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Incidence and predictors of type 2 diabetes among Koreans: A 12-year follow up of the Korean Genome and Epidemiology Study

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ABSTRACT

Aim: Because the incidence of type 2 diabetes in Korea has not been clearly defined, we examined the incidence of this condition and its association with impaired fasting glucose (IFG), impaired glucose tolerance (IGT), and other risk factors in a 12-year follow-up Korean community-based prospective cohort study.

Methods: We recruited 7542 subjects aged 40–69 years without diabetes at baseline examination from the Korean Genome and Epidemiology Study and followed these subjects for 12 years biennially. Diabetes was defined according to the 2010 American Diabetes Association criteria. The incidence of type 2 diabetes and the predictors of progression to diabetes were analyzed according to baseline glucose tolerance.

Results: The overall incidence of type 2 diabetes was 22.1 per 1000 person-years. Subjects with combined IFG-IGT at baseline had the highest incidence of diabetes, which was more than two-fold that of individuals with isolated IFG or isolated IGT (114.4 vs. 51.3 vs. 53.1 per 1000 person-years). A multivariate Cox proportional hazards model analysis showed that combined IFG-IGT, which were strong predictors of diabetes, as well as age, urban residence, family history of diabetes, smoking status, abdominal obesity, hypertension, high triglycerides and low HDL cholesterols were also independently associated with progression to diabetes.

Conclusions: The incidence of type 2 diabetes is relatively high in our Korean community-based sample. Combined IFG-IGT are strong predictors of type 2 diabetes. Measurement of 2-hour plasma glucose in addition to fasting plasma glucose is necessary for the detection of individuals at high risk for development of diabetes.

Abbreviations: IFG, impaired fasting glucose; IGT, impaired glucose tolerance; BMI, body mass index; BP, blood pressure; FPG, fasting plasma glucose; 2-h PG, 2-hour plasma glucose; HOMA-IR, homeostasis model assessment of insulin resistance; IGI, insulinogenic index; CRP, C-reactive protein

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1. Introduction

Diabetes is a worldwide public health concern with a significant impact on healthcare systems and patients' quality of life. The International Diabetes Federation estimated that 382 million individuals had diabetes in 2013, a number that surpassed earlier predictions, and this number is estimated to rise to 592 million by 2035 [1]. Specifically, Asia is considered to be on the verge of an emerging diabetes epidemic [2]. In Korea, rapid economic development, a Westernized lifestyle, and a rapid progression to an aging society have resulted in increased rates of diabetes [3]. Thus, the prevalence of diabetes in Korea has increased during the past several decades from 0.9% in 1971 to ~7–9% by the end of the 1990s [4]. According to the Korea National Health and Nutritional Examination Survey (KNHANES) studies performed from 2001 to 2013, the age-standardized prevalence of diabetes among adults 30 years of age and older increased from 8.6% to 11.0% [5]. Although estimates of the prevalence of diabetes in Korea have been calculated from the KNHANES, the incidence of type 2 diabetes in Korea has not been fully clarified, as data are lacking. Because type 2 diabetes is a heterogeneous disease that results from a combination of genetic, environmental, and societal factors, there is a need for population-based, ethnically focused, and country-specific studies to adequately determine the incidence of type 2 diabetes. Several previous incidence studies performed in Korea had limitations [6–9]. These studies included a relatively small number of participants in only rural or urban areas and had short follow-up periods. Moreover, oral glucose tolerance tests (OGTT) were not performed on all participants to confirm the diagnosis of diabetes or prediabetes. Lastly, there is no information concerning person-years at risk and diabetes incidence in terms of cases per 1000 person-years.

Prediabetes refers to a metabolic state between normal glucose homeostasis and diabetes [10]. It is known that impaired fasting glucose (IFG) is associated with insulin resistance, and impaired glucose tolerance (IGT) is associated with impaired insulin secretion [11]. The incidence of diabetes is strongly associated with prediabetes, but diabetes risk varies widely according to the particular population and is poorly documented in Korea [12].

