, the studies published before the year 2010 used FPG and OGTT[6,14], whereas the studies in Japan[17] and Korea[18] used FPG and HbA1C in the diagnosis of diabetes. It also might be due to the difference in the duration of prediabetes in patients before participating in the study and the limited data on the baseline FPG and HbA1C levels of the participants before entering the studies. Moreover, the duration of follow-up also affects the rate of progression to diabetes. Up to 93% of Chinese prediabetes patients progressed to diabetes within 20 years of follow-up[6]. The incidence of progression to T2DM in the present study was 6.43% per year, which was lower than the rate of 14.1% per year in the control group of the China Da Qing Diabetes Prevention Study and the rate of 11% per year in the placebo group of the Diabetes Prevention Program (DPP) outcomes study[19]. The rate of progression to DM in the present study was 3.1%, 5.7%, 11.8% in the first, second, and third year of follow-up, respectively, which was lower than those reported in other studies[6]. This could be due to two reasons. Firstly, diagnosis of diabetes was delayed in some patients because to diagnose DM, two abnormal test results from the same sample but using different diagnostic criteria, or in two separate test samples were required. To comply with this diagnostic scheme, the second samples were obtained when the patients returned for a follow-up visit three to six months later, which resulted in delay in establishing diagnosis of DM. Secondly, considering that these subjects were at risk of developing diabetes, intense lifestyle modification was vigorously delivered at each follow-up visits, which could lead to delayed in progression or diagnosis of diabetes.

The present study finding that prediabetes participants with IFG–/IGT+ and with IFG+/IGT+

Table 3. Review of studies involving the progression of prediabetes to diabetes in non-white participants

Study	Sample size	Inclusion criteria (at baseline)	Time period to follow-up	Diagnosis criteria for diabetes	Incidence per year	Cumulative incidence	Follow-up period and sample at the end	Risk factors	Remarks
Thailand 2020 (present study)	325	Prediabetes (FBS, HbA1C, OGTT)	Every 3 to 6 months	FBS and/or HbA1C and/or OGTT above criteria 2 times	6.4%	19.4%	3 year (n=325)	Family history IFG–/IGT+ IFG+/IGT+ FBS ≥110 mg/dL HbA1C ≥6.0%	
China Da Qing Li 2008[6]	577	576 prediabetes (FBS, OGTT)	Every 2 years	Self-reported and/or taking hypoglycemic medications and/or FBS and/or OGTT	14.1% 11.3%	65.8% 92.8%	6 year 20 year (n=563)	Intensive lifestyle intervention reduce the incidence	Randomized control trial study design
Korea Kim 2016[18]	17,971	7,208 prediabetes (FBS, HbA1C)	N/A (non-available)	FBS and/or HbA1C, or the initiation of anti-hyperglycemic medications	N/A	10% (702/7208)	5.2 year (n=7,208)	FBS 110 to 119 mg/dL HbA1C 6 to 6.4%	
Japan TOPIC3 Heianza 2011[17]	6,241	2,092 prediabetes (FBS, HbA1C)	Every year	FBS and/or HbA1C above criteria 2 times	3.1%	14% (292/2092)	4.7 year (n=2,092)	FBS 110 to 119 mg/dL HbA1C 6 to 6.4%	
Mauritius Shaw 1999[14]	3,229	755 prediabetes (FBS, OGTT)	5 years	OGTT and/or FBS or current treatment of anti-hyperglycemic medications	N/A	39% (297/755)	5 year (n=755)	IGT	

FBS=fasting blood sugar; OGTT=oral glucose tolerance test; N/A=not available; IFG=impaired fasting glucose; IGT=impaired glucose tolerance

were more susceptible to progression to diabetes than those with IFG+/GT–, similar to that of other studies. The Paris Prospective study[12] reported that 2.7% of an IFG+/IGT– population and 14.9% of IFG+/IGT+ participants progressed to diabetes in an average of 2.5 years. A long-term study in Italy also reported that 9.1% of an IFG+/IGT– subgroup and 44.4% of an IFG+/IGT+ subgroup of prediabetes participants advanced to diabetes in 11.5 years[13]. In a meta-analysis of prospective studies published between 1979 and 2004[20], the annual incidence of progression to diabetes was 4% to 6% in patients with IFG–/IGT+ and 6% to 9% in those with IFG+/IGT–, which were both lower than the 15% to 19% rate in those with IFG+/IGT+.

Both IFG and IGT have been shown to be associated with insulin resistance but at different target tissues of insulin actions. IGT is predominantly associated with the insulin resistance of skeletal muscle cells throughout the body, whereas IFG is predominantly associated with the insulin resistance of hepatocytes[21]. Patients with IGT are also associated with an increased risk of both microvascular and macrovascular complications of diabetes, such as proteinuria, neuropathy, myocardial infarction, and stroke[22], and reversion from IGT but not IFG to normoglycemia was associated with a reduction in the future risk of cardiovascular disease (CVD) and death[23]. These findings suggested that the early detection of prediabetes, especially IGT, is useful in the prevention of T2DM and diabetic complications.

Although OGTT is generally accepted as the gold standard for diagnosing diabetes and prediabetes, it is, however, time-consuming, costly, and not practical. OGTT is normally performed in research but not routinely in clinical practice, especially in Thailand. Nowadays, FPG and HbA1C are preferred over OGTT in follow-up prediabetes or diabetes cases. The Thai Clinical Practice Guideline for Diabetes 2017[24] recommended following up persons with prediabetes every one to three years; however, it is not clearly stated which test should be used for follow-up. The HbA1C level of 5.7% to 6.4%, which represents prediabetes according to the ADA criteria, can identify 109 out of 144 (76%) of IFG–/IGT+ and 86 out of 108 (80%) of IFG+/IGT+ participants. By using both FPG and HbA1C criteria, 35 out of 252 (14%) of participants were missing from the diagnosis of prediabetes. Among these, only two out of 35 (6%) persons progressed to diabetes. This suggests that FPG and HbA1C can be used in the follow-up of prediabetes.

