Trend analysis of diabetic prevalence and incidence in a rural area of South Korea between 2003–2008

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ABSTRACT

Aims/Introduction: This study determined the change in prevalence of diabetes and prediabetes over a period of 5 years in South Korea. The incidence of diabetes and prediabetes and risk factors associated with the development of diabetes were also investigated.

Materials and Methods: The Dalseong population-based cohort survey recruited 1806 subjects who were over 20-years-old in 2003. Five years later, 1287 of the original subjects were re-evaluated and 187 new subjects were added to the study. All participants completed a questionnaire, were given a physical examination, and provided blood samples for analysis including 2 h oral glucose tolerances.

Results: Age-adjusted prevalence of diabetes rose from 6.7% in 2003 to 9.1% in 2008. The prevalence of prediabetes also increased from 18.5% in 2003 to 28.4% in 2008. The incidence rates of diabetes and prediabetes were 18.3 per 1000 person-years and 55.4 per 1000 person-years, respectively. The development of diabetes was associated with impaired fasting glucose (IFG) (odds ratio [OR] 5.661), impaired glucose tolerance (IGT) (OR: 6.013), age (OR 1.013), and waist-to-hip ratio (OR 1.513). After excluding the IFG and IGT, systolic blood pressure (OR 1.023), high-sensitivity C-reactive protein (hsCRP; OR 1.097), triglyceride (OR 1.002) and waist-to-hip ratio (OR 1.696) were statistically significant risk factors in a multivariate logistic regression analysis.

Conclusions: A significant rise in the prevalence of diabetes and prediabetes was observed between 2003 and 2008. In addition, this study newly demonstrated that waist-to-hip ratio and hsCRP were associated with the development of diabetes after adjusting for several confounding factors. (J Diabetes Invest, doi: 10.1111/j.2040-1124.2010.00045.x, 2010)

KEY WORDS: Diabetes mellitus, Prevalence, South Korea

INTRODUCTION

Diabetes mellitus is increasing rapidly worldwide, especially in Asia[1]. In 2007, more than 100 million people in Asia suffered from diabetes and 60% of the world's individuals with diabetes came from Asia[2]. Rapid socioeconomic changes, such as dietary patterns, technology transfer and economic growth, have led to a diabetes epidemic in Asia. According to previous reports, the prevalence of diabetes varies throughout Asia, according to race, lifestyle, and urbanization[3–7]. South Korea is one of several countries in which a rapid change in lifestyle of individuals is occurring with a rapid progression to an aging society. However, reports on the trends in the prevalence of diabetes in South Korea are not consistent. According to one study, a significant trend toward increased prevalence of diabetes from 6.9% in 1997 to 11.7% in 2003 was observed in one population-based cohort study carried out in a rural area of South Korea[8]. In contrast, the Korea National Health and Nutrition Examination Survey (KNHANES) carried out in 1998, 2001 and 2005 reported that the prevalence of diabetes decreased from 11.1% in 1998 to 8.9% in 2001, followed by a slight increase to 9.1% in 2005[9,10]. However, in these previous surveys, a 75 g oral glucose tolerance test (OGTT) could not be completely carried out for diagnosis of diabetes and prediabetes.

Based on these considerations, we felt it was important to reinvestigate the recent change in the prevalence of diabetes and prediabetes in South Korean adults using the 75 g OGTT. At the same time, we investigated the incidence of diabetes and

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prediabetes from 2003 to 2008 to provide more information for projecting the change in prevalence in South Korea. The other aim of this survey was to determine the risk factors associated with the development of diabetes, particularly in South Korean people.