Therefore, we investigated the incidence of type 2 diabetes according to baseline glucose tolerance status in a Korean community-based prospective cohort study with a 12-year follow-up period. Additionally, we analyzed the predictors of progression to diabetes.

2. Research design and methods

2.1. *Study population*

The Ansung-Ansan Cohort Study is a prospective community-based cohort study that is part of the Korean

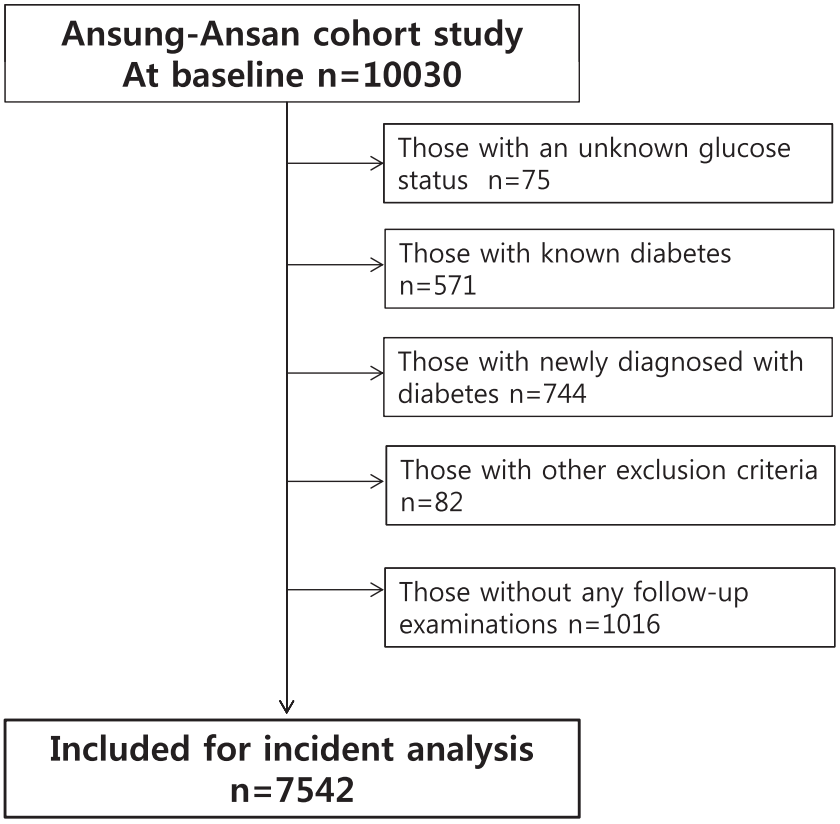

Fig. 1 – Flow diagram of the study.

Genome and Epidemiology Study (KoGES). Details of the KoGES and the methods used have been described previously [13]. The baseline survey was completed in 2001–2002, and follow-up examinations are ongoing biennially. We enrolled 10,030 subjects aged 40–69 years who lived in either the rural Ansung or urban Ansan communities. According to the 2000 census, Ansung is a rural community that has a population of 132,906, whereas Ansan is an urban community with a population of 554,998 [14]. A total of 5018 of 7192 eligible residents in Ansung were recruited using a cluster-sampling method stratified by age, sex, and residential district. Among 124,775 eligible subjects in Ansan, 5012 were surveyed using a random sampling method using the local telephone directory. A flow diagram describing the selection of study participants is shown in Fig. 1. To analyze of the incidence of diabetes, we excluded 91 individuals who had an unknown glucose status, 571 subjects with known diabetes, 744 subjects who were newly diagnosed with type 2 diabetes at baseline examination, and 82 subjects with a history of malignant diseases, liver failure, end-stage renal disease, rheumatological diseases, and acute or chronic infectious diseases, as well as those who had taken steroids in the previous 3 months. In addition, 1016 individuals were excluded because they did not undergo any follow-up examination after the baseline examination. Finally, 7542 individuals were included in the incidence analysis. Informed written consent was obtained from all participants. The study protocol was approved by the Ethics Committee of the Korean Center for Disease Control and the Ajou University School of Medicine Institutional Review Board.

