Living alone is associated with visit-to-visit HbA1c variability in men but not in women in people with type 2 diabetes: KAMOGAWA-DM cohort study

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Abstract. The purpose of this study was to evaluate the association between living alone and glycemic parameters, especially glycemic variability, in men and women with type 2 diabetes. Lifestyle factors, including living alone, were assessed by a questionnaire in this cross-sectional study. Average, standard deviation (SD), and coefficient of variation (CV) of HbA1c were calculated using the values of HbA1c, which were extracted from the medical record for 1 year. Eighteen percent of men (35/198) and 17% of women (18/103) were living alone. In men, the average of HbA1c (59.9 mmol/mol [11.0] vs. 55.7 mmol/mol [9.1], 7.6% [1.0] vs. 7.2% [0.8], p = 0.018), and CV of HbA1c (0.06 [0.03–0.08] vs. 0.03 [0.02–0.05], p < 0.001) were all significantly higher in men who were living alone than in men who weren’t. However, there were no differences in the average (53.2 mmol/mol [11.4] vs. 56.0 mmol/mol [8.8], 7.0% [1.0] vs. 7.3% [0.8], p = 0.252) or CV (0.03 [0.02–0.05] vs. 0.03 [0.02–0.04], p = 0.845) between women who were living alone and women who weren’t. Multiple regression analyses revealed that living alone was associated with CV of HbA1c after adjusting for covariates in men (β = 0.180, p = 0.005), but not in women (β = 0.085, p = 0.369). We showed that living alone is associated with visit-to-visit HbA1c variability in men, but not women, with type 2 diabetes. In clinical practice, it is necessary to pay attention to glycemic control in men who are living alone.

Key words: Lifestyle, Glycemic variability, Type 2 diabetes, Sociological aspects

THE NUMBER OF PEOPLE LIVING ALONE is increasing [1]. Likewise, the number of people with diabetes living alone is increasing, and the percentage of people with diabetes living alone was recently estimated to be around 7–15% [2]. Living alone provokes social and emotional loneliness, which can lead to various diseases, such as cardiovascular disease, and mortality [3, 4].

In addition to these reports, it has been suggested that living alone disrupts good glycemic control, through psychological and physical burden in elderly people with type 2 diabetes [2]. However, the association between mortality and living alone differs between sexes [5]. In fact, it has been reported that living alone is a risk factor for the development of diabetes, and mortality in men but not women [3, 6].

On the other hand, hemoglobin A1c (HbA1c) variability is known to be a risk factor for not only micro- and macro-vascular complications, but also all-cause mortality, independent of average HbA1c in people with type 2 diabetes [7, 8]. Thus, HbA1c variability is an important treatment target in patients with diabetes.

However, no previous studies have investigated the association between living alone and glycemic parameters, in people with type 2 diabetes, differs between men and women. Therefore, in this cross-sectional study of KAMOGAWA-DM cohort study, we researched the association between living alone and glycemic parameters, including the average, SD, and CV of HbA1c in people with type 2 diabetes, and compared findings between men and women.

Materials and Methods

Participants and study design

We initiated the KAMOGAWA-DM cohort study from 2014 to clarify the natural history, including the compli-
cations and mortality, of people with diabetes [9-11]. The Ethics Committee of Kyoto Prefectural University of Medicine approved this study (No. RBMR-E-466-7). This study was performed in University Hospital, Kyoto Prefectural University of Medicine. All people provided informed consent and written informed consent. After these process, people’s medical data was entered into a database after removing personal identification information. We extracted data from the KAMOGAWA-DM study for people with type 2 diabetes diagnosed by a physician (Kyoto, Japan), from January 2014 to January 2016 in this cross-sectional study. Many participants live in and around Kyoto city (Kyoto, Japan). The started timing varied by the participants between 2014–16 and we checked the one-year variability of HbA1c after starting the study of each participant. People undergoing steroid usage, severe renal dysfunction, defined as estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m²) [12], and people with a renal transplant or with a liver transplant were excluded, because the reliability of the HbA1c might be the low in these situations. For the same reason, people who were hospitalized during the relevant year were also excluded. People with incomplete data (blood biochemistry or questionnaires) were also excluded. To calculate the variability of HbA1c, we used five or more measurements of HbA1c per year [13]. For this reason, we excluded people whose HbA1c levels were measured less than five times a year.