MATERIALS AND METHODS
Study Population
The Dalseong County is a rural area located near Daegu metropolitan city, in the south-east of South Korea. According to the 2000 census, there were approximately 101,104 people over the age of 20 years living in Dalseong County. The present cross-sectional population-based survey was carried out in Dalseong County in August 2003 to determine the prevalence and incidence of diabetes and prediabetes. A multistage cluster sampling method was applied to select the study population. We selected nine control areas of community health centers. In each control area, two to three villages were randomly selected so that a total of 26 villages were chosen for sampling. All the voluntary subjects in each sampled village were enrolled. At the time of the initial examination, a total of 1806 people over the age of 20 years were recruited. The second survey was carried out in the same area in August 2008. Among the participants in the first survey, 207 people died or moved out of the area. Therefore, 1599 people were subjects for the second survey. As 312 subjects did not participate in the second survey, a total of 1287 people were re-evaluated for the glucose tolerance status for a follow-up rate of 80.5%. In addition, 187 new subjects were recruited in the second survey, bringing a total number of people evaluated in 2008 to 1474. The protocol for the study was approved by the institutional ethics committee and all participants provided informed consent.

Methods
All subjects underwent standardized physical examinations. Blood pressure was taken twice in a seated position with automated sphygmomanometers. Height and weight were measured. Body mass index (BMI) was calculated as the ratio of weight (kg) to standing height (m) squared (kg/m^2). Waist and hip circumference were measured in a standard manner to calculate the waist-to-hip ratio.

After an overnight fast, both capillary whole blood glucose measurement by glucose meter (Accu Check; Roche Diagnostics, Penzberg, Germany) and plasma glucose measurement (Beckman Glucose Analyzer; Beckman Instruments, Irvine, CA, USA) were obtained for every subject. It was followed by a 2-h 75 g OGTT in all participants, except for subjects with a prior history of diabetes or subjects with a fasting capillary whole blood glucose ≥11.0 mmol/L by glucometer in order to avoid a sudden rise of plasma glucose. Blood samplings for HbA$_{1c}$, lipid profiles, high-sensitivity C-reactive protein (hsCRP), uric acid, creatinine and a liver function test including aspartate transaminase (AST), alanine transferase (ALT), and γ-glutamyl-transpeptidase (γGT) were carried out.

The glucose tolerance status was classified according to the American Diabetes Association diagnostic criteria[11]. Subjects were classified as having diabetes when fasting plasma glucose (FPG) was ≥7.0 mmol/L or 2-h post-OGTT plasma glucose was ≥11.1 mmol/L. Impaired glucose tolerance (IGT) was diagnosed when 2-h post-OGTT glucose was ≥7.8, but <11.1 mmol/L. Impaired fasting glucose (IFG) was diagnosed when FPG was ≥5.6 mmol/L, but <7.0 mmol/L. Subjects with IFG or IGT were classified as prediabetes.

Statistical Analysis
The age-adjusted prevalence of diabetes and prediabetes was calculated separately for men and women, and for age categories using the Korean population aged 20–99 years from the year 2005 as the standard population. The 5-year incidence was estimated by dividing the number of incident cases by person-years at risk for diabetes at baseline. Baseline characteristics in 2003 including age, sex, BMI, waist-to-hip ratio, physical activity level, smoking status, blood pressure, lipid profiles, family history of diabetes and glucose tolerance status were considered to be possible risk factors. Differences between groups of independent variables were analyzed using a Student's t-test or a χ^2-test. Logistic regression models were carried out to assess the risk factors of diabetes. Statistical significance was defined as a P-value of 0.05 or less in all analyses. All data analyses were carried out using SPSS for Windows 15.0 (SPSS, Chicago, IL, USA).