2.2. Measurement of anthropometric and biochemical parameters

Anthropometric parameters and blood pressure (BP) were measured using standard methods. For abdominal obesity, waist circumference was measured at the midpoint between the lower limit of the ribcage and the iliac crest. Smoking status was classified into three categories: never smoker, former smoker, and current smoker. Alcohol consumption was divided into moderate (<420 kcal/week) versus heavy intake (⩾420 kcal/week) [15]. Exercise status was divided into two categories: none and regular (⩾1/week). One episode of exercise was defined as exercising for at least 30 min.

Table 1 – Clinical characteristics according to glucose tolerance status at baseline.

	Normal glucose	Isolated IFG	Isolated IGT	Combined IFG-IGT	P-value
N (% of total)	5633 (74.7)	199 (2.6)	1512 (20.0)	198 (2.6)	
Men (%)	48.2	71.9	40.1	66.7	<0.001[a,b,c,d,f]
Age (years)	51.3 ± 8.7	50.4 ± 8.3	53.1 ± 8.9	52.4 ± 8.7	<0.001[b,d]
Urban area (%)	46.1	50.3	55.8	51.5	<0.001[b]
Family history of diabetes (%)	9.7	14.6	12.1	15.2	0.001[a,b,c]
Smoking: never/former/current (%)	59.2/14.5/26.3	36.4/28.2/35.4	65.8/16.2/18.0	43.4/31.3/25.3	<0.001[a,b,c,d,f]
Alcohol consumption (%)	22.4	45.2	20.7	42.3	<0.001[a,c,d,f]
Exercise (%)	34.8	37.7	35.4	38.9	0.537
BMI (kg/m^2)	24.3 ± 3.0	25.5 ± 3.4	24.9 ± 3.2	25.4 ± 3.2	<0.001[a,b,c]
Waist circumference (cm)	81.8 ± 8.6	85.7 ± 8.6	82.9 ± 9.0	85.9 ± 8.3	<0.001[a,b,c,d,f]
Hypertension (%)	17.6	28.3	27.3	36.0	0.001[a,b,c,f]
Systolic BP (mmHg)	115.5 ± 17.2	119.7 ± 17.1	118.8 ± 18.4	123.5 ± 17.8	<0.001[a,b,c,f]
Diastolic BP (mmHg)	74.3 ± 11.3	78.3 ± 11.6	75.5 ± 11.7	79.6 ± 10.7	<0.001[a,b,c,d,f]
FPG (mg/dl)	82.7 ± 7.2	106.1 ± 5.6	85.5 ± 7.6	105.9 ± 5.3	<0.001[a,b,c,d,f]
2-h PG (mg/dl)	104.8 ± 20.7	109.7 ± 20.9	160.4 ± 15.6	167.5 ± 16.8	<0.001[a,b,c,d,e,f]
Fasting plasma insulin (IU/ml)†	7.5 ± 4.9	8.4 ± 4.1	7.7 ± 4.2	8.6 ± 4.5	<0.001[a,c,f]
2-h plasma insulin (IU/ml)†	24.4 ± 21.8	23.8 ± 19.8	41.4 ± 36.6	36.1 ± 30.4	<0.001[b,c,d,e]
HbA1c (%)	5.3 ± 0.3	5.5 ± 0.4	5.5 ± 0.4	5.7 ± 0.4	<0.001[a,b,c,e,f]
HbA1c (mmol/mol)	34.5 ± 3.7	36.4 ± 4.2	36.5 ± 4.1	38.4 ± 4.3	<0.001[a,b,c,e,f]
IGI†	0.53 ± 2.84	0.38 ± 1.01	0.22 ± 1.27	0.24 ± 0.85	<0.001[b,c,d,e]
HOMA-IR†	1.53 ± 1.02	2.20 ± 1.13	1.64 ± 0.94	2.24 ± 1.21	<0.001[a,b,c,d,f]
Total cholesterol (mg/dl)	189.8 ± 34.1	200.7 ± 34.5	198.5 ± 35.1	207.6 ± 34.3	<0.001[a,b,c,f]
HDL cholesterol (mg/dl)	46.6 ± 10.8	48.8 ± 12.4	46.3 ± 10.9	47.5 ± 11.7	0.016[a,d]
Triglycerides (mg/dl)	145.7 ± 89.7	158.2 ± 123.1	167.6 ± 103.4	192.3 ± 108.6	<0.001[b,c,e,f]
LDL cholesterol (mg/dl)	116.2 ± 32.9	124.5 ± 37.4	122.0 ± 34.6	127.0 ± 36.1	<0.001[a,b,c]
CRP (mg/dl)†	0.20 ± 0.39	0.24 ± 0.36	0.29 ± 0.90	0.27 ± 0.35	<0.001[a,b,c]

