

# Frequency and Associated Factors of Hypoglycemic Symptoms and Fear of Hypoglycemia in Elderly Patient with Type 2 Diabetes at Primary Care Unit of Songklanagarind Hospital

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## Abstract

**Objective:** To determine the frequency of symptomatic hypoglycemia and its associated factors and fear of hypoglycemia in a population of elderly patient with type 2 diabetes at primary care unit of Songklanagarind Hospital. **Methodology:** This cross-sectional study was conducted from July to October 2018 at primary care unit of Songklanagarind Hospital. The participants aged 60 and older with type 2 diabetes were included. The socio-demographic characteristic questionnaire was interviewed by a researcher or research assistants. Baseline clinical data, included body weight, height, underlying disease, duration of diabetes, complications of diabetes (diabetic retinopathy, diabetic nephropathy, cerebrovascular, peripheral vascular, neurovascular and diabetic foot complication), HbA1c, fasting plasma glucose, type and dose of glucose lowering drugs, were reviewed from the hospital information system (HIS). The participants were asked on their experiences of hypoglycemic symptoms in the previous month. Fear of hypoglycemia was measured by the Thai version of Hypoglycemia Fear Survey (HFS) covering behavior subscale (HFS-B) and worry subscale (HFS-W). The higher scores indicate higher fear of hypoglycemia. Chi-square, Wilcoxon, and Fisher tests were applied to study significant variables. Logistic regression analyses were performed to evaluate the associations between associated factors and hypoglycemic symptoms. **Results:** Overall, 160 participants were involved (mean age  $68.6 \pm 6.1$  years, 53.8% females, diabetes duration of  $10.5 \pm 6.4$  years, 57.5% diabetic complications,  $7.5 \pm 1.8\%$  HbA1c), of whom 30% reported hypoglycemic symptoms. The associated factors of hypoglycemic symptoms were diabetic complications (aOR = 2.75; 95% CI 1.23 - 6.14;  $p = 0.012$ ), glipizide use (aOR = 5.03; 95% CI 1.99 - 12.71;  $p < 0.001$ ) and fasting plasma glucose (aOR = 0.97; 95% CI 0.96 - 0.99;  $p < 0.001$ ). The mean of hypoglycemia fear survey score was  $16.9 \pm 16$ . The score on the fear of hypoglycemia (HFS) and worry subscale (HFS-W) for the patients with more frequent hypoglycemia episodes in the previous month ( $>2$  episodes) was significantly greater than another group (1-2 episodes) ( $p = 0.006$  and  $0.002$ ), indicating a greater degree of fear of hypoglycemia in the first group. **Conclusion:** The occurrence of symptoms

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of hypoglycemia is one of complications in the elderly with type 2 diabetes and their presence is associated with complications of diabetes and glipizide use. Frequent symptoms can have a negative impact on fear of hypoglycemia. Minimizing the risk of hypoglycemia represents a high priority in the diabetes treatment of the elderly people.

**Keywords:** hypoglycemia, fear of hypoglycemia, type 2 diabetes mellitus, elderly

## ความถี่และปัจจัยที่เกี่ยวข้องของอาการน้ำตาลต่ำในเลือด และความกลัวภาวะน้ำตาลต่ำในเลือด ในผู้สูงอายุโรคเบาหวานชนิดที่สอง ณ หน่วยบริการปฐมภูมิ โรงพยาบาลสงขลานครินทร์

