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ORIGINAL ARTICLE

Negative effect of a previous diagnosis of diabetes on quality of life in a Japanese population: The Gifu Diabetes Study

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Abstract
Objective To evaluate the effect of a previous indication of hyperglycemia or previous diagnosis of diabetes on quality of life (QOL) in a randomly selected population from Gifu City, Japan.
Methods In total, 452 males and 648 females were enrolled in this study. We collected information on previous indications of hyperglycemia and previous diagnoses of diabetes using a self-reported questionnaire. Participants also completed the World Health Organization Quality of Life-26 (WHOQOL-26) questionnaire and provided blood samples for the measurement of fasting plasma glucose and glycated hemoglobin levels. A 75-g oral glucose tolerance test was also performed. We compared QOL scores between the previous indication of hyperglycemia group and previous diagnosis of the diabetes group to those of the control group.
Results WHOQOL-26 scores were significantly lower in the previous diagnosis of diabetes group than in the control group (3.23 ± 0.43 vs. 3.45 ± 0.43; $p < 0.01$). However, WHOQOL-26 scores in the previous indication of hyperglycemia group were not significantly different from those of the control group. Lowering of WHOQOL-26 scores was significantly affected by the previous diagnosis of diabetes not by the plasma glucose levels.
Conclusions Our study suggests that a previous diagnosis of diabetes has a negative effect on QOL in a Japanese population. Health promotion and education that take QOL into account should be considered for people diagnosed with diabetes.

Keywords Diabetes · Hyperglycemia · Quality of life · Questionnaire

Introduction

It has been shown previously that quality of life (QOL) in diabetic patients is reduced as a result of diabetic complications, adverse effects of therapy including hypoglycemia, and the presence of comorbidities including heart failure and depression [1–4]. In the UK Prospective Diabetes Study [1] and in an Asian population [4], QOL in diabetic patients was not affected by intensive policies to improve blood glucose control. Furthermore, QOL in diabetic patients is reported to be closely correlated with symptomatic complications. As with diabetes, many chronic disease conditions have been reported to influence QOL in the general population [5, 6]. Previous studies have demonstrated the relationship between a decrease in QOL and the existence of symptoms related to

A list of all participating members in the GDSG is given in the Acknowledgement section.

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complications or treatment [7], although few studies have investigated the relationship between a previous indication of hyperglycemia or a previous diagnosis of diabetes and QOL. We hypothesized that a previous indication of hyperglycemia or diagnosis of diabetes, made by medical professionals, physicians, or nurses, might affect patients' QOL. To examine this hypothesis, we compared QOL among Japanese subjects with a previous indication of hyperglycemia, those with a previous diagnosis of diabetes, and those without either condition.

Materials and methods

Study procedures and subjects

The Gifu Diabetes Study was conducted in Gifu City, Japan. In March 2005, 2260 males and 3010 females, aged 40–78 years, were randomly selected from the residential registry. Subjects were recruited via mail, and 452 males and 648 females agreed to participate in the study. Between November 2005 and May 2007, subjects visited 1 of 35 medical institutions and provided blood samples for the measurement of fasting plasma glucose (FPG) and glycated hemoglobin (HbA1c) levels. In addition, a 75-g oral glucose tolerance test (OGTT) was performed. OGTTs were not performed on people with definite hyperglycemia or diabetes. By the end of the examination, subjects submitted a self-reported questionnaire and the World Health Organization Quality of Life-26 (WHOQOL-26) survey. The questionnaire consisted of questions related to sex, age, living situation, education level, employment, alcohol intake, smoking, exercise, past medical history, and previous hyperglycemia or diabetes diagnosis. The WHOQOL-26 is a self-reported survey that consists of 26 questions regarding QOL and is divided into five domains: physical, psychological, social, environmental, and general domains. QOL is calculated using the mean of the total score and the scores of each domain. The Japanese version of the WHOQOL-26 has been validated previously [8]. A study comparing the short form-36 (SF-36) health survey with the WHOQOL-26 in a Taiwanese population reported that the SF-36 is a better measure of health-related QOL, while WHOQOL-26 is a better measure of global QOL [9]. The WHOQOL-26 was used in our survey because it targets the general population. This study was reviewed and approved by the Ethics Review Committee of Gifu University Graduate School of Medicine (no. 17-107).