IFG, impaired fasting glucose; IGT, impaired glucose tolerance; urban area, Ansan; BMI, body mass index; BP, blood pressure; FPG, fasting plasma glucose; 2-h PG, 2-h plasma glucose; HbA1c, glycosylated hemoglobin; IGI, insulinogenic index; HDL/LDL, high-density/low-density lipoprotein; CRP, C-reactive protein. Data are presented as means ± standard deviation (SD) or %.

[a] Normal glucose vs. isolated IFG.

[b] Normal glucose vs. isolated IGT.

[c] Normal glucose vs. combined IFG-IGT.

[d] Isolated IFG vs. isolated IGT.

[e] Isolated IFG vs. combined IFG-IGT.

[f] Isolated IGT vs. combined IFG-IGT.

† Log-transformed values were used for statistical comparison. P-values represent the difference between groups for each variable using ANOVA and χ^2 tests, as appropriate.

Fasting plasma glucose (FPG), total cholesterol, triglycerides, and high-density lipoprotein (HDL) cholesterol were measured enzymatically using a 747 Chemistry Analyzer (Hitachi, Tokyo, Japan) after a 12-h fast. Low-density lipoprotein (LDL) cholesterol levels (mg/dl) were calculated using the following equation [16]: LDL cholesterol = total cholesterol (mg/dl) − HDL cholesterol (mg/dl) − (triglycerides (mg/dl)/5).

Fasting plasma insulin concentrations were measured using a radioimmunoassay (INS-IRMA Kit, BioSource, Belgium). Glycosylated hemoglobin (HbA1c) was measured using high-performance liquid chromatography (HPLC, VARIANT II; Bio-Rad Laboratories, Hercules, CA). The circulating concentration of C-reactive protein (CRP) was measured using an immunoradiometric assay (ADVIA 1650, Bayer Diagnostics, Tarrytown, NY, USA). All subjects underwent a 2-h 75-g OGTT at inclusion and every 2 years thereafter. Pancreatic β-cell function was estimated using the insulinogenic index (IGI) calculated with plasma insulin and glucose levels at 0 min and 60 min of the OGTT as follows [17]:

$$\text{IGI} = [\text{insulin}_{60\ \text{min}} - \text{insulin}_{0\ \text{min}}\ (\mu\text{IU/mL})]/[\text{glucose}_{60\ \text{min}} - \text{glucose}_{0\ \text{min}}\ (\text{mg/dl})]$$

Insulin resistance was calculated using the homeostasis model assessment of insulin resistance (HOMA-IR) using the following formula [18]:

$$\text{HOMA-IR} = [\text{fasting serum insulin}\ (\mu\text{IU/mL}) \times \text{fasting serum glucose}\ (\text{mg/dl})]/405.$$

2.3. Definitions

Diabetes was defined as FPG ⩾ 126 mg/dl, 2-h postload plasma glucose (PG) ⩾ 200 mg/dl, HbA1c ⩾ 6.5% (48 mmol/mol), or current treatment with oral anti-diabetes drugs or insulin according to the American Diabetes Association criteria [19]. Normal glucose was defined as FPG < 100 mg/dl and 2-h PG < 140 mg/dl and no diagnosis of diabetes. IFG was defined as FPG between 100 and 125 mg/dl and no diagnosis of diabetes. IGT was defined as 2-h PG levels between 140 and 199 mg/dl and no diagnosis of diabetes. Isolated IFG was defined as IFG without IGT, and isolated IGT was defined as IGT without IFG. Combined IFG-IGT was defined as the presence of IFG and IGT. Prediabetes was defined as diagnosed with IFG or IGT [10].