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### บทคัดย่อ

**วัตถุประสงค์:** เพื่อหาความถี่และปัจจัยที่เกี่ยวข้องของอาการน้ำตาลต่ำในเลือด และความกลัวภาวะน้ำตาลต่ำในเลือด ในผู้สูงอายุที่ป่วยด้วยโรคเบาหวานชนิดที่สอง ที่มารับบริการในหน่วยบริการปฐมภูมิ โรงพยาบาลสงขลานครินทร์ **ระเบียบวิธีศึกษา:** งานวิจัยนี้เป็นการศึกษาแบบภาคตัดขวาง ในผู้ป่วยด้วยโรคเบาหวานชนิดที่ 2 อายุตั้งแต่ 60 ปีขึ้นไป ระหว่างเดือนกรกฎาคม - ตุลาคม 2560 ที่หน่วยบริการปฐมภูมิ โรงพยาบาลสงขลานครินทร์ ทำการสัมภาษณ์ข้อมูลทั่วไป ลักษณะทางคลินิก และอาการน้ำตาลต่ำในเลือดในช่วงเวลา 1 เดือนที่ผ่านมา และวัดความกลัวภาวะน้ำตาลต่ำในเลือดโดยใช้แบบสอบถาม Hypoglycemia Fear Survey ฉบับแปลภาษาไทย การศึกษาวิเคราะห์หาความสัมพันธ์ระหว่างปัจจัยที่เกี่ยวข้องและอาการน้ำตาลต่ำในเลือดด้วยสถิติการถดถอยโลจิสติก **ผลการศึกษา:** ผู้เข้าร่วมวิจัยจำนวนทั้งสิ้น 160 คน มีอายุเฉลี่ย  $68.6 \pm 6.1$  ปี เป็นเพศหญิงร้อยละ 53.8 ระยะเวลาในการเป็นโรคเบาหวานเฉลี่ย  $10.5 \pm 6.4$  ปี มีภาวะแทรกซ้อนของโรคเบาหวานร้อยละ 57.5 HbA1c เฉลี่ย  $7.5 \pm 1.8\%$  พบผู้ป่วยที่มีอาการน้ำตาลต่ำในเลือดย้อยละ 30 ปัจจัยที่เกี่ยวข้องกับอาการน้ำตาลต่ำในเลือด ได้แก่ การมีภาวะแทรกซ้อนของโรคเบาหวาน (aOR = 2.75; 95% CI 1.23 - 6.14;  $p = 0.012$ ) การใช้ยา glipizide (aOR = 5.03; 95% CI 1.99 - 12.71;  $p < 0.001$ ) และค่าระดับน้ำตาลในเลือด (aOR = 0.97; 95% CI 0.96 - 0.99;  $p < 0.001$ ) พบคะแนนเฉลี่ยของความกลัวภาวะน้ำตาลต่ำในเลือดเท่ากับ  $16.9 \pm 16$  นอกจากนี้คะแนนรวมเฉลี่ยของความกลัวภาวะน้ำตาลต่ำในเลือด และคะแนนเฉลี่ยด้านความกังวล มีค่าสูงกว่าในกลุ่มที่มีความถี่ของอาการน้ำตาลต่ำในเลือดที่มากกว่าสองครั้งต่อเดือนเปรียบเทียบกับกลุ่มที่มีความถี่ 1-2 ครั้งต่อเดือนอย่างมีนัยสำคัญทางสถิติ ( $p = 0.006$  and  $0.002$ ) **สรุป:** การเกิดอาการน้ำตาลต่ำในเลือดเป็นสิ่งที่พบได้ในผู้สูงอายุโรคเบาหวานชนิดที่สอง ซึ่งปัจจัยที่เกี่ยวข้องกับอาการน้ำตาลต่ำในเลือด ได้แก่ การมีภาวะแทรกซ้อนของโรคเบาหวาน และการใช้ยา glipizide นอกจากนี้ความถี่ของอาการน้ำตาลต่ำในเลือดที่มากขึ้นส่งผลต่อความกลัวภาวะน้ำตาลต่ำในเลือด ดังนั้น การดูแลและป้องกันภาวะน้ำตาลต่ำในเลือดในผู้สูงอายุโรคเบาหวานจึงเป็นสิ่งสำคัญ

**คำสำคัญ:** อาการน้ำตาลต่ำในเลือด, ความกลัวภาวะน้ำตาลต่ำในเลือด, ผู้สูงอายุโรคเบาหวานชนิดที่สอง

### Background and Rationale

Currently, the number of older people worldwide is growing continuously.<sup>(1-2)</sup> Also, the aging Thai population is increasing over 4% per year.<sup>(3)</sup> Elderly people are different from other life

stage, due to the anatomical and physiological decline which is related to aging. This degeneration affected multiple chronic conditions that required clinical and social support.<sup>(4)</sup> Diabetes mellitus is one of the three most common diseases that is

being the risk factor of cerebrovascular and cardiovascular disease in Thai elderly people. The prevalence of diabetes mellitus has an increasing tendency in the age group 60 to 79.<sup>(5)</sup> The poorly controlled diabetes usually causes serious complications affecting quality of life, economic status of patients, family, and the nation.<sup>(6)</sup>

