

Low ambient temperatures correlate with increased risk of hypoglycemia in patients with type 2 diabetes

An ecological study in Taiwan

Shih-Wei Lai, MD^{a,b}, Wan-Chi Chang, MS^c, Cheng-Li Lin, MS^{a,d}, I-Ching Chou, MD^{e,f},
Fuu-Jen Tsai, MD, PhD^{g,h}, Yen-Jen Lai, MS, PhD^{i,*}

Abstract

Little evidence is available about the relationship between ambient temperatures and hypoglycemia in Taiwan. The purpose of the present paper is to investigate whether there is an association between ambient temperatures and hypoglycemia in patients with type 2 diabetes.

An ecological study was conducted to analyze the type 2 diabetes dataset of the Taiwan National Health Insurance Program. Every episode of hypoglycemia diagnosed at emergency department among subjects with type 2 diabetes was identified monthly between 2006 and 2013. Average monthly ambient temperatures in Celsius between 2006 and 2013 were measured according to the database of the Central Weather Bureau in Taiwan.

The incidence rates of hypoglycemia were higher during the period of cold ambient temperatures (from December to March) than the period of warm ambient temperatures (from April to November). The peak period of hypoglycemia always occurred in winter months (January and February).

Patients with type 2 diabetes in Taiwan are more susceptible to hypoglycemia during the period of cold ambient temperatures, particularly in winter months. Clinicians in Taiwan should remind patients to make a preventive strategy for hypoglycemia during the periods of cold ambient temperatures.

Abbreviation: Temperatures (°C) = temperatures in Celsius.

Keywords: ambient temperatures, diabetes, hypoglycemia

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^aSchool of Medicine, College of Medicine, China Medical University,

^bDepartment of Family Medicine, ^cDepartment of Nursing, ^dManagement Office for Health Data, China Medical University Hospital, ^eGraduate Institute of Integrated Medicine, College of Chinese Medicine, China Medical University,

^fDivision of Pediatric Neurology, China Medical University Children's Hospital,

^gSchool of Chinese Medicine, College of Chinese Medicine, China Medical University, ^hGenetic Center, Proteomics Core Laboratory, Department of Medical Research, China Medical University Hospital, Taichung, ⁱExperimental Forest, College of Bio-Resources and Agriculture, National Taiwan University, Nantou County, Taiwan.

*Correspondence: Yen-Jen Lai, Experimental Forest, College of Bio-Resources and Agriculture, National Taiwan University, No.12, Sec. 1, Qianshan Rd., Zhushan Township, Nantou County 55750, Taiwan (e-mail: alanlai@ntu.edu.tw).

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1. Introduction

Diabetes mellitus remains to be a major public health problem in the world. In addition to the microvascular and macrovascular complications of diabetes mellitus, hypoglycemia is another serious problem in diabetic patients. Hypoglycemia was frequently found in patients who tried to achieve good glucose control.^[1] Several risk factors for hypoglycemia have been well established, including old age, long duration of diabetes mellitus, insulin therapy, sulfonylurea therapy, low levels of mean blood glucose, large fluctuations in blood glucose, history of hypoglycemia, poor cognitive function, difficulty with activities of daily living, cirrhosis, cerebrovascular disease, and chronic renal failure^[2-6] but the association between ambient temperatures and hypoglycemia has not yet conclusive results. One study in Japan showed that hypoglycemia among patients with type 1 diabetes mellitus occurred often in the summer than in the winter, but the episodes of hypoglycemia among patients with type 2 diabetes mellitus were not different between the seasons.^[7] One study in Germany showed that the frequency of hypoglycemia at temperatures between 10 and 20°C was lower compared with temperatures above 20°C and below 10°C.^[8] To date, little evidence is available about the relationship between ambient temperatures and hypoglycemia in Taiwan. In order to clarify this issue, an ecological study was conducted to investigate whether there is an association between ambient temperatures and hypoglycemia in patients with type 2 diabetes.

2. Research design and methods

2.1. Data source and study design

The Taiwan National Health Insurance Program is a universal health insurance system. It was launched on March 1, 1995 and now it covers >99.7% of the 23 million people living in Taiwan.^[9,10] An ecological study was conducted to analyze the type 2 diabetes dataset of the Taiwan National Health Insurance Program. This dataset consisted of 1,700,000 subjects with newly diagnosed type 2 diabetes mellitus from 1997 to 2013. The details of this dataset have been documented in previous studies.^[11,12]

2.2. Ethics statement

The study was designed in accordance with the Declaration of Helsinki. The study was approved by the Research Ethics Committee of China Medical University and Hospital in Taiwan (CMUH-104-REC2-115). Informed consent was not required because the study used a retrospective data.

