DIABETES/METABOLISM RESEARCH AND REVIEWS
*Diabetes Metab Res Rev* 2014; **30**: 497–504.
Published online in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/dmrr.2547

**RESEARCH ARTICLE**

# Secondary diabetic ketoacidosis and severe hypoglycaemia in patients with established type 1 diabetes mellitus in China: a multicentre registration study

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*Received: 24 September 2013*
*Revised: 5 March 2014*
*Accepted: 17 March 2014*

## Abstract

**Background** Diabetic ketoacidosis (DKA) and severe hypoglycaemia are common acute complications of type 1 diabetes mellitus (T1DM). This study aimed to determine the incidence of, and risk factors for, these complications in Chinese patients with established T1DM.

**Methods** This cross-sectional study recruited patients with established T1DM from 16 centres in Guangdong Province, China. Incidence rates were expressed as episodes/100 patient–years. Regression models identified risk factors for the occurrence and recurrence of secondary DKA and severe hypoglycaemia.

**Results** A total of 611 patients with established T1DM (53.7% women) were recruited. The incidence of secondary DKA and severe hypoglycaemia was 26.4 (22.4, 31.0) and 68.8 (62.2, 76.0)/100 patient–years, respectively. Significant risk factors for secondary DKA were female gender [relative risk (RR) = 2.12], medical reimbursement rate <50% (RR = 1.84), uncontrolled diet (RR = 1.76), smoking (RR = 2.18) and poor glycaemic control [glycated haemoglobin $A_{1c}$ ($HbA_{1c}$)/1.0% increase; RR = 1.15]. Overweight/obesity was a protective factor (RR = 0.57). Significant risk factors for severe hypoglycaemia included male gender (RR = 1.71), medical reimbursement rate < 50% (RR = 1.36), longer duration of T1DM (per 5-year increase, RR = 1.22), underweight (RR = 1.44), uncontrolled diet ('never controlled' or 'sometimes controlled' vs. 'usually controlled', RR = 2.09 or 2.02, respectively), exercise <150 min/week (RR = 1.66), presence of neuropathy (RR = 1.89), smoking (RR = 1.48) and lower $HbA_{1c}$ values (per 1.0% decrease, RR = 1.46). Overweight/obesity was a protective factor (RR = 0.62). Additionally, 34.4% of secondary DKA and 81.1% of severe hypoglycaemia episodes occurred in 3.8% and 16.2% patients with recurrent events (≥two episodes), respectively.

**Conclusions** The results indicate that secondary DKA and severe hypoglycaemia occur at high rates in Chinese patients with established T1DM and that recurrence is likely to occur in high-risk patients. Comprehensive management of T1DM should include recommendations to control modifiable risk factors. Copyright © 2014 John Wiley & Sons, Ltd.

**Keywords** diabetes mellitus; type 1; diabetic ketoacidosis; severe hypoglycaemia; incidence; risk factors; Chinese

## Introduction

Diabetic ketoacidosis (DKA) and severe hypoglycaemia are common and serious acute complications of type 1 diabetes mellitus (T1DM). These conditions also have a high likelihood of recurrence. In particular, DKA is one of the leading causes of mortality in children with T1DM [1–3], and results in increased health care costs. DKA episodes are responsible for about a quarter of direct medical expenditures associated with T1DM in the USA [4].

Severe hypoglycaemia can result in serious outcomes, such as seizures, coma or even death. In the Diabetes Control and Complications Trial [5], patients with established T1DM reported a higher rate of severe hypoglycaemia than was reported by patients with type 2 diabetes mellitus [6]. Approximately 34% and 18% of intensively and conventionally treated patients with established T1DM, respectively, reported at least one episode of severe hypoglycaemia.

In China, DKA and severe hypoglycaemia are commonly encountered in daily clinical practice. The rate of occurrence may be higher in China than in other countries because of factors such as limited health resources, infrequent self-monitoring of blood glucose (SMBG) and inappropriate treatment. However, there is limited research regarding these complications in Chinese patients with T1DM. This lack of epidemiological data hinders efforts by healthcare providers to support patients with T1DM in China. Therefore, we conducted this study to determine the incidence and risk factors of secondary DKA (due to errors in diabetes management or others) and severe hypoglycaemia in Chinese patients with established T1DM in order to provide evidence for better prevention and treatment.