Classification of subjects

To elucidate the relationship between QOL and a previous indication of hyperglycemia or a previous diagnosis of diabetes, subjects were classified into three groups. Subjects were asked if they had been identified by medical professionals as having high blood glucose levels or glycosuria. Subjects who responded "yes" were classified into the previous indication of hyperglycemia group (hyperglycemia group). Subjects were asked if they had been diagnosed with diabetes previously. Those who responded "yes" were classified into the previous diagnosis of diabetes group (diabetes group). If subjects responded "no" to both questions, they were assigned to the control group. Furthermore, to investigate the influence of diabetes medical treatment on QOL, the diabetes group was divided into the medical treatment group (treated group) and untreated group, and QOL was compared.

To evaluate the effect of plasma glucose levels on QOL, all untreated subjects were classified into groups based on FPG levels, HbA1c levels, and 75 g OGTT results. Subjects were classified by FPG levels as follows: <110, 110–125, ≥ 126 mg/dl, and treated groups. Subjects were classified into four groups according to HbA1c levels: <5.9, 5.9–6.4, ≥ 6.5 %, and treated groups. Subjects were classified into four groups according to the results of the 75-g OGTT: normal, impaired glucose tolerance, diabetes, and treated groups.

Statistical analysis

The characteristics of the subjects in the hyperglycemia group and diabetes group were compared to those of the control group. Continuous data were compared using Dunnett's tests. Categorical data were compared using chi-square tests. Fisher's exact tests were applied when the number of subjects in the group was less than ten. Bonferroni correction for multiple comparisons was used. A significance cutoff (0.05 divided by two models) was set at <0.025.

To compare the WHOQOL-26 scores of the hyperglycemia group and diabetes group to those of the control group, multiple regression analysis was used, with adjustments for sex, age, body mass index (BMI), unemployment, hypertension, dyslipidemia, cerebrovascular/cardiovascular disease, and orthopedic disease. Furthermore, Dunnett's tests were used to investigate the relationship between diabetes medical treatment and QOL and to compare the WHOQOL-26 score in each plasma glucose level group. All statistical analyses were performed using JMP version 8 (SAS Institute Inc., Cary, NC, USA).

Results

Study population

A total of 1100 subjects (452 males and 648 females) volunteered to participate in this study. After excluding 47

subjects who provided incomplete responses to the WHOQOL-26 survey, 1053 subjects (440 men, 613 women) were included in the study.

Differences in Characteristics between Groups

Of the 1053 subjects, 64 (6.1 %) were assigned to the diabetes group, 97 (9.2 %) were assigned to the hyperglycemia group, and the remaining 892 (84.7 %) were assigned to the control group (Table 1). The percentage of males in the hyperglycemia group was significantly higher than that in the control group (56.7 vs. 39.7 %; $p < 0.005$ by Bonferroni correction). The mean age in the diabetes group was significantly higher than that in the control group (64.1 ± 9.0 vs. 58.8 ± 9.7 years; $p < 0.0001$). In addition, the mean BMI and percentage of obese subjects (BMI ≥ 25 kg/m^2) in the diabetes group were significantly higher in the control group (24.3 ± 3.8 vs. 23.0 ± 3.2, $p < 0.01$; 43.1 vs. 24.1 %, $p < 0.005$ by Bonferroni correction, respectively). There were a number of additional significant differences between the diabetes group and control group, including the number of unemployed subjects ($p < 0.005$ by Bonferroni correction) and the number of subjects with hypertension ($p < 0.0005$ by Bonferroni correction), dyslipidemia ($p < 0.005$ by Bonferroni correction), cerebrovascular/cardiovascular disease ($p < 0.005$ by Bonferroni correction), and orthopedic disease ($p < 0.025$ by Bonferroni correction). Of the subjects in the diabetes group, 51 (79.7 %) received diabetes medical treatment, while 13 (20.3 %) were untreated.

Effect of diabetes diagnosis on WHOQOL-26 scores

The WHOQOL-26 scores of the control, hyperglycemia, and diabetes groups are shown in Table 2. After adjusting for sex, age, BMI, employment status, hypertension, dyslipidemia, cerebrovascular/cardiovascular disease, and orthopedic disease, the mean total score of the diabetes

Table 1 Characteristics of the previous indication of hyperglycemia group and previous diagnosis of diabetes group compared to the control group