Hypoglycemia is one of diabetic complications as a cause of significant morbidity including cardiovascular disease. Hypoglycemia unawareness is prevalent among elderly patients with diabetes.<sup>(7-10)</sup> The frequent episodes of symptomatic hypoglycemia is associated with a reduction in quality of life, through nocturnal hypoglycemia disturbing sleep patterns and increasing the risk for dementia and falls in older patients with type 2 diabetes.<sup>(11-14)</sup> The fear of hypoglycemia is one of the psychological burden of diabetic patients to hypoglycemia events.<sup>(15,16)</sup> This fear influences patient health outcomes through self-treatment modifications, lifestyle change and lower patients' quality of life.<sup>(17-19)</sup> Furthermore, fear of hypoglycemia may decrease adherence to medication, which was a barrier to diabetes management.<sup>(20,21)</sup>

At the primary care unit of Songklanagarind Hospital, there has been an increase in elderly diabetic attendances. However, a few studies on hypoglycemic episodes in type 2 diabetes elderly have been published, and a comprehensive evaluation of the fear of hypoglycemia has never been made. The present research was conducted to determine the frequency of symptomatic hypoglycemia and associated factors, and to assess their fear of hypoglycemia among elderly patients

with type 2 diabetes attending primary care unit of Songklanagarind Hospital. This would be the database for future research in developing appropriate tool to improve effective care for elderly with diabetes.

## Methodology

**Study design:** Cross-sectional study.

**Participants:** The sample size was calculated by G-power program<sup>(22)</sup> for logistic regression with odds ratio = 2 from previous study of hypoglycemic episodes<sup>(23)</sup>,  $\alpha = 0.05$  and  $1-\beta = 0.95$ . The sample size was increased to 160 to allow for a 10% drop out.

The total of 160 elderly patients diagnosed with type 2 diabetes mellitus at the primary care unit of Songklanagarind Hospital who matched with the inclusion and exclusion criteria were involved in the study by purposive sampling. The study protocol was approved by the ethics committee of the Faculty of Medicine, Prince of Songkla University. (REC.61-059-9-4)

**Inclusion criteria:** The participants aged 60 years and over diagnosed with type 2 diabetes (from ICD10 code E11-E14) at the primary care unit of Songklanagarind Hospital and participants obtained informed consent.

**Exclusion criteria:** The participants with condition that could interfere with their capability to understand or answer the interview and participants with a diagnosis of depression, dementia and type 2 diabetes with diabetic ketoacidosis.

**Setting:** Primary care unit of Songklanagarind Hospital.

**Data collection:** This cross-sectional study was conducted from July to October 2018. The socio-demographic characteristic questionnaire was used to interview the participants by a researcher or research assistants. Baseline clinical data, included body weight, height, underlying disease, duration of diabetes, complications of diabetes (diabetic retinopathy, diabetic nephropathy, cerebrovascular, peripheral vascular, neurovascular and diabetic foot complication), HbA1c, fasting blood sugar, type and dose of glucose lowering drugs, were reviewed from the hospital information system (HIS) by the researcher (CC). A hypoglycemia questionnaire was administered to assess hypoglycemic symptoms, frequency and severity of hypoglycemic event. The participants were asked on their experiences of hypoglycemic symptoms in the previous month, based on a provided list of symptoms (sweating, palpitation, shaking and hunger, confusion, drowsiness, odd behavior, speech difficulty, incoordination, nausea and headache) and those symptoms were resolved with the ingestion of sugar, food or sugary drinks. The hypoglycemia symptom in this study was the event of hypoglycemia not accompanied by a plasma glucose determination based on the American Diabetes Association classification.<sup>(24)</sup> The patients with a positive recorded response were further asked frequency of each hypoglycemic symptoms as number of episodes in the previous month and to rate the severity of their episodes as mild (did not require assistance of another person to manage symptoms) or severe (leading to unconsciousness or requiring assistance from another