2.3. Study subjects

Subjects with newly diagnosed type 2 diabetes mellitus between 2006 and 2013 were selected (based on International Classification of Diseases, Ninth Revision, Clinical Modification, ICD-9 codes 250.x0 or 250.x2). All subjects included in the study had the diagnosis of type 2 diabetes mellitus. Every episode of hypoglycemia diagnosed at emergency department among these subjects with type 2 diabetes was identified monthly between 2006 and 2013 (ICD-9 codes 251.0, 251.1, and 251.2).

2.4. Ambient temperatures

According to the database of the Central Weather Bureau in Taiwan, average monthly ambient temperatures in Celsius (°C) in Taiwan were measured in the study between 2006 and 2013.^[13]

2.5. Statistical analysis

The incidence rate of hypoglycemia was estimated as the number of hypoglycemic events identified monthly divided by the number of subjects with type 2 diabetes identified monthly between 2006 and 2013. The simple correlation regression was used. All analyses were performed using the SAS statistical software

(version 9.2; SAS Institute, Inc., Cary, NC). The results were considered statistically significant when *P* values were <.05.

3. Results

3.1. Average monthly ambient temperatures (°C)

Table 1 revealed average monthly ambient temperatures in Taiwan between 2006 and 2013. The ambient temperatures were lower during December to March. The ambient temperatures were higher during April to November. In detail, the winter months were from January to February. The summer months were from June to September.

3.2. Incidence rate of hypoglycemia

Due to data missing, only 1,255,069 subjects were included in the study. Approximately 52.61% were male subjects and 47.39% were female subjects. The mean age (standard deviation) of the study subjects was 58.7 (13.9) years, ranging from 18 to 112 years.

Table 2 revealed that the overall incidence rates of hypoglycemia ranged from 0.98 to 1.97 per 1000 subjects with type 2 diabetes per month from 2006 to 2013. The incidence rate of hypoglycemia was the highest during February in 2011 (2.45 per 1000 subjects with type 2 diabetes per month).

As stratified by sex and age, the annual incidence rate of hypoglycemia seemed to be gradually increased from 2006 to 2013 (Table 3). The annual incidence rate of hypoglycemia seemed to be higher in women than in men from 2006 to 2013.

Figure 1 revealed that the annual incidence rate of hypoglycemia seemed to be higher in subjects aged ≥65 compared with the other 2 age groups from 2006 to 2013.

3.3. Interaction between incidence rates of hypoglycemia and average monthly ambient temperatures

Figure 2 revealed that the incidence rates of hypoglycemia were higher during the period of cold ambient temperatures (from December to March) than the period of warm ambient temperatures (from April to November). The peak period of hypoglycemia always occurred in winter months (January and February). Particularly, the ambient temperatures were the lowest during January to February in 2011 (13.19–15.55°C), and the incidence rate of hypoglycemia was the highest during

Table 1
Average monthly temperatures (°C) in Taiwan between 2006 and 2013.

Year/month	2006	2007	2008	2009	2010	2011	2012	2013	<i>P</i> value for trend
1	16.29	15.88	16.18	14.63	15.85	13.19	14.93	15.50	.20
2	16.65	17.60	13.59	18.94	17.09	15.55	15.35	17.67	.99
3	17.65	18.75	18.02	18.09	18.80	15.71	18.06	18.90	.95
4	21.69	20.14	21.38	20.00	19.89	19.96	21.68	20.09	.50
5	23.75	24.06	23.37	23.27	23.61	23.00	23.93	23.76	.79
6	25.45	25.87	25.43	25.75	24.76	26.25	25.46	26.40	.41
7	26.94	27.73	26.55	27.09	27.11	26.56	27.04	26.83	.43
8	26.71	26.06	26.69	27.09	27.16	26.87	26.31	26.76	.68
9	25.03	25.46	25.73	26.74	25.90	25.35	25.23	25.66	.87
10	23.76	23.14	24.21	23.29	23.07	22.79	22.57	22.90	.04
11	21.35	19.69	20.26	20.24	19.72	21.31	20.10	19.94	.58
12	17.54	17.94	17.08	16.16	16.45	16.15	16.79	15.73	.02