RESULTS
The prevalence of diabetes increased markedly from 2003 to 2008 in both sexes (Table 1). The age-adjusted prevalence of diabetes in 2003 was 6.7%, which increased to 9.1% in 2008. Among all diabetic subjects in 2003, 34.7% were previously undiagnosed. In 2008, undiagnosed diabetic subjects were slightly increased to 38.9%. The newly diagnosed cases peaked in the age group <40 years in 2003 and 50–59 years in 2008, respectively. The increasing trend of prevalence was more prominent in prediabetes, in which the age-adjusted prevalence of prediabetes was 18.5% in 2003 and 28.4% in 2008. In both 2003 and 2008, diabetes was more prevalent in women than in men; however, prediabetes was more prevalent in men. Although the prevalence of diabetes increased with age, there was no significant difference in the prevalence of prediabetes by age category in either 2003 or 2008 (Table 1). The age group ≥70 years had the highest prevalence of diabetes in both 2003 and 2008. Table 2 shows the change in the prevalence of IFG and IGT during the 5 years. The age-adjusted prevalence of IFG and IGT in 2003 was 16.0% and 5.3%, which increased to 17.2% and 16.2%, respectively. While the prevalence of both IFG and IGT (2003, IFG 11.8%, IGT 4.9% vs 2008 IFG 15.4%, IGT 16.3%) increased in women, only the prevalence of IGT, but not that of IFG (2003, IFG 23.6%, IGT 6.2% vs 2008 IFG 21.0%, IGT 16.4%) increased in men. The highest prevalence of IFG was seen in the 50–59 years age group. In contrast, the age group ≥70 years had the highest prevalence of IGT (Table 2).

By 2008, a total of 135 of 1141 subjects without diabetes at baseline developed diabetes. The 5-year cumulative age-adjusted

Table 1 | Prevalence of diabetes and prediabetes in Dalseong population-based cohort survey (2003–2008)

	2003		2008	
	Prevalence (%)			
	Prediabetes	Diabetes	Prediabetes	Diabetes
Men				
Age (years)				
≤39	25.5	2.1	14.3	0
40–49	31.3	4.5	40.4	8.5
50–59	27.6	11.5	35.8	16.4
60–69	25.5	18.4	29.0	21.9
≥70	22.4	15.8	32.8	24.6
Total	26.3	12.8	32.8	20.1
Adjusted†	27.0	6.4	35.47	8.0
Women				
Age (years)				
≤39	6.5	2.6	14.3	0
40–49	13.3	5.6	22.5	10.8
50–59	23.9	9.3	26.6	16.3
60–69	23.7	14.5	30.0	25.2
≥70	20.8	17.3	35.8	24.9
Total	20.2	11.5	30.0	21.1
Adjusted†	13.8	6.9	25.0	9.9
Total				
Age (years)				
≤39	13.7	2.4	14.3	0
40–49	19.9	5.2	28.2	10.1
50–59	25.4	10.2	30.3	16.3
60–69	24.3	15.9	29.6	24.0
≥70	21.5	16.6	34.6	24.8
Total	22.5	12.0	31.1	20.8
Adjusted†	18.5	6.7	28.4	9.1

†Age-adjusted prevalence.

Table 2 | Prevalence of prediabetes in Dalseong population-based cohort survey (2003–2008)

	2003		2008	
	Prevalence (%)			
	IFG†	IGT‡	IFG†	IGT‡
Men				
Age (years)				
≤39	21.3	7.0	14.3	14.3
40–49	29.7	4.5	29.8	21.7
50–59	25.3	4.7	29.9	12.1
60–69	20.8	6.2	19.2	16.5
≥70	17.2	11.4	17.9	22.0
Total	22.6	6.8	22.2	17.8
Adjusted§	23.6	6.2	21.0	16.4
Women				
Age (years)				
≤39	6.5	1.3	14.3	14.3
40–49	10.8	6.3	12.7	15.5
50–59	20.2	6.6	15.8	17.1
60–69	19.9	8.7	20.6	18.5
≥70	15.8	10.5	20.3	23.6
Total	16.7	7.6	18.5	19.4
Adjusted§	11.8	4.9	15.4	16.3
Total				
Age (years)				
≤39	12.1	3.4	14.3	14.3
40–49	17.7	5.7	18.1	17.5
50–59	22.3	5.8	21.4	15.1
60–69	20.2	7.8	20.1	17.8
≥70	16.4	10.9	19.4	23.0
Total	19.0	7.3	19.9	18.8
Adjusted§	16.0	5.3	17.2	16.2

†Impaired fasting glucose, ‡Impaired glucose tolerance, §Age-adjusted prevalence.

