Endocrine Journal 2018, **65** (5), 527-536

Original

Twelve-year trends of increasing overweight and obesity in patients with diabetes: the Shiga Diabetes Clinical Survey

Itsuko Miyazawa[1)], Aya Kadota[2), 3)], Katsuyuki Miura[2), 3)], Motozumi Okamoto[4)], Takashi Nakamura[5), 8)], Tsuyoshi Ikai[6), 8)], Hiroshi Maegawa[1)] and Atsushi Ohnishi[7), 8)]

[1)] *Department of Medicine, Shiga University of Medical Science, Otsu 520-2192, Japan*
[2)] *Department of Public Health, Shiga University of Medical Science, Otsu 520-2192, Japan*
[3)] *Center for Epidemiologic Research in Asia, Shiga University of Medical Science, Otsu 520-2192, Japan*
[4)] *Japanese Red Cross Otsu Hospital, Otsu 520-8511, Japan*
[5)] *Department of Cardiology, Saiseikai Shiga Hospital, Ritto 520-3046, Japan*
[6)] *Wakakusa Clinic, Kusatsu 525-0045, Japan*
[7)] *Ohnishi Clinic, Kusatsu 525-0054, Japan*
[8)] *Shiga Medical Association, Ritto 520-3031, Japan*

Abstract. The prevalence of obesity is increasing globally in patients with diabetes. This study aimed to examine 12-year trends of increasing obesity in Japanese patients with diabetes, and their clinical features. The study used results of the Shiga Diabetes Clinical Survey, which recorded medical performance in diabetic patients in 2000, 2006 and 2012. Data were analyzed from 14,205, 14,407 and 21,449 adult patients in these three years, respectively. Overweight and obesity prevalence and the clinical features of diabetes patients were examined, stratified by body mass index (BMI) and age. The prevalence of overweight (BMI 25–30 kg/m^2) and obesity (BMI ≥30 kg/m^2) were 27.0% and 5.1% in 2000, 28.9% and 7.3% in 2006 and 30.9% and 10.0% in 2012. Glycemic control, blood pressure and serum lipid profile improved over 12 years in all BMI categories. However, glycemic and triglyceride control were insufficient in obese patients aged <65 years (hemoglobin A1c 7.5 ± 1.4%, triglyceride 197.7 ± 178.4 mg/dL in 2012). The percentage of patients who used antihypertensive and lipid-lowering drugs increased and patients with higher BMI had increased frequency of using these drugs, both in young and old age groups. Higher BMI was significantly and positively associated with albuminuria. In summary, overweight and obesity have increased in Japanese diabetic patients, particularly for younger generations. Findings suggest that obesity may lead to poorer glycemic control, blood pressure and lipid profiles. Overweight and obesity are important modifiable risk factors for diabetes, suggesting that more active weight-control interventions are warranted.

Key words: Overweight, Obesity, Diabetes mellitus, Albuminuria, Clinical survey

THE PREVALENCE OF OBESITY is increasing globally [1], and is a common comorbidity in patients with diabetes [2]. Obesity is an established cause of type 2 diabetes and is also an independent risk factor for cardiovascular disease (CVD) [3]. Furthermore, concurrent type 2 diabetes and obesity is associated with poor control of risk factors for CVD, regardless of ethnicity [2, 4-6]. The prevalence of obesity, defined as body mass index (BMI) ≥30 kg/m², is low in most Asian countries compared with Western countries [2, 7]. However, the prevalence of overweight, defined as BMI 25–30 kg/m^2, is substantially higher than that of obesity [7]. Asian individuals, including Japanese, tend to develop type 2 diabetes at a lower BMI [8] because, in general, they are more insulin resistant compared with other ethnicities [9]. The influence of overweight on the clinical management of diabetes tends to be more pronounced in Asian people. Therefore, it is important to examine trends in the prevalence of overweight and obesity Japanese diabetic patients, along with their clinical characteristics.

Submitted Sep. 29, 2017; Accepted Jan. 30, 2018 as EJ17-0415
Released online in J-STAGE as advance publication Mar. 10, 2018
Correspondence to: Itsuko Miyazawa, Department of Medicine, Shiga University of Medical Science, Seta Tsukinowa-cho, Otsu, Shiga 520-2192, Japan.
E-mail: shimojo@belle.shiga-med.ac.jp

The Japan Diabetes Clinical Data Management (JDDM), which examines the clinical performance of patients with diabetes, has reported that mean BMI has generally increased in Japanese diabetic patients, albeit slightly decreasing since 2014 [10]. The JDDM is a study that mainly involves diabetologists. In contrast, the Shiga Diabetes Clinical Survey (SDCS) covers all medical institutions including diabetologists and primary care clinics in the Shiga Prefecture. Therefore, the SDCS is able to assess the actual condition of diabetic patients in Japan. In addition, there is no survey which is carried out repeatedly over a long period in Japan.