Table 2**Incidence rate of hypoglycemia among patients with type 2 diabetes in Taiwan between 2006 and 2013.**

Year/month	2006	2007	2008	2009	2010	2011	2012	2013	P value for trend
1	1.19	1.43	1.43	2.05	2.02	2.23	2.33	2.14	.002
2	1.04	1.52	1.65	1.54	2.00	2.45	2.11	2.32	.002
3	1.03	1.10	1.61	1.37	1.90	2.04	2.26	1.72	.01
4	0.92	1.30	1.38	1.37	1.76	2.20	1.88	1.56	.03
5	0.85	1.20	1.30	1.33	1.87	1.78	2.01	1.86	<.001
6	0.90	1.18	1.30	1.48	1.71	1.62	1.92	1.90	<.001
7	0.99	1.16	1.27	1.39	1.61	1.74	1.97	1.78	.001
8	0.82	1.22	1.39	1.63	1.69	1.77	1.75	1.67	.006
9	0.92	1.24	1.29	1.52	1.61	1.59	1.69	1.60	.003
10	1.00	1.08	1.38	1.48	1.65	1.66	1.91	1.56	.003
11	1.05	1.07	1.22	1.40	1.58	1.59	1.79	1.75	<.001
12	1.11	1.23	1.39	1.49	1.69	1.69	2.04	1.85	<.001
Overall	0.98	1.22	1.38	1.50	1.75	1.85	1.97	1.81	<.001

Incidence rate: per 1000 patients with type 2 diabetes per month.

Table 3**Annual incidence rate of hypoglycemia among patients with type 2 diabetes in Taiwan between 2006 and 2013, stratified by sex and age.**

Year	2006	2007	2008	2009	2010	2011	2012	2013	P value for trend
Men									
Aged ≤39	3.16	3.23	5.02	4.67	5.75	5.27	6.38	7.17	<.001
Aged 40–64	2.62	3.24	3.65	3.79	4.74	5.06	5.19	5.27	<.001
Aged ≥65	7.66	9.61	10.30	11.49	12.92	13.52	13.98	12.90	.001
Overall	4.41	5.46	6.07	6.54	7.67	8.06	8.40	8.21	<.001
Women									
Aged ≤39	2.13	3.47	3.79	4.08	6.06	5.94	5.22	5.66	.005
Aged 40–64	2.49	2.57	3.12	3.57	3.67	3.96	4.53	4.79	<.001
Aged ≥65	9.26	11.57	12.81	13.29	15.40	16.26	16.37	14.81	.003
Overall	5.31	6.46	7.37	7.88	8.98	9.58	10.0	9.68	<.001

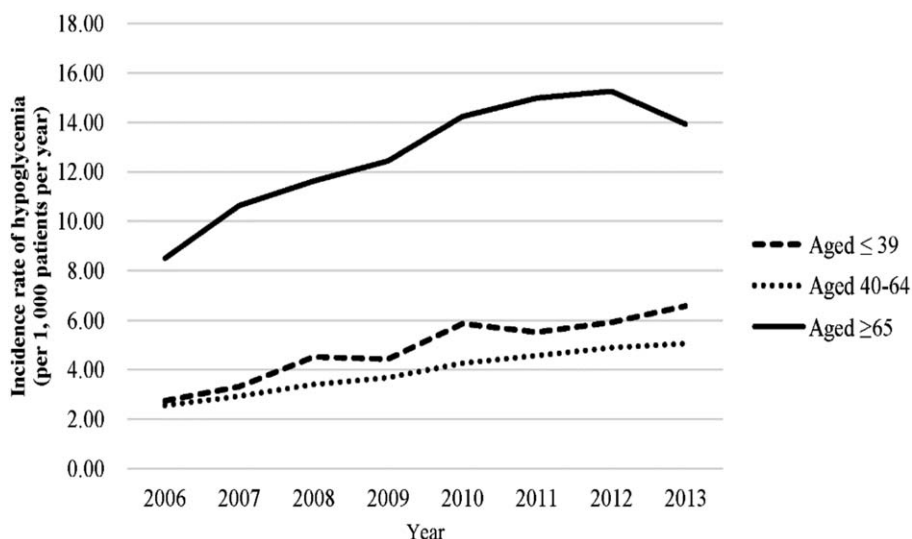
Incidence rate: per 1000 patients with type 2 diabetes per year.

this period (2.23–2.45 per 1000 subjects with type 2 diabetes per month).