Questionnaire and measurements

Lifestyle-related factors was assessed by a questionnaire survey. People who indicated they regularly performed sport at least once a week, were defined as regular exercisers [14]. Daily alcohol drinkers were defined as alcohol drinkers [15]. Smoking was defined as current tobacco use [15, 16]. A positive answer to the question of “Are you living alone?” is defined as living alone.

Body mass index (BMI) was calculated as follows: 
BMI = weight (kg) / height in meters squared (m²). Venous blood was collected after an overnight fast and was used to measure fasting plasma glucose, triglycerides, total cholesterol, and high-density lipoprotein (HDL) cholesterol levels.

We also researched diabetic medication being used by study participants, and categorized them as nutrient load reducers, insulin sensitizers, insulin secretagogues or insulin [9]. Nutrient load reducers included sodium-glucose cotransporter inhibitors and α-glucosidase inhibitors; insulin sensitizers included metformin and pioglitazone; and insulin secretagogues included glinides, sulfonylureas, dipeptidyl peptidase-4 inhibitors, and glucagon-like peptide-1 receptor agonist [9].

Definition of HbA1c variability

We extracted HbA1c values from the medical record for the one year following enrollment, and average HbA1c, standard deviation (SD) of HbA1c, and the coefficient of variation (CV) of HbA1c were calculated. CV of HbA1c was defined as SD / average HbA1c (%).

Statistical analysis

We performed statistical analyses by software of JMP ver. 12.0 (SAS Institute, Cary, NC, USA) or EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria) [17]. A p < 0.05 defined as statistically significant. Mean, median, and frequencies of potential confounding variables were calculated. Continuous variables were presented as the mean (SD) or the median (interquartile range [IR]) when the variables were skewed. Normal distribution was evaluated by Shapiro-wilk normality test and then homogeneity of variance was evaluated by F test. According to the status of living alone, participants were divided into two groups in each sex. Either Student’s t-test, or the Mann-Whitney U test was performed to evaluate the statistical significance of differences between groups. Categorical variables were presented as numbers, and the chi-squared test was performed to assess the statistical significance of differences between groups.

To clarify the effect of living alone on glycemic parameters, including average of HbA1c and CV of HbA1c, we used multiple regression analyses, adjusting for potential confounders; age, BMI, duration of diabetes, lifestyle-related factors [18], including alcohol, smoking, and exercise, nutrient load reducers, insulin sensitizers, insulin secretagogues, insulin treatment, and average HbA1c. To investigate the multicollinearity, we checked the variance inflation factor (VIF). We confirmed that all the VIF was less than 2.

Results

This study initially involved 646 peoples (405 men and 241 women), but 345 (205 men and 137 women) were excluded. In total, 301 people (198 men and 103 women) were included in the overall study population (Fig. 1).

The study participants’ clinical characteristics are presented according to sex and living-alone status in Table 1. Mean (SD) of age and median (IR) of diabetes duration were 67.0 (11.0) years and 10 (6–20) years, respectively. Mean (SD) of HbA1c was 56.1 mmol/mol (9.5) (7.3% [0.9]). Among them, 35 men (18%) and 18 women (17%) were living alone.
The average (SD) of HbA1c was significantly higher in men who lived alone than in men who did not (59.9 mmol/mol [11.0] vs. 55.7 mmol/mol [9.1], 7.6% [1.0] vs. 7.2% [0.8], p = 0.018). In addition, both SD (IR) and CV (IR) of HbA1c were significantly higher in men who lived alone than in men who did not (0.39 [0.17–0.62] vs. 0.24 [0.16–0.36], p < 0.001 and 0.06 [0.03–0.08] vs. 0.03 [0.02–0.05], p < 0.001, respectively). However, average, SD, and CV of HbA1c were not different between women who lived alone and women who did not (Table 1).

Multiple regression analyses showed that living alone was associated with CV of HbA1c after adjusting for covariates ($\beta = 0.142, p = 0.006$) (Supplemental Table 1). Furthermore, multiple regression analyses showed that living alone was associated with CV of HbA1c after adjusting for covariates in men ($\beta = 0.180, p = 0.005$), whereas living alone was not associated with CV of HbA1c after adjusting for covariates in women ($\beta = 0.085, p = 0.369$) (Table 2).