incidence rates were 9.62% in men, 8.87% in women and 9.14% in total. Figure 1 shows the incidence rate of diabetes in subjects without diabetes at baseline by age category. The incident cases of diabetes increased with age, except for a small decline in the incidence rate of subjects aged ≥70 years. A total of 228 of 792 subjects with normal glucose tolerance (NGT) at 2003 developed prediabetes after 5 years. Age-adjusted incidence rate of prediabetes was 27.7% (29.2% in men, 27.0% in women). The progression rates to IFG and IGT from baseline NGT were 15.6 and 19.8%, respectively. The incidence rate from NGT to prediabetes did not increase significantly with age (Figure 2). When the incident diabetes and prediabetes cases were distributed equally throughout the 5 years, the age-adjusted incidence of diabetes and prediabetes were 18.3 per 1000 person-years and 55.4 per 1000 person-years, respectively.

Factors associated with diabetes development are shown in Table 3. Age, blood pressure, BMI, waist-to-hip ratio, AST, ALT, total cholesterol, triglyceride, γGT and hsCRP were significantly higher among those who developed diabetes compared with those who continued to have NGT. In a univariate logistic regression analysis with baseline characteristics of 2003, age (odds ratio [OR] 1.024, $P < 0.008$), systolic blood pressure (OR 1.024, $P < 0.001$), diastolic blood pressure (OR 1.039, $P < 0.001$), BMI (OR 1.118, $P < 0.001$), waist to hip ratio (OR 2.069, $P < 0.001$), AST (OR 1.015, $P < 0.003$), ALT (OR 1.017, $P < 0.003$), total cholesterol (OR 1.006, $P < 0.024$), triglyceride (OR 1.002, $P < 0.001$), γGT (OR 1.005, $P < 0.011$), hsCRP (OR 1.099, $P < 0.006$), IFG (OR 6.636, $P < 0.001$) and IGT (OR 7.440, $P < 0.001$) were significant risk factors for development of diabetes. Multiple logistic regression analysis showed that IFG, IGT, age and waist-to hip-ratio were statistically significant factors for development of diabetes (Table 4). As IFG and IGT are very well-known to strongly influence the development of diabetes, we re-analyzed the risk factors after excluding IFG and IGT. On this basis, systolic blood pressure, hsCRP, triglyceride, and waist-to-hip ratio were statistically significant risk factors (Table 5).
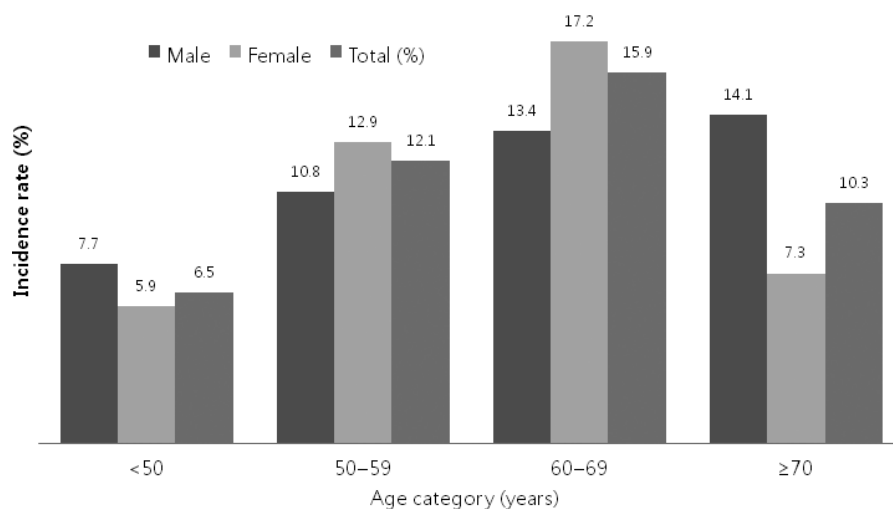
Figure 1 | Cumulative incidence rate of subjects with normal glucose tolerance or prediabetes to those with diabetes according to their age group over 5 years (2003–2008).
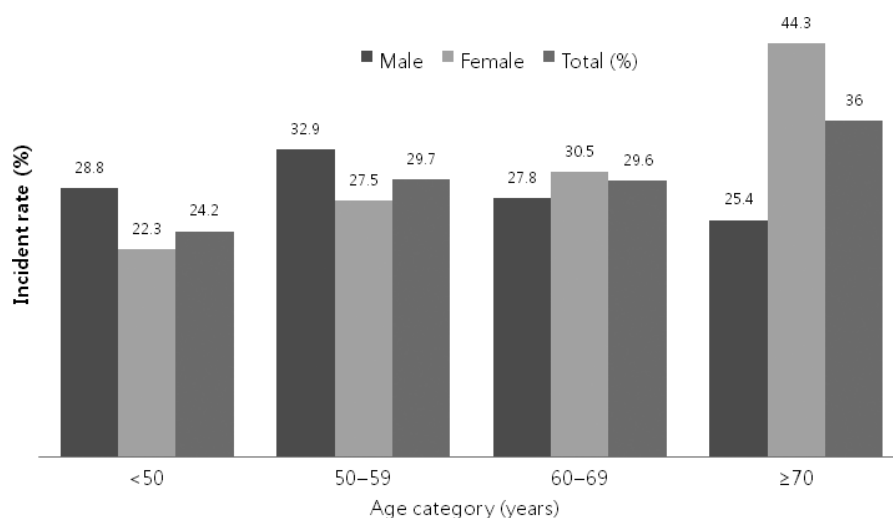