person to manage symptoms).<sup>(11),(25-27)</sup> The fear of hypoglycemia was measured by the Hypoglycemia Fear Survey II (HFS-II). The 15 items in the behavior subscale (HFS-B) measured behaviors the patients took to avoid hypoglycemic episodes and negative consequences. The 18 items in the worry subscale (HFS-W) measured specific concern that patients had with their hypoglycemic episodes. The items were rated on a five-point Likert scale ranging from 0 (never) to 4 (always). The fear of hypoglycemia score has no definite cutoff score, the higher score the higher fear of hypoglycemia.<sup>(28-32)</sup> The Thai version of Hypoglycemia Fear Survey developed from forward and backward translations with internal consistency reliability (Cronbach's alpha) of 0.77 was used.

**Data editing:** The data from questionnaires were double entered into EpiData version 3.1 for detecting any inaccuracies.

**Data analysis:** The R Studio version 3.3.3 was used for data analysis. The frequencies and percentages were analyzed for discrete variables. The mean, standard deviation, median and interquartile were analyzed for continuous variables. The Chi-square test, Fisher's exact test, and Wilcoxon Rank Sum were applied to study the variables with hypoglycemic symptoms. The logistic regression analyses with a backward selection were performed to evaluate the associations between the significant associated factors and hypoglycemic symptoms. The fear of hypoglycemia scores were reported as median and interquartile. The frequency of hypoglycemic symptoms in the previous month

(1-2 episodes/more than 2 episodes) was compared with fear score by using Wilcoxon Rank Sum Test. A  $p < 0.05$  was regarded as statistical significance in the models.

## Results

Overall, 160 participants who met the criteria for inclusion, had the following characteristics: 53.8% females, mean age of  $68.6 \pm 6.1$  years, and 34.4% unemployed. The mean diabetes duration was  $10.5 \pm 6.4$  years, 57.5% of diabetic complications,  $7.5 \pm 1.8\%$  of HbA1c.

Thirty percent of participants ( $n = 48$ ) reported hypoglycemic symptoms in the previous month. The mean frequency of hypoglycemic episodes in the previous month was  $2.35 \pm 2.8$ . The most frequent hypoglycemic event was one

episode per month (56.2%). Most of hypoglycemic symptoms that the patients reported were hunger (79.2%), palpitation (58.3%) and sweating (54.2%).

Clinical and socio-demographic characteristics of the study sample according to the hypoglycemic symptoms in the previous month showed that the diabetic complications of the hypoglycemic group were higher than the no hypoglycemic group (56.2% versus 36.6%;  $p = 0.033$ ), the participants using glipizide was higher in hypoglycemic symptoms group (46.8% versus 27.9%;  $p = 0.037$ ), the median fasting plasma glucose level was lower in hypoglycemic symptoms group (125 versus 133;  $p = 0.034$ ). There was no significant difference of the participants using insulin, metformin, glibenclamine and pioglitazone. (Table 1)

**Table 1** Socio-demographic characteristics and clinical baseline data of the study population according to hypoglycemic symptoms in the previous month