4. Discussion

In this ecological study, we observed that patients aged ≥65 had a higher incidence rate of hypoglycemia. The incidence rates of

hypoglycemia were higher during the period of cold ambient temperatures (from December to March) than the period of warm ambient temperatures (from April to November). Taiwan is a subtropical country, so 4 seasons are not distinct. According to the official records (Table 1), the ambient temperatures were lower during December to March. The winter months were from January to February.

**Figure 1.** Annual incidence rates of hypoglycemia between 3 age groups in Taiwan between 2006 and 2013.

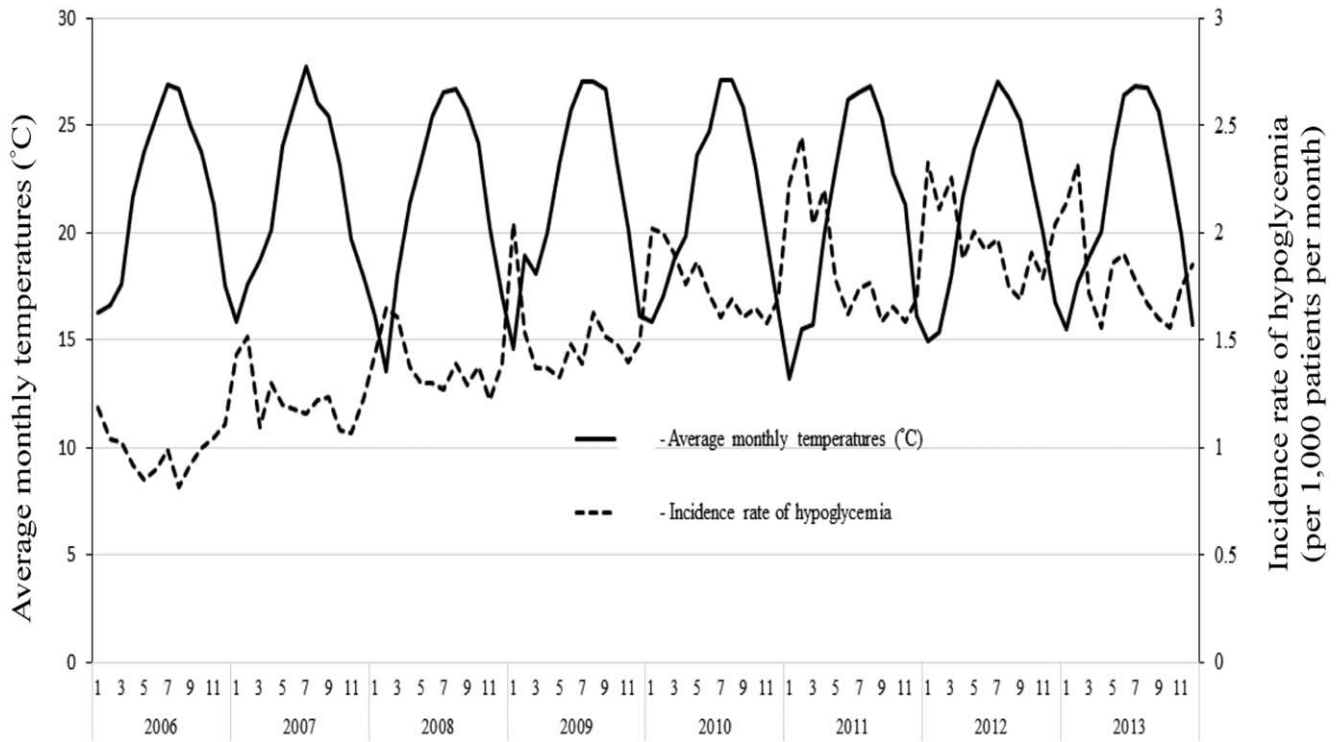


Figure 2. Interaction between incidence rates of hypoglycemia and average monthly ambient temperatures in Taiwan between 2006 and 2013.