The aim of this study was to assess trends of increasing overweight and obesity in Japanese diabetic patients, which tends to be a leaner population than that of Western countries. Using data from the SDCS, clinical characteristics stratified by age, sex and BMI category were examined and their 12-year trends were assessed.

Materials and Methods

The Shiga Medical Association established the SDCS in 2000. The association has carried out this large-scale survey of medical care in diabetes, which targets all medical institutions in Shiga, every 6 years since 2000. Details of the cohort have been reported previously [11]. Briefly, in 2000, registration forms were sent to all medical institutions in Shiga. In 2006 and 2012, the association sent registration forms to 266 and 241 medical institutions, respectively, because forms were sent to those facilities that were interested in participating. Data were collected in November in 2000 and in October and November for the years 2006 and 2012.

Information was collected on weight, height, blood pressure, the most recent data for hemoglobin A1c (HbA1c), other laboratory data, and drug therapy. Estimated glomerular filtration rate (eGFR) has been included since 2012. Each facility provided these data in a registration form. This study comprised patients aged ≥20 years with available data on BMI. We analyzed 14,205 patients in 2000, 14,407 in 2006 and 21,449 in 2012. Most of the blood examination data were not fasting data; fasting data were 37.1% in 2000, 24.7% in 2006 and 15.5% in 2012.

HbA1c, which was measured as outlined in the methods of Japan Diabetes Society (JDS), was estimated as the National Glycohemoglobin Standardization Program (NGSP) equivalent value by the following formula: HbA1c (NGSP) (%) = 1.02 × HbA1c (JDS) (%) + 0.25 [12].

BMI was calculated as bodyweight in kilograms divided by height in meters squared. Obesity class was defined according to World Health Organization (WHO) criteria as follows: non-obese (BMI <25 kg/m^2), overweight (BMI 25–30 kg/m^2), obesity class I (BMI 30–35 kg/m^2) and obesity class II or higher (BMI ≥35 kg/m^2), although the WHO's criteria was different from that of Japan Society for the Study of Obesity. (Obesity class defined by Japan Society for the Study of Obesity was as follows: non-obese (BMI <25 kg/m^2), obesity class I (BMI 25–30 kg/m^2), obesity class II (BMI 30–35 kg/m^2) and obesity class II or higher (BMI ≥35 kg/m^2)). eGFR was calculated using the simplified equation proposed by the Japanese Society of Nephrology [13] as follows: eGFR (mL/min/1.73 m^2) = 194 × [age (years)]$^{-0.287}$ × [serum creatinine (mg/dL)]$^{-1.094}$ × 0.739 (for females) [13].

Albuminuria was assessed by albumin-creatinine ratio (ACR) in spot urine samples.

This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Shiga University of Medical Science (No. 27-135).

Statistical analysis

All continuous variables were expressed as means ± standard deviation. For comparison among two groups, *t*-tests were used for continuous variables and the chi-square test for categorical variables. Kruskal-Wallis test was used to compare ACR between BMI categories. Logistic regression analysis was used to examine trends in prevalence of obesity stratified by age, sex and obesity class.

Statistical significance was defined as a p value of <0.05. All statistical analyses were conducted using SAS software (version 9.4, Cary, NC, USA).

Results

Trends in the prevalence of overweight and obesity

The proportion of patients with overweight and obesity (BMI ≥25 kg/m^2) was 32.1% in 2000, 36.2% in 2006 and 40.9% in 2012. The prevalence of BMI ≥25 kg/m^2 was significantly higher in women than men (28.4% v 36.2% in men and women, respectively, $p < 0.001$ in 2000; 34.7% v 38.1%, $p < 0.001$ in 2006; and 39.1% v 43.5%, $p < 0.001$ in 2012). There was statistically significant interaction between sex and age on the trend of

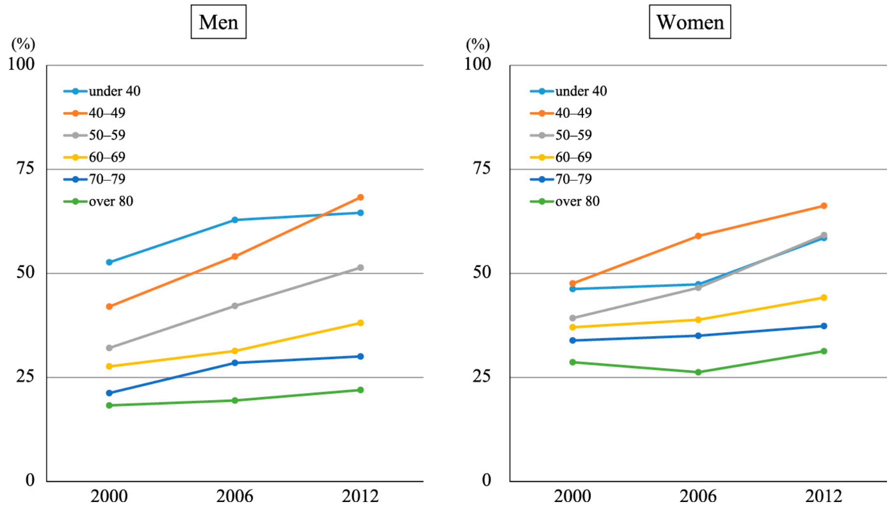

Fig. 1 Trends in the prevalence (%) of overweight and obesity (body mass index (BMI) ≥25 kg/m^2) among Japanese diabetic patients stratified by age in the three survey years (14,205 patients in 2000, 14,407 patients in 2006, 21,449 patients in 2012).