	Control group ($N = 892$)	Previous indication of hyperglycemia group[a] ($N = 97$)	p	Previous diagnosis of diabetes group[b] ($N = 64$)	p
Sex (% male)	39.7	56.7	0.0007*	48.4	0.3045
Age (years)	58.8 ± 9.7	60.0 ± 10.3	0.4490	64.1 ± 9.0	<0.0001
Body mass index (kg/m^2)	23.0 ± 3.2	22.6 ± 3.1	0.3743	24.3 ± 3.8	0.0051
Body mass index ≥ 25 kg/m^2 (%)	24.1	22.7	0.7508	43.1	0.0013*
Living alone (%)	6.2	11.3	0.0525	10.9	0.1803
Education ≤ 9 years (%)	18.0	21.1	0.4705	26.6	0.0906
Unemployed (%)	37.0	36.5	0.9137	58.7	0.0006*
Alcohol intake > 20 g/day (%)	22.2	30.9	0.0525	21.9	0.9522
Current smoker (%)	14.7	15.5	0.8375	15.6	0.8379
Exercise < 1 h/week (%)	21.9	22.9	0.8270	19.7	0.6779
Hypertension (%)	22.1	24.7	0.5508	59.4	<0.0001*
Dyslipidemia (%)	32.0	43.3	0.0241*	50.0	0.0030*
Cerebrovascular/cardiovascular disease (%)	7.2	9.3	0.4162	18.8	0.0009*
Orthopedic disease (%)	9.6	15.5	0.0721	20.3	0.0068*
Cancer (%)	5.7	8.3	0.3621	9.4	0.2659
Mental disease (%)	3.8	3.1	1.0000	4.7	0.7322
Treated diabetes (%)	0	0		79.7	
Fasting plasma glucose (mg/dl)	91.8 ± 12.2	103.6 ± 27.7	<0.0001	126.4 ± 37.9	<0.0001
HbA1c (%)	5.71 ± 0.46	6.14 ± 0.82	<0.0001	7.14 ± 1.47	<0.0001

Data for age, body mass index (BMI), fasting plasma glucose, and glycated hemoglobin (HbA1c) are presented as the mean ± standard deviation. All other information is presented as numbers or percentages. Dunnett's tests were used to compare continuous variables. Chi-square tests or Fisher's exact tests were used to compare categorical variables, and Bonferroni correction was used for multiple comparisons

* Significant at $p < 0.025$ (Bonferroni correction)

[a] People who had noticed or determined that they had high blood glucose levels or glycosuria

[b] People who had been diagnosed with diabetes

Table 2 World Health Organization Quality of Life-26 scores of the previous indication of hyperglycemia group and previous diagnosis of diabetes group compared to the control group

	Control group	Previous indication of hyperglycemia group	p^a	Previous diagnosis of diabetes group	p^a
Total score	3.45 ± 0.43	3.44 ± 0.46	0.9993	3.23 ± 0.43	0.0030
Physical domain	3.64 ± 0.52	3.63 ± 0.53	0.9952	3.33 ± 0.54	0.0012
Psychological domain	3.44 ± 0.54	3.43 ± 0.59	0.9692	3.24 ± 0.52	0.0350
Social domain	3.38 ± 0.51	3.30 ± 0.59	0.7284	3.30 ± 0.52	0.9612
Environmental domain	3.37 ± 0.49	3.40 ± 0.51	0.8327	3.21 ± 0.47	0.0166
General domain	3.19 ± 0.62	3.18 ± 0.64	0.9825	2.78 ± 0.56	<0.0001

Data are presented as the mean ± standard deviation

[a] Adjusted for sex, age, body mass index, unemployment, hypertension, dyslipidemia, cerebrovascular/cardiovascular disease, and orthopedic disease

group was significantly lower than that of the control group (3.23 ± 0.43 vs. 3.45 ± 0.43; $p < 0.01$). The scores of all domains, other than the social domain, were significantly lower in the diabetes group than in the control group (physical domain, $p < 0.01$; psychological domain, $p < 0.05$; environmental domain, $p < 0.05$; general domain, $p < 0.0001$). In contrast, there were no significant differences in the total and domain scores between the hyperglycemia group and control group.

To identify the effect of "previous diagnosis" not "treatment" on QOL levels, target subjects were divided into the three groups: previous diagnosis of diabetes with treatment, previous diagnosis of diabetes without treatment, and control. Analyzed with Dunnett's tests for comparison of WHOQOL-26 scores, the total and physical domain scores of the diabetes group with/without treatment were significantly lower than those in the control group (Table 3).

To make sure that the suppressed QOL level was not due to plasma glucose levels, when all untreated subjects were classified according to FPG levels, HbA1c levels, or 75-g OGTT results, there were no significant differences in the WHOQOL-26 scores between the each plasma glucose level group (Table 4). On the other hand, the WHOQOL-26 score in the treated group was significantly lower than those of all various plasma glucose level groups, although the average plasma glucose level was not significantly different in HbA1c between the treated group and ≥6.5 % in the HbA1c group without treatment.