The present study showed that Thai prediabetes individuals who had a family history of T2DM in first-degree relatives, those who had FPG level of 110 mg/dL or more and an HbA1C level of 6.0% or more had a higher risk of developing T2DM than those who had none of these risk factors after an average follow-up duration of two years or 25.5 months. Compared with the previous studies[25], a family history of T2DM was an independent risk factor associated with the progression of T2DM in most studies, similar with the present findings. However, smoking, BMI, and hypertension or high systolic blood pressure were independent factors in some studies[25], but not in the present study. A recent retrospective cohort study in a Japanese population[26] showed that waist circumference but not BMI or blood pressure was associated with an increased risk of diabetes. The reason for the different risk factors in each study is not clear, however, it might be due to ethnic differences. Prediabetes participants with an FPG level 110 mg/dL or more and HbA1C level 6.0% or more were strongly associated with the progression of diabetes, which was similar to a study with 7,208 Korean prediabetes participants[18]. The results showed that prediabetes participants with a higher FPG of 110 to 124 mg/dL, and HbA1C of 6.0% to 6.4%, had a substantially higher likelihood of progressing to diabetes than those with a lower FPG of 100 to 109 mg/dL, and HbA1C of 5.7% to 5.9%. The cumulative incidence of diabetes at 5.6 years in Japanese participants with both FPG 110 to 124 mg/dL and HbA1C 6.0% to 6.4% was 100%[27].

In conclusion, the present study findings suggested that Thai prediabetes individuals with the risk factors described above should be followed up at least every year. These subgroups should undergo more intensive and motivative lifestyle modification to diminish the development of diabetes and to delay complications in the future.

Advantages and limitations of the study

The present study is the first study aimed at evaluating the rate of progression from prediabetes to T2DM in a Thai population. Although the present study was designed as a cohort study, all the participants had a 75-g OGTT test at baseline to exclude normal glucose tolerance or pre-existing T2DM cases before enrollment into the study. All the participants that met the criteria were enrolled in the present study and this should reduce the selection bias. The sample size enrolled was less than in other studies, as shown in Table 3, but was

more than the calculated sample size and had enough power to estimate of the progression rate and some of the associated risk factors. Participants in the present study were followed up every three to six months, which was more frequent compared with the other studies. This increased the accuracy to detect the progression rate of prediabetes to T2DM. However, there were some limitations in the present study. Patients had a previous abnormal FPG level but had not performed 75-g OGTT before enrolling on the study. Therefore, the authors did not know the duration of "prediabetes" stage at the baseline. Patients that currently smoked (6%) or had thiazide use (2%) or herbal use (1%) were too small to allow detecting any significant differences. There were no medical records about waist circumference, which might otherwise have been found to be an associated risk factor of progression to T2DM[25]. Lastly, the rate of progression to DM in each year in the present study was quite lower than the previous study[6]. This could be due to delay in establishing diagnosis of DM by using two abnormal results from the two separate samples, obtained several months apart and the regular delivery of intense lifestyle modification to these subjects at every visit.

Clinical implications

The present study suggested that participants with prediabetes and had a first-degree relative or family member with DM or had comorbidity with hypertension and dyslipidemia should be followed up at least every year. FPG and HbA1C should be performed to enable early detection of the progression to DM. However, people with FPG of 110 mg/dL or more, and HbA1C of 6.0% or more should be screened more frequently, perhaps every three to six months. Otherwise, lifestyle modification should be strongly emphasized to prevent to delay development of DM in these prediabetes people.

Conclusion

In the present study, about one-fifth or 19.4% of individuals with prediabetes progressed to diabetes within three years. The progression rate for DM development each year was 3.1%, 5.7%, 11.8% in the first, second, and third year of follow-up, respectively. The average incidence was 6.43% per year and the mean time of progression to T2DM was 25.5 months.

High risk prediabetes based on IFG–/IGT+ or IFG+/IGT+ by 75-g OGTT with a family history of T2DM in first-degree relatives, FPG of 110 mg/dL or more, and HbA1C of 6.0% or more should be screened to prevent T2DM development. Exercise of at least moderate intensity together with DSME attainment should be advised.

What is already known on this topic?

The prediabetes stage is associated with an increased risk of the development of T2DM and the cumulative rate of progression from prediabetes to T2DM in other countries has been reported to vary from 10% to 39% during 5-year follow-up. However, the incidence of diabetes and the associated risk factors in Thai populations with prediabetes has not yet been well established.

What this study adds?

About one-fifth of individuals with prediabetes in the Thai cohort progressed to diabetes within three years. The progression rate of DM development each year was 3.1%, 5.7%, and 11.8% in the first, second, and third year, respectively. The average incidence was 6.43% per year. Prediabetes, especially in subjects with IFG–/IGT+ or IFG+/IGT+ by 75-g OGTT, a family history of T2DM in first-degree relatives, FPG of 110 mg/dL or more, and HbA1C of 6.0% or more, showed a high risk of T2DM development.

Acknowledgement

The authors gratefully acknowledge the support from Professor Sutin Sriussadaporn and Professor Sathit Vannasaeng for their expert advice, and Miss Khemajira Karaketklang for assistance with the statistical analysis.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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