prevalence of BMI ≥25 kg/m^2 (p for interaction <0.001). We showed trends in the prevalence of BMI ≥25 kg/m^2 by sex and age in Fig. 1. The prevalence of BMI ≥25 kg/m^2 increased over time in both men and women and in all age groups (Fig. 1). The prevalence of BMI ≥25% has been over 50% in men aged <40 years since 2000, aged 40–49 since 2006 and aged 50–59 years since 2012. In women, the prevalence of BMI ≥25 kg/m^2 was also increased in younger age groups (<60 years), a trend that was almost the same in men.

Next, trends in BMI ≥25 kg/m^2 stratified by obesity class were explored. The percentage of all classes of obesity has increased over 12 years (Fig. 2A). Results stratified by age group are shown in Fig. 2B. In those aged <50 years, the prevalence of obesity class I and obesity class II or higher increased. In those aged 50–59 years, the prevalence of all obesity classes increased remarkably. In the 60–69 and 70–79 years age groups, the prevalence of all obesity classes increased, but to a lesser extent than in those aged 50–59 years of age. The prevalence in those aged >80 years changed only slightly. The trend of obesity in old generation were statistically significant but the slope were almost flat and it has no clinically meaning.

Trends in clinical characteristics stratified by BMI category

Mean BMI in the SDCS cohort has increased for 12 years (23.7 ± 3.6 kg/m^2 in 2000, 24.2 ± 3.8 kg/m^2 in 2006 and 24.6 ± 4.3 kg/m^2 in 2012, p for trend <0.001). The clinical characteristics of each study population stratified by age and BMI category are shown in Table 1. Both in the groups aged <65 years (hereinafter referred to as 'young') and ≥65 years (referred to as 'old'), patients with a higher BMI were younger and had higher HbA1c levels in all survey years. Patients with a higher BMI tended to have higher blood pressure and higher HbA1c, both in young and old groups. Young patients had higher total cholesterol, non-high-density lipoprotein cholesterol (HDL) and triglycerides but lower HDL cholesterol levels with increases in BMI. Old patients showed the same tendencies in lipid profile in 2000 and 2006 but those with obesity class I and II or higher had almost the same lipid profile in 2012. The percentage of patients who received treatment for diabetes including insulin therapy has increased for 12 years. Insulin was not commonly prescribed for obese patients in 2000, but the percentage prescribed insulin has gradually increased over time, both in young and old groups. The percentage of patients using antihypertensive or lipid-lowering drugs has also increased for 12 years. Patients with higher BMI had a higher frequency of antihypertensive and lipid-lowering drug prescribing, both in young and old groups. Old patients had a higher frequency of antihypertensive drug prescribing than young patients, but there was no difference between young and old age groups for lipid-lowering drugs.

Next, we compared the clinical characteristics stratified by obesity category between hospitals and primary care clinics. Patients with higher BMI were younger and