Hypertension was defined as systolic BP ⩾ 140 mmHg or diastolic BP ⩾ 90 mmHg or treatment with antihypertensive medication. A family history of diabetes was coded when there was at least one first-degree relative with diabetes. Abdominal obesity was defined using the Korean-specific waist circumference cutoff values of ⩾90 cm for men and ⩾85 cm for women [20]. High triglycerides were defined as serum triglyceride levels ⩾150 mg/dL, and low HDL cholesterol was defined as levels <40 mg/dL in men and <50 mg/dL in women [21].

2.4. Statistical analysis

Continuous variables are expressed as means ± standard deviation (SD), and categorical variables are expressed as numbers and percentages. Skewed values, such as fasting plasma insulin, 2-h plasma insulin, IGI, HOMA-IR, and CRP, were normalized using logarithmic transformation before all analyses. One-way analysis of variance (ANOVA) was used to assess differences in means according to metabolic phenotype for continuous variables. The χ^2 test was used for categorical data, as appropriate. Person-years of diabetes were

Table 2 – Incidence of type 2 diabetes according to gender and baseline glucose tolerance status.

	Normal glucose	Isolated IFG	Isolated IGT	Combined IFG-IGT	Prediabetes
All					
No. developing diabetes	657	81	624	138	843
Cumulative incidence (%)	11.7	40.7	41.3	69.7	44.2
Person-years	534,561	1579	11,744	1206	14,529
Incidence[a]	12.3	51.3	53.1	114.4	58.0
HR (95% CI[b])	1	3.98 (3.16–5.02)	4.50 (4.03–5.02)	9.50 (7.90–11.43)	4.85 (4.38–5.38)
Men					
No. developing diabetes	350	61	268	97	426
Cumulative incidence (%)	12.9	42.7	44.2	73.5	48.4
Person-years	25,325	1129	4463	768	6361
Incidence[a]	13.8	54.0	60.0	126.2	67.0
HR (95% CI[c])	1	3.89 (2.96–5.11)	4.42 (3.77–5.19)	9.90 (7.89–12.41)	4.95 (4.29–5.70)
Women					
No. developing diabetes	307	20	356	41	417
Cumulative incidence (%)	10.5	35.7	39.3	62.1	40.6
Person-years	28,136	450	7280	438	8168
Incidence[a]	10.9	44.5	48.9	93.6	51.1
HR (95% CI[c])	1	4.26 (2.71–6.71)	4.57 (3.92–5.32)	8.46 (6.10–11.73)	4.76 (4.11–5.52)

IFG, impaired fasting glucose; IGT, impaired glucose tolerance; HR, hazard ratio; CI, confidence interval. Prediabetes was defined as diagnosed with IFG or IGT.

[a] Incidence (per 1000 person-years).

[b] Adjusted for age and sex.

[c] Adjusted for age.

calculated from the baseline examination until the event developed or until the last examination. The 12-year incidence of diabetes was calculated per 1000 person-years by dividing the number of individuals who developed diabetes during follow up by the total person-time. The cumulative incidence rate was calculated by dividing the number of individuals who developed diabetes during follow up by the number of individuals without diabetes at baseline. A multivariate Cox proportional hazard model was used to determine the association between various factors and progression to diabetes. The data were analyzed using the SPSS software version 22.0 (SPSS Inc., Chicago, IL, USA). A two-sided *p*-value <0.05 was considered to indicate statistical significance.