Discussion

In a Japanese population, QOL scores are lower in those with a previous diagnosis of diabetes than in those without a previous diagnosis of diabetes. Furthermore, there was no relationship between QOL scores and a previous indication of hyperglycemia. In addition, QOL was not influenced by FPG levels, HbA1c levels, or the results of the 75-g OGTT, indicating that QOL was not affected by plasma glucose levels.

The International Quality of Life Assessment Project, which was conducted in eight countries, reported that the presence of at least one chronic medical condition, including diabetes, on the physical health scale had a noteworthy effect on QOL [5]. Consistent with this, we found that a previous diagnosis of diabetes was associated with lower QOL. Furthermore, in a study of various Asian

Table 3 World Health Organization Quality of Life-26 scores of the medical treatment (treated group) and untreated subgroups of the previous diagnosis of diabetes group as compared with the control group

	Control group ($N = 892$)	Previous diagnosis of diabetes group ($N = 64$)			
		Untreated group ($N = 13$)	P	Treated group ($N = 51$)	P
Total score	3.45 ± 0.43	3.17 ± 0.40	0.0406	3.25 ± 0.43	0.0028
Physical domain	3.64 ± 0.52	3.29 ± 0.53	0.0308	3.35 ± 0.55	0.0003
Psychological domain	3.44 ± 0.54	3.17 ± 0.43	0.1383	3.25 ± 0.55	0.0364
Social domain	3.38 ± 0.51	3.13 ± 0.59	0.1563	3.35 ± 0.50	0.906
Environmental domain	3.37 ± 0.49	3.14 ± 0.46	0.1723	3.23 ± 0.47	0.0854
General domain	3.19 ± 0.62	2.88 ± 0.65	0.1412	2.75 ± 0.54	<0.0001

Data are presented as the mean ± standard deviation or numbers

Dunnett's tests were used (not adjusted)

Table 4 World Health Organization Quality of Life-26 scores subdivided according to fasting plasma glucose levels, HbA1c levels, and 75-g oral glucose tolerance test results

	Fasting plasma glucose (mg/dl)			
	<110 ($N = 927$)	110–125 ($N = 50$)	≥126 ($N = 24$)	Treated group ($N = 51$)
Mean ± SD	90.3 ± 7.8	115.8 ± 4.9	161.5 ± 46.8	128.9 ± 34.8[a]
Total score	3.44 ± 0.43	3.44 ± 0.45	3.51 ± 0.60	3.25 ± 0.43*
	HbA1c (%)			
	<5.9 ($N = 668$)	5.9–6.4 ($N = 278$)	≥6.5 ($N = 54$)	Treated group ($N = 51$)
Mean ± SD	5.53 ± 0.24	6.06 ± 0.15	7.25 ± 1.33	7.29 ± 1.32[b]
Total score	3.44 ± 0.44	3.45 ± 0.40	3.46 ± 0.54	3.25 ± 0.43*
	75 g OGTT			
	Normal ($N = 628$)	IGT ($N = 297$)	Diabetes ($N = 65$)	Treated group ($N = 51$)
Total score	3.45 ± 0.42	3.41 ± 0.45	3.50 ± 0.46	3.25 ± 0.43*

OGTT oral glucose tolerance test, *IGT* impaired glucose tolerance

* Significant at $p < 0.01$ by Dunnett's tests

[a] Fasting plasma glucose (FPG) of the treated group was significant lower than the ≥126 mg/dl in FPG group without treatment

[b] HbA1c of the treated group was not significantly different from the ≥6.5 % in the HbA1c group without treatment

ethnicities, diabetes was shown to have a negative impact on QOL, physical functioning, and general health [6]. Similarly, we found that QOL scores for the physical, psychological, environmental, and general domains were significantly lower in the diabetes group than in the control group. Moreover, it has been shown in a Korean population that diabetes is associated with impaired health-related QOL, independent of comorbidities [10]. Our results suggested that a diagnosis of diabetes itself was related to lower QOL, even after adjusting for hypertension, dyslipidemia, cerebrovascular/cardiovascular disease, and orthopedic disease.