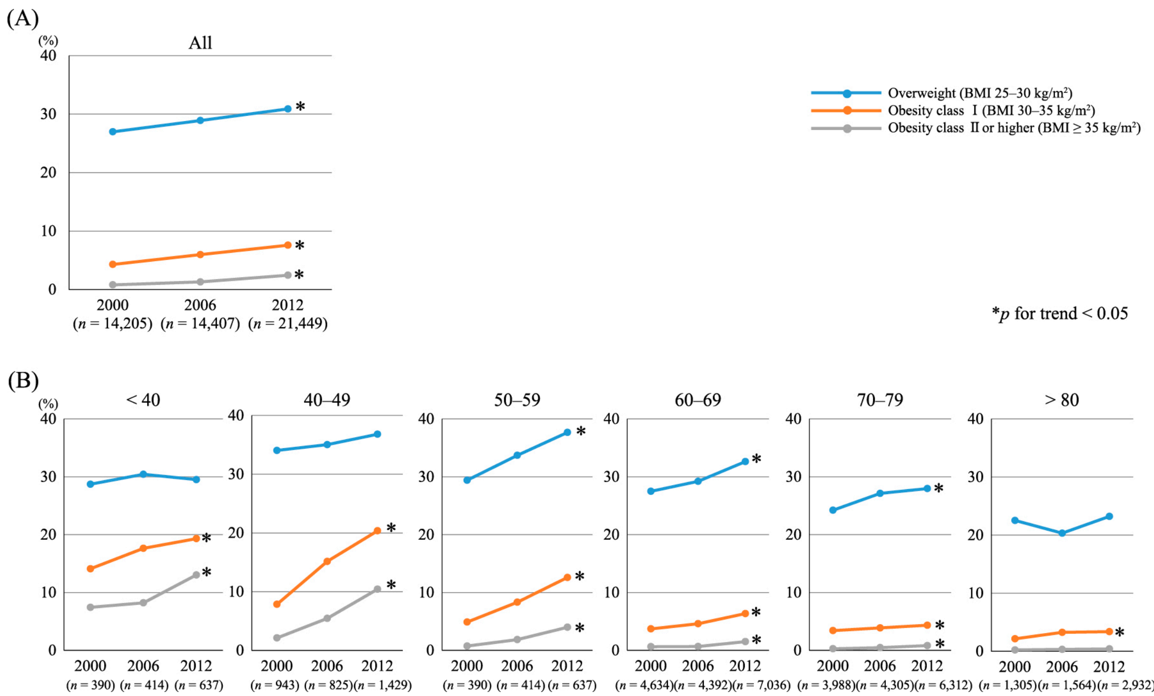

Fig. 2 Trends in the prevalence (%) of obesity classes among Japanese diabetic patients with BMI ≥25 kg/m^2 in the three survey years (4,556 patients in 2000, 5,211 patients in 2006, 8,776 patients in 2012). (A) Trend for all age groups, (B) Trend stratified by age group.

had higher HbA1c and poor control of blood pressure and lipid profile both in hospitals and primary care clinics. The trends of results between them were almost same (Supplementary Table 1).

Trends in glycemic control among diabetic patients with overweight and obesity

We limited the patients to BMI ≥25 kg/m^2 (4,556 patients in 2000, 5,211 patients in 2006 and 8,776 patients in 2012). Patients with BMI ≥25 kg/m^2 were divided into three age groups: <65 years, 65–75 years and ≥75 years, and differences in glycemic control between the three groups were examined. Because the target value of glycemic control is different between 65–75 years and ≥ 75 years according to the guidelines of the Japan Diabetes Society [14]. Fig. 3 shows trends in rates of achieving target HbA1c <7.0% among patients with BMI ≥25 kg/m^2. The percentage of patients with HbA1c <7.0% was higher in 2012 than in 2000 and 2006 for all age groups and was higher in the older group in all survey years. More than half of patients aged ≥75 years with overweight and obesity achieved HbA1c <7.0% over 12 years.

The association between urinary albumin and BMI

Last, the association between urinary albumin and BMI in the cross-sectional analysis of the year 2012 was examined. The number of participants who had data for ACR was 8,097. Mean ACR was 81.5 mg/gCre in the non-obese group, 105.8 mg/gCre in the overweight group and 132.5 mg/gCre in the obese group (p < 0.001). We categorized participants by ACR into three groups: normoalbuminuria (<30 mg/gCre), microalbuminuria (30–300 mg/gCre) and macroalbuminuria (≥300 mg/gCre). The percentage of each group was 64.3% for normoalbuminuria, 28.9% for microalbuminuria and 6.8% in macroalbuminuria. Fig. 4 shows results stratified by age group. Both in young and old groups, the percentage of microalbuminuria and macroalbuminuria increased according to BMI category.

Discussion

Overweight and obesity have been increasing in Japanese diabetic patients. Glycemic, blood pressure and serum lipid control have improved over 12 years in all BMI categories. However, glycemic and triglyceride control remain insufficient in younger obese patients,

Table 1 Trends in clinical characteristics of Japananese diabetic patients stratified by BMI category in young and old age groups

Young (<65 years)