## Materials and methods

This cross-sectional study recruited patients with established T1DM during the period 6 August 2010 to 31 March 2012 from 16 tertiary hospitals in Guangdong Province (Table S1). Endocrinologists in the local hospitals diagnosed T1DM using the criteria recommended by the American Diabetes Association (ADA) [7] and the World Health Organization [8] reports for the classification of diabetes. The protocol and consent processes were approved by the Ethics Committee of the Third Affiliated Hospital of Sun Yat-Sen University. Written informed consent was obtained from patients (aged $\geq$18 years) or their legal guardians (aged $<$18 years).

After diagnosis, data were collected every 3 months. Questionnaires were used to collect information about patient demographics, medical history related to T1DM, including treatment and any acute/chronic complications, smoking/drinking status, diet, exercise and the results of physical examination. Diet and physical activity were self-reported. Usually controlled, sometimes controlled and never controlled diets were defined as $\geq$2/3, 1/3–2/3 and $<$1/3 meals in a week, respectively, were based on diabetes diet principles. Mixed-meal tests were performed in study visit, whereas fasting and 2-h postprandial serum C-peptide were measured. The total calories of the mixed meal were 162 kcal (60% carbohydrate, 9.9% protein and 18–19% fat). Body mass index (BMI) was calculated using the measured weight (kg) divided by the square of measured height (m). Age-specific and sex-specific BMI criteria for underweight, normal weight, overweight and obese categories for Chinese children and adolescents aged 2–18 years were derived from published epidemiological studies [9,10] (Table S2). For patients aged $>$18 years, BMI cut-offs for the underweight, normal weight, overweight and obese categories were set at $>$18.5, 18.5–23.9, 24.0–27.9 and $\geq$28.0 kg/m$^2$, respectively [10]. Age-specific targets for glycated haemoglobin A1c ($HbA_{1c}$) values recommended by the Chinese Diabetes Society (CDS) [11] and the ADA [12] were used to evaluate blood glucose levels.

Diagnosis of DKA was based on the criteria of the CDS [3], ADA [13], Lawson Wilkins Pediatric Endocrine Society and the European Society for Paediatric Endocrinology [1]: hyperglycaemia (blood plasma glucose $>$13.9 mmol/L), blood bicarbonate $<$15 mmol/L and/or pH $<$ 7.30 (arterial) and elevated level of ketones in the urine or blood. For a definition of severe hypoglycaemia, the recommendations of the CDS [3] and ADA [14] were used: an event requiring assistance of another person to actively administer carbohydrate, glucagons or other resuscitative actions.

### Biochemical analysis

For all patients, $HbA_{1c}$ and stimulated C-peptide levels were assessed at every visit. The mean $HbA_{1c}$ and stimulated C-peptide were calculated from all available measurements in each subject. Ethylenediaminetetraacetic acid-anticoagulated whole blood (for $HbA_{1c}$) and serum (for C-peptide) samples were collected and frozen at $-20$ °C in each hospital and then shipped on dry ice to the Third Affiliated Hospital of Sun Yat-Sen University and the Beijing North Institute of Biological Technology, respectively. $HbA_{1c}$ levels were measured using high-performance liquid chromatography (Bio-Rad D10 $HbA_{1c}$ analyser; reference range 4.3–6.1%, intra-batch and interbatch coefficients of variation 0.46% and 0.99%, respectively). C-peptide levels were measured using an iodine ($^{125}$I) radioimmunoassay kit (reference range:



DOI: 10.1002/dmrr

fasting, 200.0–1133.3 pmol/L and five times after stimulation; intra-batch and interbatch coefficients of variation 0.46% and 0.99%, respectively).