3. Results

3.1. *Baseline clinical characteristics according to glucose tolerance status*

The baseline demographic and biochemical characteristics of the four glucose tolerance status groups are shown in Table 1. Of the 7542 participants (mean age 51.7 ± 8.8 years, men 47.7%), 1909 (25.3%) were classified as having prediabetes. The majority of participants with prediabetes were diagnosed using 2-h PG values. The prediabetes group consisted of the following: isolated IFG, 10.4%; isolated IGT, 79.2%; and combined IFG-IGT, 10.4%. Compared with subjects with normal glucose, those with isolated IFG, isolated IGT, and combined IFG-IGT had a higher BMI, waist circumference, systolic BP, diastolic BP, FPG, 2-h PG, HbA1c, HOMA-IR, total cholesterol, LDL cholesterol, and CRP and were significantly more likely to have family history of diabetes. The isolated IFG group had higher HOMA-IR and IGI values compared with the isolated IGT group. Moreover, the combined IFG-IGT group had higher HOMA-IR and lower IGI values, which reflected a state of increased insulin resistance with impaired insulin secretion.

3.2. *Incidence of diabetes at 12-year follow-up*

The final follow-up examination was performed in 2013–2014. The total person-years of follow up were 67,990 years. A total of 1500 of 7542 individuals without diabetes at baseline developed diabetes. The incidence of diabetes for the entire cohort was 22.1 per 1000 person-years, and the 12-year cumulative incidence of diabetes was 19.9%.

Participants with baseline prediabetes had a higher incidence of diabetes compared with those with normal glucose (58.0 vs. 12.3 per 1000 person-years, Table 2). Subjects with combined IFG-IGT at baseline had the highest incidence of diabetes, by more than two-fold, compared with individuals with isolated IFG or isolated IGT (114.4 vs. 51.3 vs. 53.1 per 1000 person-years). An analysis of gender-stratified data revealed a similar pattern.

We further evaluated the incidence of diabetes in subjects with normal glucose by dividing them into two subgroups (normal glucose-1-h-low and normal glucose-1-h-high) based on their 1-h plasma glucose concentration (greater or less than 155 mg/dl) after excluding 11 subjects without 1-h glucose levels. The incidence of diabetes in subjects with normal glucose-1-h-low and normal glucose-1-h-high were 7.5 and 25.3 per 1000 person-years, respectively (Supplementary Table 1).

3.3. *Risk factors for development of type 2 diabetes*

Using multivariate Cox proportional hazard models, we investigated the predictors for the development of diabetes during the follow-up period. After adjusting for various clinical parameters, isolated IFG, isolated IGT, and combined IFG-IGT were strong predictors of diabetes (Table 3). Additionally, age, urban residence, family history of diabetes, smoking status, abdominal obesity, hypertension, high triglycerides, and low HDL cholesterol were also independently associated with progression to diabetes.

Table 3 – Predictors of the incidence of type 2 diabetes.

Variables	HR (95% CI)	P
Prediabetes		
Isolated IFG (vs. normal glucose)	3.61 (2.85–4.57)	<0.001
Isolated IGT (vs. normal glucose)	4.06 (3.62–4.55)	<0.001
Combined IFG-IGT (vs. normal glucose)	8.21 (6.79–9.94)	<0.001
Age (year)	1.02 (1.02–1.03)	<0.001
Urban area (vs. rural area)	1.38 (1.23–1.55)	<0.001
Family history of diabetes	1.47 (1.27–1.71)	<0.001
Smoking		
Former (vs. never)	1.18 (1.02–1.36)	0.028
Current (vs. never)	1.61 (1.42–1.83)	<0.001
Abdominal obesity	1.35 (1.20–1.51)	<0.001
Hypertension	1.25 (1.11–1.41)	<0.001
High triglyceride	1.55 (1.38–1.73)	<0.001
Low HDL cholesterol	1.17 (1.04–1.31)	0.006

IFG, impaired fasting glucose; IGT, impaired glucose tolerance; urban area, Ansan; rural area; Ansung; HDL, high-density lipoprotein.
Multivariate Cox proportional hazard model adjusted for age, sex, residential area, family history of diabetes, smoking status, alcohol consumption, exercise, abdominal obesity, hypertension, high triglycerides, and low HDL cholesterol.