In order to add the accuracy of hypoglycemia diagnosis, hypoglycemic subjects were defined as those who had a diagnosis of hypoglycemia at emergency department. In the present study, we observed that hypoglycemia was more frequent during the period of cold ambient temperatures than the period of warm ambient temperatures. The peak period of hypoglycemia always occurred in winter months (January and February). These findings were compatible with a previous study,^[14] but contrary to others revealing that hypoglycemia was more often in summer months than in winter months.^[15]

Although the mechanisms of the association between ambient temperatures and hypoglycemia are beyond the scope of the present study, we reviewed the relevant literature to discuss it. Some studies reported that due to different cultural and dietary effects on diabetic patients, the levels of fasting glucose and hemoglobin A1c would reveal seasonal fluctuations in different populations.^[16,17] That is, some diabetic patients had higher levels of fasting glucose and hemoglobin A1c in winter months and thus the risk of hypoglycemia was low in winter months. This phenomenon partially explains why conflicting results exist between previous and our studies. One study in Taiwan reported that patients with type 2 diabetes were at higher risk of HbA1c >7% in the winter than those in the summer (adjusted odds ratio 1.13 and 95% confidence interval 1.04–1.22), but hypoglycemia was not examined in the study.^[18] Therefore, the relationship between hypoglycemia and hemoglobin A1c remained unsettled. To our opinion, hypoglycemia is an acute episode. Whenever patients use anti-diabetes medications but without oral intake, hypoglycemia might happen. Ambient temperatures could be a precipitating factor for hypoglycemia among those patients having risky behaviors. Based on the above discussion, we think that there could be a seasonal variation of hypoglycemia between

countries. It depends on the country's data to make a preventive strategy of hypoglycemia during the period of seasonal alternation. Currently we suggest that clinicians in Taiwan should remind patients with type 2 diabetes to prevent hypoglycemia during the period of cold ambient temperatures, especially in patients aged ≥ 65 .

Some limitations should be discussed. First, due to the inherent limitation of the dataset used, the diagnosis criteria of hypoglycemia was not recorded. Only ICD-9 codes for hypoglycemia were used for instead. Second, due to the same limitation, the levels of blood glucose and hemoglobin A1c were not recorded in the dataset when hypoglycemia was diagnosed. We could not assess the relationship between hypoglycemia, ambient temperatures, blood glucose, and hemoglobin A1c. Whether ambient temperatures have an effect on glycemic control needs other data for confirmation. We suggest that when hypoglycemia is diagnosed, blood glucose and hemoglobin A1c should be checked simultaneously. Then the relationship between hypoglycemia, blood glucose, and hemoglobin A1c can be clarified. Third, due to the same limitation, the duration of diabetes mellitus was not recorded. We could not assess the relationship between hypoglycemia and the duration of diabetes mellitus. Fourth, some factors, such as dietary habits and behaviors of taking medications, could be associated with hypoglycemia, but the information of these factors was not recorded in the dataset. Fifth, patients with type 2 diabetes often took combined medications. It was difficult to examine which individual medication would pose patients at risk of hypoglycemia.

Some strengths should be discussed. This is the first ecological study to investigate the relationship between ambient temperatures and hypoglycemia in patients with type 2 diabetes in Taiwan. The diagnosis of hypoglycemia was made by physicians at emergency department. The ambient temperatures were

exactly recorded by the Central Weather Bureau in Taiwan. All of study data were official records and well certified. The sample size is large enough to increase its statistical power. The validity of study analysis is high. The results can be convinced.

5. Conclusions

We conclude that patients with type 2 diabetes in Taiwan are more susceptible to hypoglycemia during the period of cold ambient temperatures, particularly in winter months. Clinicians in Taiwan should be aware of the risk of hypoglycemia and remind patients to make a preventive strategy for hypoglycemia during the period of cold ambient temperatures, especially in patients aged ≥ 65 .

Author contributions

Conceptualization: Shih-Wei Lai.

Data curation: Shih-Wei Lai, Yen-Jen Lai.

Formal analysis: Wan-Chi Chang, Cheng-Li Lin, I-Ching Chou, Fuu-Jen Tsai, Yen-Jen Lai.

Methodology: Shih-Wei Lai.

Validation: Shih-Wei Lai.

Writing – original draft: Shih-Wei Lai.

Writing – review & editing: Shih-Wei Lai.

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