	2000			2006			2012		
BMI (kg/m^2)	Non-obese <25	Overweight 25–30	Obese ≥30	Non-obese <25	Overweight 25–30	Obese ≥30	Non-obese <25	Overweight 25–30	Obese ≥30
Number (*n*)	4,067	1,898	447	3,502	2,027	684	4,080	3,088	1,457
Men (%)	2,494 (61.3)	1,079 (56.9)	192 (43.0)	2,187 (62.5)	1,254 (61.9)	355 (51.9)	2,649 (64.9)	1,995 (64.6)	772 (53.0)
Age (year)	55.2 ± 7.8	54.4 ± 8.0	50.2 ± 10.5	56.6 ± 7.7	55.3 ± 7.9	51.1 ± 9.3	56.3 ± 8.3	55.0 ± 8.3	50.3 ± 9.5
Systolic blood pressure (mmHg)	131.9 ± 17.9	136.7 ± 16.9	141.0 ± 17.7	130.0 ± 16.3	134.2 ± 15.3	136.2 ± 16.5	127.9 ± 16.0	131.9 ± 15.0	134.6 ± 15.6
Diastolic blood pressure (mmHg)	76.5 ± 10.6	80.4 ± 10.2	83.9 ± 10.8	75.4 ± 10.1	79.0 ± 10.2	81.4 ± 10.9	75.0 ± 10.6	78.6 ± 10.6	80.4 ± 11.5
BMI (kg/m^2)	22.0 ± 2.0	27.0 ± 1.3	33.0 ± 3.2	22.1 ± 2.0	27.0 ± 1.4	33.1 ± 3.0	22.1 ± 2.0	27.2 ± 1.4	33.9 ± 3.9
Hemoglobin A1c (%)	7.5 ± 1.5	7.6 ± 1.5	7.7 ± 1.7	7.4 ± 1.3	7.6 ± 1.4	7.8 ± 1.5	7.1 ± 1.2	7.3 ± 1.3	7.5 ± 1.4
Total cholesterol (mg/dL)	198.8 ± 36.1	206.5 ± 35.4	211.4 ± 37.7	199.5 ± 35.4	204.7 ± 35.5	208.8 ± 36.7	188.6 ± 37.0	190.7 ± 36.8	194.0 ± 38.2
Triglyceride (mg/dL)	141.5 ± 106.4	191.2 ± 140.2	203.1 ± 130.1	137.7 ± 98.0	176.3 ± 114.0	193.3 ± 123.5	141.6 ± 110.0	179.6 ± 131.9	197.7 ± 178.4
High-density lipoprotein-cholesterol (mg/dL)	57.6 ± 17.7	51.1 ± 15.5	50.3 ± 14.6	58.8 ± 17.5	52.2 ± 14.1	50.8 ± 14.5	59.1 ± 17.0	52.3 ± 13.6	50.7 ± 12.3
Non-high-density lipoprotein-cholesterol (mg/dL)	141.2 ± 36.7	154.9 ± 35.2	162.0 ± 38.0	140.7 ± 37.0	152.4 ± 36.4	157.2 ± 36.8	130.5 ± 35.0	139.1 ± 35.8	144.3 ± 37.9
Creatinine (mg/dL)	—	—	—	—	—	—	0.9 ± 0.9	0.9 ± 0.8	0.8 ± 0.6
eGFR (mL/min/1.73 m^2)	—	—	—	—	—	—	79.4 ± 22.3	77.6 ± 21.8	82.6 ± 24.3
Medication for Diabetes (%)	77.1	73.3	71.4	79.9	80.3	81.3	86.7	87.8	87.4
Use of insulin (%)	22.6	15.1	14.3	27.0	21.0	21.1	31.5	24.9	26.3
Use of antihypertensive drugs (%)	31.1	46.3	60.6	35.4	50.7	60.4	38.8	55.7	64.5
Use of lipid-lowering drugs (%)	23.5	33.7	32.4	29.9	40.8	43.7	41.9	54.2	50.3

Old (≥65 years)

	2000			2006			2012		
BMI (kg/m^2)	Non-obese <25	Overweight 25–30	Obese ≥30	Non-obese <25	Overweight 25–30	Obese ≥30	Non-obese <25	Overweight 25–30	Obese ≥30
Number (*n*)	5,582	1,935	276	5,694	2,137	363	8,593	3,537	694
Men (%)	2,869 (36.8)	779 (40.3)	78 (28.3)	3,061 (53.8)	1,050 (49.1)	126 (34.7)	4,983 (58.0)	1,878 (53.1)	257 (37.0)
Age (year)	73.4 ± 6.1	72.9 ± 5.9	72.4 ± 5.2	74.8 ± 6.3	73.8 ± 5.8	73.8 ± 5.8	74.7 ± 6.6	73.7 ± 6.3	72.7 ± 6.1
Systolic blood pressure (mmHg)	138.0 ± 17.1	141.9 ± 16.0	143.0 ± 15.2	135.0 ± 16.1	138.0 ± 15.2	139.4 ± 16.7	131.3 ± 16.3	133.9 ± 14.8	135.7 ± 14.9
Diastolic blood pressure (mmHg)	74.4 ± 10.4	77.5 ± 9.7	78.4 ± 10.2	72.9 ± 10.0	75.7 ± 9.9	76.8 ± 9.4	70.9 ± 10.7	72.8 ± 10.2	73.6 ± 10.5
BMI (kg/m^2)	21.7 ± 2.2	26.8 ± 1.3	32.1 ± 2.3	21.8 ± 2.1	26.9 ± 1.3	32.2 ± 2.2	21.8 ± 2.2	26.9 ± 1.3	32.6 ± 2.9
Hemoglobin A1c (%)	7.1 ± 1.3	7.2 ± 1.3	7.3 ± 1.4	7.2 ± 1.2	7.2 ± 1.1	7.3 ± 1.1	6.9 ± 0.9	7.0 ± 1.0	7.1 ± 1.0
Total cholesterol (mg/dL)	192.6 ± 33.7	200.1 ± 33.6	204.0 ± 31.0	191.8 ± 34.1	196.2 ± 31.2	200.1 ± 34.8	180.3 ± 34.7	181.5 ± 34.7	179.7 ± 31.2
Triglyceride (mg/dL)	128.8 ± 75.7	156.8 ± 84.6	164.5 ± 105.7	124.3 ± 73.6	150.0 ± 78.0	156.6 ± 86.6	124.2 ± 73.2	153.4 ± 90.0	155.4 ± 83.6
High-density lipoprotein-cholesterol (mg/dL)	55.6 ± 16.7	51.3 ± 14.1	51.5 ± 13.1	56.3 ± 16.8	51.1 ± 14.0	52.3 ± 15.1	57.1 ± 16.3	52.5 ± 14.6	52.7 ± 12.5
Non-high-density lipoprotein-cholesterol (mg/dL)	137.8 ± 33.4	148.3 ± 33.2	152.1 ± 31.2	135.3 ± 33.2	144.8 ± 30.9	146.2 ± 33.4	124.6 ± 32.1	129.7 ± 33.2	126.5 ± 29.5
Creatinine (mg/dL)	—	—	—	—	—	—	0.9 ± 0.7	0.9 ± 0.6	0.9 ± 0.5
eGFR (mL/min/1.73 m^2)	—	—	—	—	—	—	65.0 ± 20.5	62.7 ± 19.5	62.6 ± 20.0
Medication for Diabetes (%)	71.5	71.9	76.1	75.5	76.2	74.1	84.0	84.8	88.5
Use of insulin (%)	17.7	14.4	9.8	19.7	18.2	19.0	24.7	23.7	26.5
Use of antihypertensive drugs (%)	53.7	67.5	77.2	58.8	73.1	81.3	60.9	74.2	82.6
Use of lipid-lowering drugs (%)	27.0	35.7	44.6	31.6	40.5	49.3	45.2	55.6	60.2