| Variable                    | Overall<br>n (%)<br>(n = 160) | No hypoglycemic<br>symptoms<br>(n = 112) | Hypoglycemic<br>symptoms<br>(n = 48) | p value            |
|-----------------------------|-------------------------------|--|--------------------------------------|--------------------|
| Sex                         |                               |  |                                      | 0.809 <sup>a</sup> |
| Male                        | 74 (46.2)                     | 53 (47.3)                                | 21 (43.8)                            |                    |
| Female                      | 86 (53.8)                     | 59 (52.7)                                | 27 (56.2)                            |                    |
| Age (years)                 | $68.6 \pm 6.1^\dagger$        | $67 (64,72.2)^{\ddagger\dagger}$         | $69 (64,72)^{\ddagger\dagger}$       | 0.712 <sup>b</sup> |
| Education status            |                               |  |                                      | 0.199 <sup>c</sup> |
| No education                | 10 (6.2)                      | 8 (7.1)                                  | 2 (4.2)                              |                    |
| Primary school              | 80 (50)                       | 49 (43.8)                                | 31 (64.6)                            |                    |
| High school                 | 41 (25.6)                     | 32 (28.6)                                | 9 (18.8)                             |                    |
| Bachelor degree             | 29 (18.1)                     | 22 (19.6)                                | 6 (12.5)                             |                    |
| Occupation                  |                               |  |                                      | 0.010 <sup>c</sup> |
| Unemployed                  | 55 (34.4)                     | 35 (31.2)                                | 20 (41.7)                            |                    |
| Gardener                    | 25 (15.6)                     | 16 (14.3)                                | 9 (18.8)                             |                    |
| Retired government official | 48 (30)                       | 39 (34.8)                                | 9 (18.8)                             |                    |
| Merchant                    | 18 (11.2)                     | 13 (11.6)                                | 5 (10.4)                             |                    |
| Self-employed               | 10 (6.2)                      | 9 (8)                                    | 1 (2.1)                              |                    |
| Other                       | 4 (2.5)                       | 0 (0)                                    | 4 (8.3)                              |                    |

**Table 1** Socio-demographic characteristics and clinical baseline data of the study population according to hypoglycemic symptoms in the previous month (continued)

| Variable                             | Overall<br>n (%)<br>(n = 160) | No hypoglycemic<br>symptoms<br>(n = 112) | Hypoglycemic<br>symptoms<br>(n = 48) | p value            |
|--------------------------------------|-------------------------------|--|--------------------------------------|--------------------|
| Weight (kg)                          | 64.7 ± 12.2 <sup>†</sup>      | 63 (56.8,72) <sup>††</sup>               | 64.5 (54,68) <sup>††</sup>           | 0.578 <sup>b</sup> |
| Height (cm)                          | 159 ± 8.2 <sup>†</sup>        | 159.5 ± 8 <sup>†</sup>                   | 157.7 ± 8.5 <sup>†</sup>             | 0.199 <sup>d</sup> |
| Body mass index (kg/m <sup>2</sup> ) | 25.63 ± 4.6 <sup>†</sup>      | 25.1 (23.1,27.1) <sup>††</sup>           | 24.6 (22.3,28.2) <sup>††</sup>       | 0.743 <sup>b</sup> |
| Smoking                              |                               |  |                                      | 0.844 <sup>c</sup> |
| No                                   | 145 (90.6)                    | 103 (92)                                 | 42 (87.5)                            |                    |
| Yes                                  | 15 (9.4)                      | 9 (8)                                    | 6 (12.5)                             |                    |
| Dyslipidemia                         |                               |  |                                      | 0.148 <sup>c</sup> |
| No                                   | 15 (9.6)                      | 8 (7.3)                                  | 7 (14.9)                             |                    |
| Yes                                  | 142 (90.4)                    | 102 (92.7)                               | 40 (85.1)                            |                    |
| Cardiovascular disease               |                               |  |                                      | 0.725 <sup>c</sup> |
| No                                   | 148 (94.3)                    | 103 (93.6)                               | 45 (95.7)                            |                    |
| Yes                                  | 9 (5.7)                       | 7 (6.4)                                  | 2 (4.3)                              |                    |
| Cerebrovascular disease              |                               |  |                                      | 0.675 <sup>c</sup> |
| No                                   | 150 (95.5)                    | 104 (94.5)                               | 46 (97.9)                            |                    |
| Yes                                  | 7 (4.5)                       | 6 (5.5)                                  | 1 (2.1)                              |                    |
| Chronic kidney disease               |                               |  |                                      | 0.779 <sup>c</sup> |
| No                                   | 141 (89.8)                    | 98 (89.1)                                | 43 (91.5)                            |                    |
| Yes                                  | 16 (10.2)                     | 12 (10.9)                                | 4 (8.5)                              |                    |
| Duration of diabetes (years)         | 10.5 ± 6.4 <sup>†</sup>       | 10 (5,15) <sup>††</sup>                  | 10 (7.8,15) <sup>††</sup>            | 0.405 <sup>b</sup> |
| Complications of diabetes            |                               |  |                                      | 0.033 <sup>a</sup> |
| No                                   | 92 (57.5)                     | 71 (63.4)                                | 21 (43.8)                            |                    |
| Yes                                  | 68 (42.5)                     | 41 (36.6)                                | 27 (56.2)                            |                    |
| Diabetic retinopathy                 |                               |  |                                      | 0.668 <sup>a</sup> |
| No                                   | 51 (75)                       | 32 (78)                                  | 19 (70.4)                            |                    |
| Yes                                  | 17 (25)                       | 9 (22)                                   | 8 (29.6)                             |                    |
| Diabetic nephropathy                 |                               |  |                                      | 0.668 <sup>a</sup> |
| No                                   | 32 (47.1)                     | 22 (53.7)                                | 10 (37)                              |                    |
| Yes                                  | 36 (52.9)                     | 19 (46.3)                                | 17 (63)                              |                    |
| Cerebrovascular complication         |                               |  |                                      | 0.514 <sup>c</sup> |
| No                                   | 66 (97.1)                     | 39 (95.1)                                | 27 (100)                             |                    |
| Yes                                  | 2 (2.9)                       | 2 (4.9)                                  | 0 (0)                                |                    |
| Peripheral vascular complication     |                               |  |                                      | 1 <sup>c</sup>     |
| No                                   | 59 (86.8)                     | 35 (85.4)                                | 24 (88.9)                            |                    |
| Yes                                  | 9 (13.2)                      | 6 (14.6)                                 | 3 (11.1)                             |                    |
| Neurovascular complication           |                               |  |                                      | 0.149 <sup>c</sup> |
| No                                   | 63 (92.6)                     | 36 (87.8)                                | 27 (100)                             |                    |
| Yes                                  | 5 (7.4)                       | 5 (12.2)                                 | 0 (0)                                |                    |