## Statistical analysis

Categorical variables are presented as counts (percentages), and continuous data that were not normally distributed are presented as median [first quartile (Q1)–third quartile (Q3)]. Differences between groups were analysed by Mann–Whitney U test. Incidence rates of secondary DKA and severe hypoglycaemia are presented as events /100 patient-years, proportions were compared by Fisher's exact test. To determine risk factors for secondary DKA and severe hypoglycaemia, a Poisson regression model was used. Separate backwards stepwise logistic regression analyses were used to identify risk factors for the recurrence of secondary DKA and severe hypoglycaemia. All analyses were performed using SAS v. 9.2 software (SAS, Cary, NC, USA). Statistical significance was designated at $p < 0.05$.

# Results

## Demographic and clinical characteristics

Table 1 summarizes the demographic and clinical characteristics of the patients with established T1DM enrolled in this study. The sample consisted of 611 patients with established T1DM (53.7% women) who participated in a median of 3.2 (range 2.2–4.5) visits. T1DM onset occurred most frequently (46.6%) at age 20–39 (median 22.7) years. According to BMI [9,10], underweight, overweight and obese patients accounted for 19.6%, 10.8% and 1.0% of the sample, respectively. Of the total sample, 71.8% reported that they 'usually controlled' their diet, and 52.7% reported exercising ≥150 min/

**Table 1. Demographic and clinical characteristics of patients with type 1 diabetes mellitus (T1DM) ($n$ = 611)**

| Characteristics | Data | Characteristics | Data |
|---|---|---|---|
| Gender: female (%) | 328 (53.7) | Duration of T1DM (years) | 4.3 (1.7–7.9) |
| Current age (years) | 27.8 (19.5–37.3) | 0–1 (%) | 84 (13.7) |
| 0–6 (%) | 7 (1.1) | 1–5 (%) | 254 (41.6) |
| 7–12 (%) | 48 (7.9) | 5–15 (%) | 239 (39.1) |
| 13–19 (%) | 104 (17.0) | > 15 (%) | 34 (5.6) |
| 20–39 (%) | 335 (54.8) | BMI categories | |
| 40–59 (%) | 94 (15.4) | Underweight (%) | 120 (19.6) |
| ≥ 60 (%) | 23 (3.8) | Normal (%) | 419 (68.6) |
| Age at onset of diabetes (years) | 22.7 (14.0, 31.4) | Overweight (%) | 66 (10.8) |
| 0–6 (%) | 41 (6.7) | Obese (%) | 6 (1.0) |
| 7–12 (%) | 97 (15.9) | Medical reimbursement rates (%) | |
| 13–19 (%) | 124 (20.3) | 0–19 (%) | 106 (17.3) |
| 20–39 (%) | 285 (46.6) | 20–49 (%) | 262 (42.9) |
| 40–59 (%) | 54 (8.8) | 50–79 (%) | 206 (33.7) |
| ≥ 60 (%) | 10 (1.6) | 80–100 (%) | 37 (6.1) |
| $HbA_{1c}$ (%) at age (years) | 8.4 (7.0–10.2) | Patients reaching $HbA_{1c}$ target (%) | 161 (26.4) |
| 0–6 (%) | 8.3 (8.2–11.7) | Age 0–6 years (%) | 4 (57.1) |
| 7–12 (%) | 8.5 (7.5–10.4) | Age 7–12 years (%) | 17 (35.4) |
| 13–19 (%) | 9.6 (8.0–12.4) | Age 13–19 years (%) | 18 (17.3) |
| > 20 (%) | 8.1 (6.9–9.9) | Age ≥ 20 years (%) | 122 (27.0) |
| Exercise ≥150 min/week (%) | 322 (52.7) | Diet control status | |
| Smoker (%) | 69 (11.3) | Usually controlled (%) | 439 (71.8) |
| Alcohol intake ≥70 g/week (%) | 28 (4.6) | Sometimes controlled (%) | 114 (18.7) |
| Frequency of SMBG (per day) | 0.4 (0.1–1.4) | Never controlled (%) | 58 (9.5) |
| Frequency of SMBG (per day) in insulin pump users [a] | 2.0 (0.7–3.0) | Insulin regimen | |
| Frequency of SMBG (per day) in non-insulin pump users | 0.4 (0.1–1.0) | Injection frequency <3/day (%) | 221 (36.2) |
| Fasting C-peptide (pmol/L) | 29.9 (0.0–132.0) | Injection frequency ≥3/day (%) | 308 (50.4) |
| Stimulated C-peptide (pmol/L) | 40.0 (0.0–190.0) | Insulin pump (%) | 82 (13.4) |
| Per capita annual family income (1000 Chinese Yuan) [b] | 25.0 (10.0–48.0) | Basal insulin categories ($n$ = 198) | |
| Insulin dosage (IU/kg/day) | 0.7 (0.5–0.8) | Insulin glargine | 132 (66.7) |
| | | NPH | 66 (33.3) |