Data are % or mean ± standard deviation.

BMI, body mass index; eGFR, estimated glomerular filtration rate

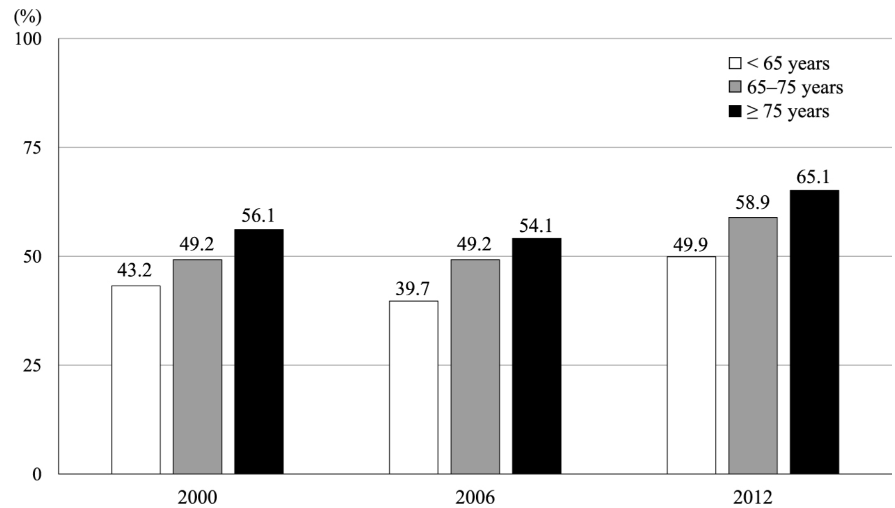

Fig. 3 Trends in the proportion (%) of patients with BMI ≥25 kg/m² with HbA1c <7.0% in the three survey years (4,556 patients in 2000, 5,211 patients in 2006, 8,776 patients in 2012).