4. Discussion

This study evaluated the incidence of type 2 diabetes as well as the predictors of the development of diabetes in a representative sample of the general population of Korea, including residents of both rural and urban areas. The overall incidence of diabetes in this community-based cohort was 22.1 per 1000 person-years during a 12-year follow-up. Whereas the incidence of diabetes varies according to country and ethnicity, the incidence in our study is relatively high. A recent meta-analysis of Japanese studies reported an incidence of 9.0 per 1000 person-years [22], whereas an Asian Indian cohort study reported an incidence of 33.1 per 1000 person-years [23]. Studies with Caucasians reported much lower incidence rates (~10.0–11.3 per 1000 person-years) [24–26]. Moreover, a recent Italian population-based study reported an incidence of diabetes of 4 per 1000 person-years during 2002–2007 [27], whereas a Swedish study reported an incidence of 4.34 and 3.16 per 1000 person-years in men and women, respectively, in 2005–2013 [28].

Several previous studies have estimated the incidence of diabetes in Korea. During the 1990s, a 2-year follow-up study in rural areas reported an annual age-adjusted incidence of 3.2% in men and 1.5% in women [6]. Moreover, between 1997 and 1999, the adjusted annual incidence of diabetes for subjects over 40 years of age was 1.3% in urban areas [29]. Another rural cohort study conducted between 1997 and 2003 reported that the age- and sex-adjusted incidence of diabetes was 16.3 per 1000 person-years [8], whereas that reported in a rural area-based cohort survey conducted between 2003 and 2008 was 18.3 per 1000 person-years [9]. The incidence of diabetes in the current study is relatively higher than those in past studies. This may be due to several factors, including residence in both rural and urban areas, older age (40–69 years), and longer duration of follow up. This cohort study is the largest community-based prospective cohort specifically designed to study trends and characteristics in Korean patients with diabetes using reliable sampling designs and standardized data collection; thus, it is reflective of the incidence of diabetes in the Korean population.

Of those with prediabetes, 79.2% were identified using only 2-h PG and had isolated IGT. This suggests that FPG alone is not sufficient for screening individuals with abnormal glucose tolerance. The proportion of individuals with isolated IGT among individuals with prediabetes was 12.5% in American Indians [30] and 54.5% in South Asian Indians [23]. These results indicate that ethnic variations exist for the epidemiological and physiological characteristics of prediabetes and diabetes [31]. Therefore, 2-h PG as well as FPG may be crucial for the proper screening of prediabetes and diabetes in the Korean population. According to the recently published 2015 Korean Diabetes Fact Sheet, approximately 8.4 million Korean individuals (25.0%) aged 30 years or older had IFG in 2013 [32]. Because this prior survey did not carry out OGTT, we assume that more than 3 folds of this estimated subjects with prediabetes remain undetected, based on the proportion of individuals with prediabetes in our study.

The incidence of diabetes among individuals in our cohort with prediabetes was 58.0 per 1000 person-years. The progression rate from combined IFG-IGT to diabetes was more than two-fold greater than that from isolated IFG or isolated IGT to diabetes, which is consistent with previous studies in other populations [25,30,33,34]. After adjusting for various risk factors, combined IFG-IGT was the strongest predictor of the development of diabetes. IFG and IGT reflect different physiological abnormalities in glucose homeostasis; fasting hyperglycemia results from an increase in hepatic glucose output in the presence of hyperinsulinemia, whereas IGT is characterized by defects in the β-cell secretory response [11,35]. As demonstrated in Table 1, combined IFG-IGT includes defects in both insulin sensitivity and insulin secretion, and, therefore, is associated with a very high risk of progression to diabetes. On the basis of these result, although performing an OGTT is relatively inconvenient compared with measuring FPG alone, it can identify individuals at high risk for developing diabetes who require an intensive preventative strategy.