Discussion

We demonstrated that in men with type 2 diabetes, both the average and variability of HbA1c were higher in people living alone than in people not living alone. In addition, we found that living alone was independently associated with glycemic variability in men, but not women, with type 2 diabetes. Previous studies revealed that the impact of living alone on mortality differs between sexes [3, 5]. For example, men living alone tend to be regular smokers [6], and living alone is risk factor for mortality in men but not in women [3]. No previous studies have revealed the association between living alone and glycemic parameters differs between sexes in people with type 2 diabetes. This study is the first to show that living alone is associated with glycemic variability is only evident in men. HbA1c variability is known to be a risk factor for not only micro- or macro-vascular complications, but also all-cause mortality, independent of average HbA1c in people with diabetes [7]. Thus, our study may explain why mortality increases in men but not women who live alone [3].

There are several possible explanations for the association of living alone with glycemic variability in men, but not women. In Japan, consciousness differs between men and women regarding household assignment. In fact, the burden of household is more on women than on men and mainly women prepare meals [19]. It has been reported that the ratio of men who cook for themselves is lower in men who live alone than in men who do not [20]. However, the ratio of women who cook for themselves is similar in women who live alone to women who do not [20]. In addition, it has been reported that people who regularly eat at home have lower risk of developing diabetes compared with people who often eat out [21]. Because eating out often results in high calorie intake and disturbed nutritional balance, such as reduced vitamin intake, and fruit and vegetable, eating out is a risk factor for diabetes [21, 22]. Living alone may be associated with poor glycemic variability in men because men who live alone have less opportunities to cook for themselves and more opportunities to eat out, compared to men who live with other people, although we did not include ratios of eating out in this study population. In fact, it has been reported that diet is associated with HbA1c variability [23].
Table 1  Clinical characteristics of study people according to the presence of living alone

|                      | Total  | Living alone (−) | Living alone (+) | p       | Living alone (−) | Living alone (+) | p       |
|----------------------|--------|------------------|------------------|---------|------------------|------------------|---------|
|                      | n = 301| (n = 163)        | (n = 35)         |         | (n = 85)         | (n = 18)         |         |
| Age (year)           | 68     | (62–74)          | 68               | (61–74) | 66               | (57–73)          | 0.144   | 69     | (63–74) | 0.044   |
| Duration of diabetes (year) | 10     | (6–20)           | 10               | (6–20)  | 10               | (5–18)           | 0.624   | 12     | (7–19)  | 0.104   |
| Body mass index (kg/m²) | 23.6   | (21.2–25.3)      | 23.7             | (22.0–25.2) | 24.0            | (21.5–25.6)      | 0.913   | 23.4   | (19.9–25.3) | 0.755   |
| Average Hemoglobin A1c (%) | 7.1    | (6.7–7.8)        | 7.1              | (6.6–7.8) | 7.6             | (6.8–8.3)        | 0.043   | 7.1    | (6.7–7.7) | 0.252   |
| Average Hemoglobin A1c (mmol/mol) | 54.3   | (49.5–61.2)      | 53.8             | (49.0–61.2) | 59.7            | (50.7–67.2)      | 0.043   | 54.4   | (49.7–60.7) | 0.252   |
| SD of Hemoglobin A1c | 0.24   | (0.16–0.37)      | 0.24             | (0.16–0.36) | 0.39            | (0.17–0.62)      | 0.005   | 0.24   | (0.17–0.34) | 0.126   |
| CV of Hemoglobin A1c | 0.03   | (0.02–0.05)      | 0.03             | (0.02–0.05) | 0.06            | (0.03–0.08)      | 0.005   | 0.03   | (0.02–0.04) | 0.190   |
| Fasting plasma glucose (mmol/L) | 7.5    | (6.5–9.0)        | 7.7              | (6.6–9.0) | 8.2             | (6.7–9.5)        | 0.370   | 7.1    | (6.2–8.2) | 0.774   |
| Total cholesterol (mmol/L) | 4.8    | (0.8)            | 4.6              | (0.8)   | 4.7             | (0.6)            | 0.814   | 5.0    | (0.9)   | 0.318   |
| Triglycerides (mmol/L) | 1.2    | (0.9–1.8)        | 1.2              | (0.9–1.9) | 1.4             | (1.0–2.3)        | 0.179   | 1.1    | (0.8–1.6) | 0.183   |
| HDL cholesterol (mmol/L) | 1.4    | (1.2–1.8)        | 1.3              | (1.2–1.7) | 1.3             | (1.1–1.7)        | 0.581   | 1.7    | (1.4–2.0) | 0.514   |
| Exercise (−/+ )      | 133/168| 64/99           | 18/17            | 0.185   | 40/45           | 11/7             | 0.279   |
| Current smoker (−/+ ) | 262/39 | 137/26          | 31/4             | 0.498   | 79/6            | 15/3             | 0.190   |
| Alcohol drinking (−/+ ) | 231/70 | 110/53         | 25/10            | 0.650   | 80/5            | 16/2             | 0.423   |
| Insulin (−/+ )       | 229/72 | 127/36         | 24/11            | 0.239   | 63/22           | 15/3             | 0.407   |
| Insulin secretagogues (−/+ ) | 74/227 | 42/121       | 4/31             | 0.068   | 22/63           | 6/12             | 0.519   |
| Insulin sensitizers (−/+ ) | 183/118 | 96/67      | 22/13            | 0.665   | 55/30           | 10/8             | 0.465   |
| Nutrient load reducers (−/+ ) | 250/51 | 138/25      | 29/6             | 0.790   | 66/19           | 17/1             | 0.102   |