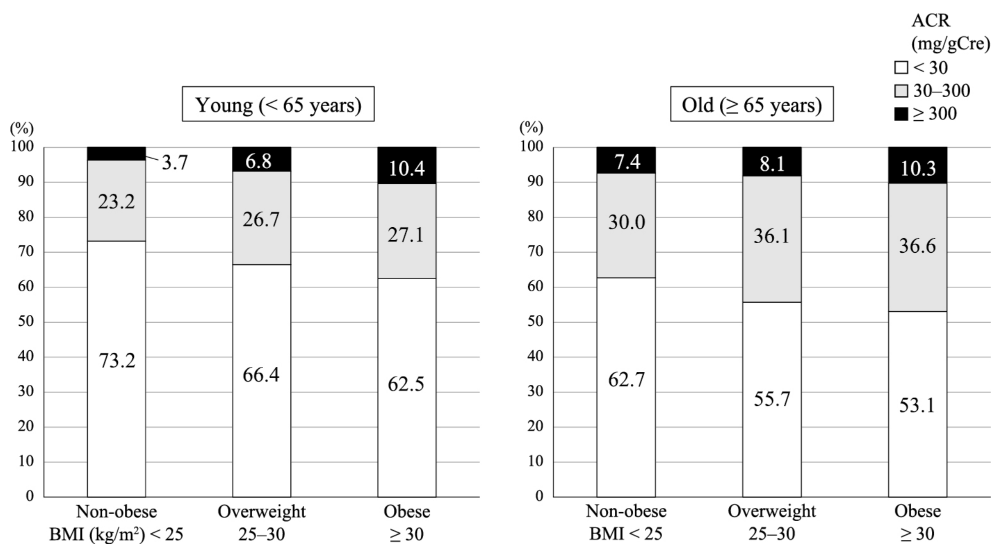

Fig. 4 The association between urinary albumin creatinine ratio (ACR) and BMI in 2012 (8,097 patients).

despite a higher frequency of medication use, because the prevalence of morbid obesity (obesity class II or higher) has increased. Higher BMI was significantly and positively associated with albuminuria in this study.

According to the latest National Nutrition Survey of Japan, mean BMI has remained constant in men and decreased in women, with a prevalence of BMI ≥25 kg/m² of 29.5% in men and 19.2% in women [15]. The prevalence of overweight was 20.1% and obesity was 3.8% in the Japanese general population [16]. In contrast, our results show that the prevalence of overweight and obesity in patients with diabetes has increased both in men and women. The trend of National Nutrition Survey of Japan and our study was different because the percentage of those who have diabetes was low in Japanese general population; 19.5% in men, 9.2% in women [15], respectively. Reports from Western countries show that the prevalence of obesity among diabetes patients has increased since the 1980s [17, 18]. A review of diabetes patients showed that the prevalence of obesity, defined as BMI ≥30 kg/m² or waist circumference ≥102 cm in men and ≥88 cm in women, was 50.9–98.6% in

Europe and 56.1% in Asia [2]. The percentage of Japanese patients with BMI ≥25 kg/m^2 was reported to be 33.9% in 2004 [19], which is similar to the findings from 2006 in our study. In another Asian study, conducted in Taiwan, the prevalence of overweight and obesity was 33.5% and 13%, respectively, again similar to our study [20]. The percentage of morbidly obese patients increased in our study, especially in young patients. Younger people were reported to have less amount of vegetable intake and higher percentage of fat intake to total energy [15]. In addition, mean step counts/day has decreased [15]. It suggests lifestyle becomes rapidly westernized and might influence increased morbid obesity.

BMI was inversely related to age in this study. This relationship between BMI and age is consistent with previous studies, which also demonstrated an inverse association with duration of diabetes [6, 21]. Japanese patients with diabetes have quite limited insulin secretory capacity and are becoming obese during the early stages of the disease [22]. It has also been reported that obesity in younger patients at first diagnosis of diabetes has increased over time in Japan [23]. It has been suggested that people of Asian ethnicity should pay more attention to increased BMI compared with other ethnicities—both in the pre-diabetic and diabetic stages.

In the baseline survey of the Japan Diabetes Complications Study (JDCS) in 1996, a prospective study examining the incidence of diabetic complications, patients with higher BMI tended to be younger, have higher blood pressure, higher triglyceride levels and lower HDL-cholesterol levels [22]. These results are comparable with our study. HbA1c level increased with BMI in our study but it was poorly correlated with BMI in the JDCS. Other studies have reported that diabetic patients with obesity had poor control of blood glucose, blood pressure and serum lipids, although they were more likely to be receiving antihypertensive drugs and lipid-lowering drugs compared with non-obese patients [4, 5]. In our study, patients in the older age group had glycemic, blood pressure and serum lipid control that was almost acceptable, even in those with BMI ≥30. Patients aged ≥75 years had continued good glycemic control. However, in 2012 in the young and obese group, glycemic control was insufficient, and triglyceride levels were also high, despite the increased use of medication over 12 years. In young patients with obesity, insulin resistance can be the result of visceral obesity and tends to be metabolic disorders, which is a clustering of CVD risk factors such as hypertension or dyslipidemia. Conversely, in older patients obesity tended to be milder, and could be explained by sarcopenia—the degenerative loss of skeletal muscle mass caused by aging. These differences in the pathophysiology of obesity and diabetes between young and old patients warrant attention.

According to the JDCS, a higher proportion of insulin therapy was seen in patients in the lower BMI categories [22]. We also observed that in 2000 the percentage of insulin use decreased with increasing BMI. However, this trend gradually diminished over the study period. One reason underlying increased insulin use might be the increasing use of combination therapy with oral hypoglycemic agents (OHAs) and insulin. More OHAs for use in combination with insulin have become available, and basal-insulin supported oral therapy has become popular in Japan [11].