**Table 1** Socio-demographic characteristics and clinical baseline data of the study population according to hypoglycemic symptoms in the previous month (continued)

| Variable   | Overall<br>n (%)<br>(n = 160) | No hypoglycemic<br>symptoms<br>(n = 112) | Hypoglycemic<br>symptoms<br>(n = 48) | p value            |
|--|-------------------------------|--|--------------------------------------|--------------------|
| Diabetic foot complication                       |                               |  |                                      | 0.352 <sup>a</sup> |
| No   | 42 (61.8)                     | 23 (56.1)                                | 19 (70.4)                            |                    |
| Yes  | 26 (38.2)                     | 18 (43.9)                                | 8 (29.6)                             |                    |
| Family history of diabetes                       |                               |  |                                      | 0.329 <sup>a</sup> |
| No   | 91 (56.9)                     | 67 (59.8)                                | 24 (50)                              |                    |
| Yes  | 69 (43.1)                     | 45 (40.2)                                | 24 (50)                              |                    |
| Self-monitoring of blood glucose                 |                               |  |                                      | 0.964 <sup>a</sup> |
| No   | 132 (82.5)                    | 93 (83)                                  | 39 (81.2)                            |                    |
| Yes  | 28 (17.5)                     | 19 (17)                                  | 9 (18.8)                             |                    |
| Fasting plasma glucose (mg/dL)                   | 138.2 ± 33.5 <sup>†</sup>     | 133 (120,160) <sup>††</sup>              | 125 (112.5,140.8) <sup>††</sup>      | 0.034 <sup>b</sup> |
| HbA1c (%)  | 7.5 ± 1.8 <sup>†</sup>        | 7.1 (6.3,8) <sup>††</sup>                | 7.3 (6.6,8.4) <sup>††</sup>          | 0.296 <sup>b</sup> |
| Insulin (any type)                               |                               |  |                                      | 0.218 <sup>a</sup> |
| No   | 122 (81.3)                    | 87 (84.5)                                | 35 (74.5)                            |                    |
| Yes  | 28 (18.7)                     | 16 (15.5)                                | 12 (25.5)                            |                    |
| Metformin  |                               |  |                                      | 0.229 <sup>c</sup> |
| No   | 13 (8.7)                      | 7 (6.8)                                  | 6 (12.8)                             |                    |
| Yes  | 137 (91.3)                    | 96 (93.2)                                | 41 (87.2)                            |                    |
| Glipizide  |                               |  |                                      | 0.040 <sup>a</sup> |
| No   | 99 (66)                       | 74 (71.8)                                | 25 (53.2)                            |                    |
| Yes  | 51 (34)                       | 29 (28.2)                                | 22 (46.8)                            |                    |
| Glibenclamide                                    |                               |  |                                      | 1 <sup>c</sup>     |
| No   | 139 (92.7)                    | 95 (92.2)                                | 44 (93.6)                            |                    |
| Yes  | 11 (7.3)                      | 8 (7.8)                                  | 3 (6.4)                              |                    |
| Pioglitazone                                     |                               |  |                                      | 0.100 <sup>a</sup> |
| No   | 119 (79.3)                    | 86 (83.5)                                | 33 (70.2)                            |                    |
| Yes  | 31 (20.7)                     | 17 (16.5)                                | 14 (29.8)                            |                    |
| Dose of glucose lowering agents<br>(mg per day)  |                               |  |                                      |                    |
| Insulin (any type)                               | 23.7 ± 14.6                   | 20 (14.2,27.5) <sup>††</sup>             | 21 (10,28) <sup>††</sup>             | 0.871 <sup>b</sup> |
| Metformin  | 1360.1 ± 628.2 <sup>†</sup>   | 1500 (1000,1775) <sup>††</sup>           | 1000 (1000,1750) <sup>††</sup>       | 0.968 <sup>b</sup> |
| Glipizide  | 10 ± 5.4                      | 10 (5,10) <sup>††</sup>                  | 10 (5,10) <sup>††</sup>              | 0.447 <sup>b</sup> |
| Glibenclamide                                    | 4.5 ± 1                       | 5 (4.4,5) <sup>††</sup>                  | 5 (5,5) <sup>††</sup>                | 0.340 <sup>b</sup> |
| Pioglitazone                                     | 28.5 ± 8.1                    | 30 (30,30) <sup>††</sup>                 | 30 (30,30) <sup>††</sup>             | 0.100 <sup>b</sup> |
| Hospital admission due to severe<br>hypoglycemia | 1 (0.6)                       | 0 (0)                                    | 1 (2.1)                              | 0.300 <sup>c</sup> |