It has been reported that treatment of diabetes influenced health-related QOL in a Japanese population [11]. Data from a recent meta-analysis revealed that the risk of depression was not higher among subjects with impaired glucose metabolism, normal glucose metabolism, or undiagnosed diabetes and that the risk of depression was significantly lower in these three groups than in subjects who had been previously diagnosed with type 2 diabetes [12]. In addition, the results of the meta-analysis showed that plasma glucose levels and the incidence of complications in each group were not associated with an increase in depressive symptoms, leading the authors to conclude that the burden of a chronic disease such as diabetes, which requires continued treatment to control the condition, might have some effect on the incidence of depression. In the 2 years following the diagnosis of diabetes, in the absence of complications, O'Connor et al. showed that the risk of depressive disorders increases [13]. These results are in line with the results found in our study, which showed an association between low QOL scores and a previous diagnosis of diabetes. People with a diabetes diagnosis are instructed to control their diet and to exercise and/or are prescribed medications and urged to measure their plasma glucose levels regularly. It is understandable that these additional responsibilities and behavioral changes might negatively affect QOL scores. In a large community-based study of older people with diabetes, a relationship between well-being and treatment satisfaction has been shown, with the well-being score of the insulin therapy group significantly lower than the well-being scores of the diet modification and tablet therapy groups [7]. In addition, although about 20 % of patients were not treated in the diabetes group in this study, their QOL scores were lower than those in the control group. They might be not able to go to the hospital regularly because of physical (diagnosed with other illnesses such as an orthopedic disease), economic, and domestic constraints (family member who required care, lack of understanding, etc.). However, it is not known whether their lowered QOL was due to disturbed regular medical visits or previous diabetes diagnosis in this group. Therefore, only prospective study following up their QOL levels with/without medical treatment after diabetes diagnosis should be clarified. A positive intervention considering QOL is also required for people who have not received medical treatment in diagnosing diabetes.

When the participants in our study were classified by FPG levels, HbA1c levels, and OGTT results, there were no significant differences in QOL, indicating that QOL was

not affected by plasma glucose levels. Similarly, Kleefstra et al. [14] showed that unrecognized hyperglycemia/diabetes does not reduce QOL. In our study, the diagnosis of diabetes and other medical information were obtained from a self-reported questionnaire; the reliability of data was not completely accurate. However, the Nord-Trøndelag diabetes study reported that the reliability of self-reported data is approximately 95 % [15], and this method has been used in previous studies [16–18]. As our study focused on the recognition of hyperglycemia or diabetes by the subjects, the self-reported questionnaire was considered adequate.

QOL is an important health outcome and the ultimate goal of all health interventions [19]. Multiple studies have reported that the duration of diabetes and disease severity are related to QOL [11, 20]. Therefore, if people with diabetes receive appropriate treatment from an early stage, serious complications may be prevented and QOL may thus be maintained. The Hoorn Screening Study demonstrated that QOL was significantly negatively affected in newly diagnosed diabetes patients; however, a year after diagnosis, QOL scores were positively affected by diabetes treatment [21]. In order to maintain QOL scores, not only the quality of medical treatment but also the appropriateness of the education and support systems for patients are important.

Our study had several limitations. First, we did not assess the effect of diabetic complications or clinical changes on QOL. Additional research is required to eliminate the effects of diabetic complications on QOL, as QOL is known to be affected by complications [1, 2]. Second, we did not assess the effects of medical interventions in subjects with a previous indication of hyperglycemia. Knowledge of diabetes and the mental/physical stress induced by medical interventions intended to promote lifestyle modification may have an influence on QOL. This relationship should be examined in the future. Third, our study used cross-sectional data. Therefore, we could not confirm whether QOL decreased immediately following a diagnosis of diabetes. To overcome this limitation, an additional follow-up study could provide insight into the relationship between QOL and a diagnosis of diabetes with medical interventions.

In our study, QOL was evaluated using the WHOQOL-26, which assesses general QOL in general populations; in most previous studies, QOL was evaluated using the SF-36 or EQ-5D and EQ-VAS, which are focused on health-related QOL. No population study examining the relationship between diabetes and QOL using the WHOQOL-26 has previously been reported. WHOQOL-26 was developed to measure comprehensive and subjective QOL and differs from other methods of measuring health-related QOL. The SF-36 is thought to measure health-related QOL more effectively, whereas the WHOQOL-26 is a better measure of global QOL [9]. It is significant that our results show that diabetes affects QOL, despite using a different method of assessment than previous studies.

In conclusion, we found that a previous diagnosis of diabetes had a negative effect on QOL in the Japanese population. These results suggest that a more careful promotion and education approach, taking QOL into account, should be considered when caring for individuals within the general population who have been diagnosed with diabetes.

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Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

Human rights statement and informed consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Informed consent or a substitute for it was obtained from all patients for being included in the study.

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