We also examined the cross-sectional association between BMI and albuminuria using the 2012 survey (the 2000 and 2006 surveys were not used because of insufficient data on albuminuria). ACR increased with BMI both in the young and old age groups. eGFR was not associated with BMI in the young group but decreased with BMI in the old group. We presume that younger age in the higher BMI categories might be associated with higher eGFR both in young and old groups and that eGFR in the young group is affected by glomerular hyper-filtration, which is observed in the early stages of diabetic nephropathy. Previous reports have shown higher BMI to be a risk factor for end-stage renal disease [24] and suggest that obesity is a risk factor for renal dysfunction. In this study, albuminuria could not be distinguished from diabetic nephropathy or obesity-related glomerulopathy (ORG), which is caused by obesity and also results in proteinuria. In diabetes of long duration, microalbuminuria and macroalbuminuria seem to be caused by diabetic nephropathy. Although duration of diabetes was unknown in our study, mean age was younger in the higher BMI categories. It should be recognized that obese patients may have albuminuria or proteinuria regardless of age or duration of diabetes. Previous reports from the JDDM showed a similar prevalence of microalbuminuria and macroalbuminuria [25] and the same tendency that nephropathy defined by ACR ≥30 mg/gCre increased with higher BMI levels [26]. This suggests our findings are reasonable. Weight loss interventions reduce microalbuminuria and proteinuria in obese patients, both with and without diabetes [27-29]. Obesity is a modifiable risk factor, and weight-loss interventions for obese patients should be done intensively. It must be noted that ACR is not sufficient as a marker for preventing ORG in diabetic patient, and it is necessary to establish novel predictive markers for ORG.

This study has several limitations. First, the cohort comprised both patients with type 1 and type 2 diabetes, although the majority are likely to have had type 2 diabetes because the incidence of type 1 diabetes is very low in Japan ($2.25/10^5$) [30]. Second, our study has the possibility of selection bias because medical institutes that have a particular interest in diabetes care may have participated more frequently. The response rate was unclear in this study, although we presume that most medical institutes that provide medical care to diabetic patients participated. Third, HbA1c measurement was carried out at each clinic or hospital and was not centralized. However, inter-laboratory differences in glycohemoglobin measurement in Japan are reported to have been reduced to a clinically acceptable level [31]. Fourth, quite few hemodialysis patients might be captured in this study. The proportion of patients with eGFR <15 mL/min/1.73 m^2 was 0.57%. Fifth, most of the blood examination data were not fasting data. Triglyceride level might be influenced by postprandial state. Sixth, we could not examine inter-subject or inter-institution variability. Because the SDCS data was anonymized, both individuals and institutions could not be identified. Finally, we did not have any information about exercise and diet habits in participants, including drinking habits.

In conclusion, the prevalence of overweight and obesity increased in this cohort of Japanese patients with diabetes. Our findings suggest that obesity may lead to worsened control of glycemic and cardiovascular risk factors. Overweight and obesity are important modifiable risk factors for diabetes. Reducing the prevalence of overweight and obesity will lead to an improvement in the medical performance of diabetic patients.

Acknowledgments

We thank all the members of the Shiga Medical Association for their participation in this study.

Members of the Shiga Diabetes Clinical Survey Group: Atsunori Kashiwagi (Department of Medicine, Shiga University of Medical Science), Masayuki Shigenaga (Shigenaga Clinic), Yuichi Orita (Orita Clinic), Tsuyoshi Otaka (Otaka Clinic), Nobuisa Mizuno, Hirohumi Fukumoto (Department of Medicine, Shiga Medical Center for Adults), Takamasa Miura (Miura Clinic), Yasuhiro Nishida (Department of Ophthalmology, Shiga University of Medical Science), Naoyuki Takashima, Hirotsugu Ueshima (Department of Health Science, Shiga University of Medical Science), Katsuhito Yoshitoku (Yoshitoku Clinic), Hideki Yano (Department of Medicine, Hikone Municipal Hospital), Makoto Konishi (Konishi Clinic), Hideki Noda, Masataka Nishimura (Department of Medicine, Nagahama City Hospital), Kenji Kamiuchi (Department of Medicine, Otsu Municipal Hospital), Masanori Iwanishi (Department of Medicine, Kusatsu General Hospital), Hideo Kawamura (Kawamura Clinic), Naoya Ochiai (Miyaji Clinic), Yukimasa Shimosaka (Shimosaka Clinic), Jun Morita (Morita Dental Clinic), Atsuo Ohnishi (Ohnishi Clinic), Takashi Nakamura (Saiseikai Shigaken Hospital), Tsuyoshi Ikai (Wakakusa Clinic).

Writing Committee: Itsuko Miyazawa, Hiroshi Maegawa (Department of Medicine, Shiga University of Medical Science), Aya Kadota, Katsuyuki Miura (Department of Public Health, Center for Epidemiologic Research in Asia, Shiga University of Medical Science), Motozumi Okamoto (Japanese Red Cross Otsu Hospital).

Disclosure

The authors declare no conflicts of interest.

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