Data are expressed as mean (SD), median (interquartile range) or number. HDL, High-density lipoprotein. The difference between groups was analyzed by Student’s t-test, Mann-Whitney U-test or Chi-square test.

Insulin secretagogues included sulfonylureas, glinides, dipeptidyl peptidase-4 inhibitors and glucagon-like peptide-1 receptor agonist; insulin sensitizers included pioglitazone and metformin; and nutrient load reducers included α-glucosidase inhibitors and sodium-glucose cotransporter inhibitor.

Another possible reason is the timing of dinner. In this study, among the people whose dinner time could be assessed by the questionnaire, the mean (SD) dinner time for men who lived alone was significantly later than that of men who did not (19.5 h [1.5] vs. 19.0 h [1.0] (in 24-hour notation), p = 0.036), but dinner time was similar between women who lived alone and women who did not (18.6 [0.8] vs. 18.9 [0.9], p = 0.300). Late-night-dinner considerably prolongs postprandial glucose levels [24–26], and is risk for poor glycemic control [9]. Taking these findings together, living alone is associated with poor glycemic variability in men, but not in women.

In addition, psychological and physical burdens may differ between men and women who live alone. One of the reasons for living alone is marital status, which affects mental control and diabetes management, particularly in men [27]. Thus, living alone could lead to poor glycemic control through psychological and physical burdens in men. In fact, it has been reported that high stress is associated with HbA1c variability [28]. Furthermore, it has been reported that high average HbA1c is associated with high SD of HbA1c in people with type 2 diabetes [29].
Women: R² = 0.321 for CV of HbA1c. R² = 0.232 for average of HbA1c.

Men: R² = 0.315 for CV of HbA1c. R² = 0.163 for average of HbA1c.
diabetes [7]. In this study, the average HbA1c was higher in men who lived alone than men who did not, and this may explain why the SD and CV of HbA1c in men who lived alone were also higher.

In this study, we also showed that BMI and poor HbA1c are associated with CV of HbA1c, which are the same as previous studies [23]. Possible examination is that higher BMI is associated with metabolic abnormalities, which might be affected by inadequate diet and exercise. Possible examination is that higher BMI is associated with metabolic abnormalities, which might be affected by inadequate diet and exercise. Previous studies also revealed that exercise, younger age, and poor treatment adherence are associated with HbA1c variability [23, 28-30].

We should mention several limitations of this study. First, this is a cross-sectional study, so the causal relationship between living alone and glycemic parameters was unclear. Second, we did not assess the reasons for living alone, which can include divorce, bereavement, and unmarried status. However, a previous study reported that marital status does not significantly affect HbA1c level [31]. Moreover, we did not have a data of social support from the network, contacts to network, and academic history, which also might be have impact on glycemic control. Third, because HbA1c values have seasonal variation [32], the seasonality of the sampling month might cause the bias of HbA1c values. Fourth, we could not adjust the effect of original variability of measured HbA1c, which vary within 0.12–0.18% standard deviation. Fifth, the employment status before and after retirement are important. However, we did not have data of the employment status. Sixth, the measurement with questionnaire may be less accurate. Lastly, participants in this study were all Japanese, so it is difficult to generalize our results to all people with type 2 diabetes.

In conclusion, we demonstrate that living alone is associated with visit-to-visit HbA1c variability in men, but not women, with type 2 diabetes. In clinical practice, medical professionals need to check the living conditions of men with type 2 diabetes and provide nutritional support to reduce the future micro- and macro-vascular complications. Further studies are needed to identify methods to help men who live alone attain stable glycemic control.

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Conflicts of Interest

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