<sup>†</sup> [mean ± SD], <sup>††</sup> [median (IQR)]

<sup>a</sup> Chi-square test, <sup>b</sup> Rank Sum test, <sup>c</sup> Fisher's exact, <sup>d</sup> t-test



**Table 2** Hypoglycemic symptoms and associated factors: logistic regression analysis (n=48)

| Factors                   | adjusted OR (95%CI) | p value |
|---------------------------|---------------------|---------|
| Complications of diabetes | 2.75 (1.23 - 6.14)  | 0.012   |
| Fasting plasma glucose    | 0.97 (0.96 - 0.99)  | < 0.001 |
| Glipizide use             | 5.03 (1.99 - 12.71) | < 0.001 |

**Table 3** Fear of hypoglycemia scores according to the frequency of hypoglycemic symptoms

| Fear of hypoglycemia score | Frequency hypoglycemic symptoms<br>(episode in previous month) |              | p value* |
|----------------------------|--|--------------|----------|
|                            | 1 - 2  | > 2          |          |
|                            | (n = 9)  | (n = 39)     |          |
| HFS <sup>†</sup>           | 11 (4 - 18)  | 39 (14 - 54) | 0.006    |
| HFS-B <sup>†</sup>         | 4 (1.5 - 10.5)   | 6 (4 - 18)   | 0.202    |
| HFS-W <sup>†</sup>         | 5 (0 - 11)   | 21 (9 - 32)  | 0.002    |

<sup>†</sup> [median (IQR)]

\* Rank sum test

The associated factors of hypoglycemic symptoms were diabetic complications (aOR = 2.75; 95% CI 1.23 - 6.14;  $p = 0.012$ ), glipizide use (aOR = 5.03; 95% CI 1.99 - 12.71;  $p < 0.001$ ). A unit of increase in fasting plasma glucose was associated with 0.03 time reduction in hypoglycemic symptoms (aOR = 0.97; 95% CI 0.96 - 0.99;  $p = < 0.001$ ). The results of the adjusted multivariate analysis are shown in Table 2.