Figure 2 | Cumulative incidence rate of subjects with normal glucose tolerance to those with prediabetes according to their age group over 5 years (2003–2008).

DISCUSSION

This survey is the first comprehensive study that measured the prevalence and incidence of diabetes and prediabetes with a 5-year follow-up by using the OGTT in South Korea. Our data show a remarkable increase in the prevalence of diabetes and prediabetes in the Dalseong area of South Korea during the past 5 years (6.7% in 2003, 9.1% in 2008). The prevalence of diabetes increased from 6.9% in 1997 to 11.7% in 2003 in a survey of a Korean rural population[8]. In contrast, the Korea National Health and Nutrition Examination Survey (KNHANES) carried out in 1998, 2001 and 2005 reported that the recent prevalence of diabetes has not changed significantly based on the data that the prevalence decreased from 11.1% in 1998 to 8.9% in 2001 and increased slightly to 9.1% by 2005[9,10]. The average annual

risk of developing diabetes for someone with IFG or IGT is approximately 5–10% per year[12]. In the present study, we found a remarkable increase in prediabetes for 5 years (2003, 18.5% vs 2008, 28.4%). Although there is controversy as to whether the prevalence of diabetes will rapidly increase in South Korea, our survey suggested the presence of a large pool of people with the potential to develop diabetes in the near future. Similar to our data, the increasing prevalence of diabetes and/or prediabetes has been reported in other Asian countries. In urban areas of China, the prevalence of diabetes and prediabetes was 12.2% and 15.4% in 2002, and increased to 18.8% and 28.7% in 2006[7]. Studies from other Asian countries have shown a prevalence of diabetes of 9.0% for Singapore in 1998[13], 12.1% for India in 2000[14], 6.7% for Thailand in 2004[15] and 10.3% for Sri Lanka in

Table 3 | Baseline characteristics of the study population according to incident diabetes status (2003–2008)