Similar to other studies [2,23,24,30,36], we observed that age, urban residence, family history of diabetes, smoking, abdominal obesity, hypertension, high triglycerides, and low HDL cholesterol were also important predictors for progression to diabetes.

It has been recently suggested that a 1-h post-load glucose levels ⩾155 mg/dl in those with normal glucose levels can be used to identify individuals at increased risk for the development of type 2 diabetes [37–39]. In particular Fiorentino et al. [39] reported that a 1-h post-load glucose level ⩾155 mg/dl is a stronger predictor of type 2 diabetes than is IFG. In our study, subjects with normal glucose-1 h-high exhibited a higher risk of developing type 2 diabetes than those with normal glucose-1 h-low, but they also demonstrated a lower risk than those with IFG.

From 2010 ADA criteria, an intermediate range of HbA1c 5.7–6.4% has been added as an indicator for high risk of type 2 diabetes [19]. When we defined prediabetes according to this criteria, the incidence of diabetes in subjects with prediabetes (n = 2721) was 49.7 per 1000 person-years. Cederberg et al. [40] compared fasting glucose, 2-h glucose, and HbA1c as predictors of type 2 diabetes at 10 years. According to this study, the combination of fasting glucose and 2-h glucose was more strongly associated with the incidence of type 2 diabetes than was the combination of fasting glucose and HbA1c. Thus, OGTT may be more helpful than measuring fasting glucose and HbA1c for predicting diabetes.

The present study has several strengths. First, this study included a large sample and had a long follow-up duration. Various risk factors for diabetes as well as indices for β-cell function and insulin resistance were included in the analyses. Next, glucose tolerance status was determined using an OGTT at baseline and at follow up, thereby ensuring an accurate estimate of the incidence of diabetes. Studies that use self-reports of diabetes diagnosis or administrative databases may underestimate the incidence due to overlooking undiagnosed or untreated diabetes [22]. Lastly, prediabetes status was analyzed in individuals with isolated IFG, isolated IGT, and combined IFG-IGT; thus, the incidence rates were presented for the isolated states as well as for the combined

state. Several limitations of this study must be considered. As this study was based on residents of the Ansung and Ansan communities, caution should be taken when generalizing the results to the Korean population as a whole. Because 30-min glucose and insulin values were not available, we used IGI at 60 min as the index of β-cell function. IGI at 60 min correlates well with IGI at 30 min and is an acceptable surrogate of early insulin secretion [41]. Furthermore, we did not consider changes in the modifiable risk factors that can affect the incidence of diabetes. Concomitant use of anti-hypertensive agents and lipid-lowering agents can affect incidence of diabetes. Angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers are associated with a decreased incidence of new-onset diabetes, whereas β-blockers, diuretics, and statins have a negative effect on glucose metabolism [42,43]. Because data on the specific classes of anti-hypertensive agents and lipid-lowering agents were not available for this study, we could not analyze the effect of these drugs on the incidence of diabetes. Nevertheless, this study provides the most reliable up-to-date information on the incidence and predictors of type 2 diabetes in the Korean population.

In conclusion, this 12-year prospective study carried out with the Korean population showed an incidence of type 2 diabetes of 22.1 per 1000 person-years, which is relatively high. IFG and IGT were highly predictive of diabetes, and their effects were additive. The measurement of 2-h PG is needed in addition to FPG levels to identify individuals at high risk for developing diabetes. These results emphasize the need to develop community health promotion strategies for the early detection and prevention of diabetes.

Authors contributions

Concept and design – SJH, NHC; acquisition of data – SHJ, HJK, DJK; analysis and interpretation of data – SHJ, HJK, DJK, KWL, NHC; drafting of the manuscript – SJH; revising the article critically for important intellectual content – SHJ, HJK, DJK, KWL, NHC; final approval of the version– SHJ, HJK, DJK, KWL, NHC.

Conflict of interest

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.diabres.2016.10.004.

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