The mean and standard deviation of hypoglycemia fear survey score was  $16.9 \pm 16$ , the behavior (HFS-B) and worry (HFS-W) subscale score was  $7.5 \pm 7.9$  and  $9.4 \pm 11.9$ . The median score on the fear of hypoglycemia (HFS) and worry subscale (HFS-W) for the patients with more frequency of hypoglycemia episodes in previous

month (>2 episodes) was significantly greater than the less frequent group (1-2 episodes) ( $p = 0.006$  and 0.002), indicating a greater degree of fear of hypoglycemia in the more frequent group (see Table 3).

## Discussion

Our study shows that thirty percent of the elderly patients with type 2 diabetes reported hypoglycemic symptoms in the previous month. The associated factors of hypoglycemic symptoms were complications of diabetes and glipizide usage. The frequency of hypoglycemic symptoms (more than two episodes per month) affected on the fear of hypoglycemia.

The numbers of patients reported hypogly-





cemic symptoms in the present study were somewhat lower when compared with the cross-sectional observational study of patients with type 2 diabetes in Italy<sup>(11)</sup>, Spain<sup>(19)</sup> and Asia-Pacific<sup>(20)</sup> that founded 44.6%, 45% and 35.8% of hypoglycemic episodes respectively. These discrepancies might be explained by the difficulties in recognizing hypoglycemic symptoms in elderly due to the non-specific symptoms and the little warning or unawareness of autonomic symptoms.<sup>(33)</sup>

Complication of diabetes was a significant associated factor of hypoglycemic symptom (56.2% versus 36.6%;  $p = 0.033$  and aOR = 2.75; 95% CI 1.23 - 6.14;  $p = 0.012$ ). This finding can be explained by the importance of the frailty of the patients with diabetes complications or proxy indicators for hypoglycemic unawareness as the risk factor for hypoglycemia.<sup>(34)</sup>

We also found that glipizide users had a higher risk of hypoglycemia symptoms consistent with the article of the Canadian Diabetes Association presenting that sulfonylurea was an associated risk for hypoglycemia, especially in patients with advanced age and general disability.<sup>(35)</sup> A unit of increase in fasting plasma glucose was associated with 0.03 time reduction in hypoglycemic symptoms (aOR = 0.97; 95% CI 0.96 - 0.99;  $p < 0.001$ ). This finding suggested that diabetic patients who had lower level of fasting plasma glucose may have tightly controlled, that hypoglycemia occurred more often in the intensive therapy group.<sup>(36)</sup>

We found a greater degree of the fear of hypoglycemia on the HFS-II and worry subscale

for the patients with more frequent hypoglycemia episodes, consistent with the previous studies that concluded the frequency of episodes of symptomatic hypoglycemia in elderly patients with type 2 diabetes was associated with a higher fear of hypoglycemia.<sup>(11)</sup>

The present study had some limitations. First, we cannot conclude the cause-effect relationships because of the cross-sectional study design. The recall bias from self-reported information on the frequency of hypoglycemic episodes of participants is the second limitations. Third, we did not objectively measure hypoglycemia. Some patients might feel confused between hunger and hypoglycemia or “normal feeling”. Elderly patients were likely to experience unspecific symptoms. However, clinical practice at the primary care unit indicated very relevant symptoms of patient hypoglycemic reports. Another strength was that the present study used psychometric instruments, including the Hypoglycemia Fear Survey the Thai version which proved to be simple to administer. The present study contributes to be a good database for future research to develop the appropriate tool to improve the effectiveness of care for elderly diabetes patients.

## Conclusion

The occurrence of symptoms of hypoglycemia was one of complications in the elderly with type 2 diabetes. The presence of hypoglycemic symptoms was associated with complications of diabetes and glipizide use. Frequent symptoms were also associated with fear of hypoglycemia.

Minimizing the risk of hypoglycemia should be a high priority in the diabetes treatment of the elderly people.

Longitudinal study, especially objectively self-monitoring of plasma glucose by the patients, should be done in the future to assess the clinical outcomes and causal relationships of the associated factors with hypoglycemic symptoms.

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