No. subjects	No. incident diabetes	Incident diabetes	P-value
	1006	135	
Age (years)	58 ± 11	61 ± 9	0.002
Systolic BP (mmHg)	130 ± 18	139 ± 21	<0.001
Diastolic BP (mmHg)	82 ± 11	87 ± 12	<0.001
HbA$_{1c}$ (%)	5.3 ± 0.6	5.7 ± 0.5	0.111
Body mass index (kg/m^2)	23.5 ± 3.1	24.6 ± 3.2	<0.001
Waist circumference (cm)	81.7 ± 8.7	84.0 ± 8.8	<0.001
Waist-to-hip ratio			
Male	0.87 ± 0.07	0.92 ± 0.06	0.003
Female	0.87 ± 0.07	0.90 ± 0.06	<0.001
AST (IU/L)	24 ± 14	29 ± 21	0.017
ALT (IU/L)	37 ± 13	42 ± 25	0.028
Cholesterol (mg/dL)	197 ± 36	204 ± 37	0.023
Triglyceride (mg/dL)	150 ± 111	192 ± 139	0.001
HDL cholesterol (mg/dL)	52 ± 13	53 ± 23	0.456
LDL cholesterol (mg/dL)	115 ± 35	112 ± 41	0.463
γGT (IU/L)	28 ± 46	44 ± 45	0.003
hsCRP (mg/L)	1.28 ± 2.21	2.16 ± 3.67	0.028
Parental diabetes history (%)	5.5	6.8	0.862
Smoking Current smoker	23.1	26.2	0.375
Ex-smoker	13.3	16.4	
Never-smoker	65.3	57.5	

ALT, alanine transferase; AST, aspartate transaminase; BP, blood pressure; HDL, high-density lipoprotein; hsCRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein; γGT, γ-glutamyl-transpeptidase.

Table 4 | Adjusted odds ratios (95% confidence intervals) of developing diabetes including impaired fasting glucose and impaired glucose tolerance obtained from logistic regression analysis (2003–2008)

	Odds ratio	P-value	95% CI†
Impaired fasting glucose	5.661	<0.001	3.442–9.308
Impaired glucose tolerance	6.013	<0.001	3.225–11.213
Age (years)	1.013	0.047	1.000–1.063
Waist-to-hip ratio	1.513	0.049	1.002–2.285

†This model was adjusted for systolic blood pressure, diastolic blood pressure, body mass index, aspartate transaminase, alanine aminotransferase, total cholesterol, triglyceride, γ-glutamyl-transpeptidase and high-sensitivity C-reactive protein. CI, confidence intervals.

2006[16]. We observed that the prevalence of diabetes increased with age. However, other Korean studies have reported that the prevalence reached its peak in those in the 60–70 years age group and then declined[8]. This pattern was also observed in India[17]. The authors suggested the possibility of either premature death of diabetic patients aged ≥70 years or false negatives in isolated post-challenge hyperglycemic diabetes because of the lack of OGTT[8]. Our data suggest that the pattern in Korea is similar to those of Europe, America and China, which is

Table 5 | Adjusted odds ratios (95% confidence intervals) of developing diabetes excluding impaired fasting glucose and impaired glucose tolerance obtained from logistic regression analysis (2003–2008)

	Odds ratio	P-value	95% CI†
Systolic blood pressure (mmHg)	1.023	<0.001	1.010–1.035
hsCRP (mg/dL)	1.097	0.008	1.024–1.174
Triglyceride (mg/dL)	1.002	0.023	1.000–1.035
Waist-to-hip ratio	1.696	0.007	1.154–2.492

†This model was adjusted for age, diastolic blood pressure, body mass index, aspartate transaminase, alanine aminotransferase, total cholesterol, γ-glutamyl-transpeptidase. CI, confidence intervals.

consistent with the observation that diabetes has been increasing with age[17].

The increasing trend of prevalence of prediabetes was attributed to a marked change of prevalence of IGT. Previous reports have suggested that IFG is predominantly related to genetic factors and male sex, whereas IGT is predominantly related to physical inactivity and an unhealthy diet[18,19]. Our data show that a potential causative factor leading to the remarkable increase of prediabetes is peripheral insulin resistance associated with socioeconomic change, such as westernized diet patterns and physical inactivity. Furthermore, this result showed that the OGTT has an important role in screening for prediabetes. A fasting glucose level without OGTT might underestimate the incidence of IGT.

The highest prevalence of prediabetes was seen in the 50–59 years age group in 2003 and ≥70 years age group in 2008. It was postulated that the age of the total population of cohort increased in 2008. In addition, we found that the prevalence of IFG did not increase with age, but IGT increased more in the elderly, which is consistent with observations in other Asian and European countries[20,21]. Prediabetes is not only a significant risk factor for progression to diabetes, but is also considered a risk factor for cardiovascular disease. Several lines of prospective studies have shown that cardiovascular events increased at plasma glucose levels well below those diagnostic of diabetes. The Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe (DECODE) study, for example, showed a graded increase between 2-h plasma glucose and cardiovascular disease mortality[22]. In the present data, the incidence rate of prediabetes was high in the less than 50 years age group (24.2%). The result was that prediabetes has developed more extensively in the middle-aged group, suggesting that we should focus on the identification and the management of undiagnosed prediabetes patients for cardiovascular disease prevention, especially those with IGT.

Another main issue in the present survey was the risk factors that affected the development of diabetes. The present data showed that prediabetes status, age and waist-to-hip ratio were variables that could predict the development of diabetes. In accordance with previous studies, prediabetes status was a most powerful predictor of diabetes. Impaired glucose tolerance

(OR 6.013) was associated more strongly than IGT (OR 5.661) with the development of diabetes, which is consistent with other reports[12,23].

To establish new risk factors along with conventional risk factors, such as IGT and IFG, we evaluated the association between the incident diabetic cases with the risk factors measured at baseline excluding IFG and IGT, because prediabetes is considered to be an intermediary category along the continuum to overt diabetes. Systolic blood pressure, hsCRP, triglyceride, and waist-to-hip ratio were independent risk factors for predicting diabetes.

In the present study, we confirmed that the waist-to-hip ratio, a measure indicative of central obesity, is a major risk factor of diabetes. The result that waist-to-hip ratio was still associated with diabetes after adjusting the BMI showed that central obesity contributes independently to the progression to diabetes. Despite the fact that Asians have lower BMI than western counterparts, some Asian countries have a similar or even higher prevalence of diabetes than western countries. This finding is explained by the observation that Asian populations are more prone to abdominal obesity with increased insulin resistance compared with their western counterparts. Therefore, central obesity is a useful marker as a risk of type 2 diabetes, especially in individuals with normal BMI values[24]. While high blood pressure and triglyceride are well known risk factors of diabetes, we observed that a relatively high level of hsCRP at baseline predicts the development of diabetes. However, there is controversy over whether CRP is an independent risk factor of diabetes. Results from a meta-analysis showed that CRP is significantly associated with the incidence of diabetes, but the association was completely attenuated after adjusting waist-to-hip ratio, γGT, and adiponectin[25]. A prospective study carried out in Finland showed a positive association between CRP and diabetes risk after adjusting other related factors[26]. The present results have also shown CRP was still a risk factor of diabetes after adjusting for the confounding factors by multiple regression analysis, which is in agreement with results of the prospective study. To prevent the development of diabetes, identifying patients with these risks early is still a major issue of growing clinical concern. There was no significant relationship between incident diabetes cases and parental diabetic histories, although the incidence rates of diabetes according to parental diabetes history were different (with parental diabetes, 14.5% vs without parental diabetes, 11.5%). Some people in old age could not accurately remember their parental medical history, which might have attenuated the relationship.

Although the present study was limited in size, relative parameters of diabetes and prediabetes were evaluated widely, and OGTT was carried out for exact diagnosis of glucose tolerance status, which has not been previously reported in South Korea. However, caution should be taken in interpreting the results as a generalized epidemiology of Korea's diabetes, because the Dalseong cohort could appear as a well-controlled epidemiologic survey, but might not be representative of the population throughout Korea.

In conclusion, the prevalence of diabetes and prediabetes significantly increased over the course of a 5-year study. In addition to IFG, IGT, hypertension, dyslipidemia and age, we could identify other risk factors, such as hsCRP and waist-to-hip ratio associated with diabetes development. With an observation of a particularly high incidence rate of prediabetes in middle age, the present survey suggests that health promotion and lifestyle intervention are urgently required to prevent a further increase in the prevalence of diabetes in South Korea.

ACKNOWLEDGEMENTS

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