Data are presented as counts (%) for categorical variables or median (Q1–Q3) for continuous variables.
T1DM, type 1 diabetes mellitus; BMI, body mass index; $HbA_{1c}$, glycated haemoglobin $A_{1c}$; SMBG, self-monitoring of blood glucose.
[a] $P < 0.05$ as compared with non-insulin pump users.
[b] On 31 March 2012, 1000 Chinese Yuan = 158.73 USD.



DOI: 10.1002/dmrr

week. Non-smokers and non-drinkers represented 95.4% and 88.7% of the sample, respectively. The median frequency of SMBG was 0.4 (range 0.1–1.4) times/day. Median-stimulated C-peptide level was 40.0 (range 0.0–190.0) pmol/L. Overall, 26.4% patients reached age-specific $HbA_{1c}$ targets.

## Secondary DKA

The incidence of secondary DKA was 26.4 (22.4, 31.0)/100 patient–years. At least one secondary DKA event occurred in 20.0% ($n = 122$) of the 611 patients. The incidence was 27.1 (18.1, 38.9)/100 patient–years in patients younger than 18 years and 26.3 (21.8, 31.4)/100 patient–years in adult patients ($P > 0.05$ between different age groups). There were no significant differences in incidence between patients treated with insulin glargine ($n = 132$) and patients treated with neutral protamine Hagedorn (NPH) insulin ($n = 66$) [22.4 (14.6, 32.8) vs. 25.5 (14.6, 41.4)/100 patient–years; $P > 0.05$].

Figure 1 illustrates the RR of the significant risk factors for secondary DKA. These included female gender (RR = 2.12), medical reimbursement rate <50% (RR = 1.84), uncontrolled diet ('never controlled' vs. 'usually controlled', RR = 1.76), smoking (RR = 2.18) and poor glycaemic control ($HbA_{1c}$/1.0% increase, RR = 1.15). Additionally, 34.4% of secondary DKA episodes represented recurrent events (≥ two episodes) in 3.8% of the patients. The recurrence of secondary DKA was associated with female gender (RR = 10.56), smoking (RR = 6.99), poor $\beta$ cell function (stimulated C-peptide/100 pmol/L decrease, RR = 4.22) and poor glycaemic control ($HbA_{1c}$/1.0% increase, RR = 1.16) (Table 2).

## Severe hypoglycaemia

The incidence of severe hypoglycaemia was 68.8 (62.2, 76.0)/100 patient–years. At least one severe hypoglycaemia event occurred in 28.6% ($n = 175$) of the 611 patients. The incidence was 70.9 (55.9, 88.7)/100 patient–years in patients younger than 18 years and 68.4 (61.0, 76.3)/100 patient–years in adult patients ($P > 0.05$ between different age groups). There were no significant differences in incidence between patients treated with insulin glargine ($n = 132$) and patients treated with NPH insulin ($n = 66$) [55.1 (42.4, 70.3) vs. 65.4 (46.9, 88.7)/patient-years; $P > 0.05$].

Figure 2 illustrates the RR of the significant risk factors for severe hypoglycaemia. These included male gender (RR = 1.71), medical reimbursement rate <50% (RR = 1.36), longer diabetes duration (per 5-year increase,

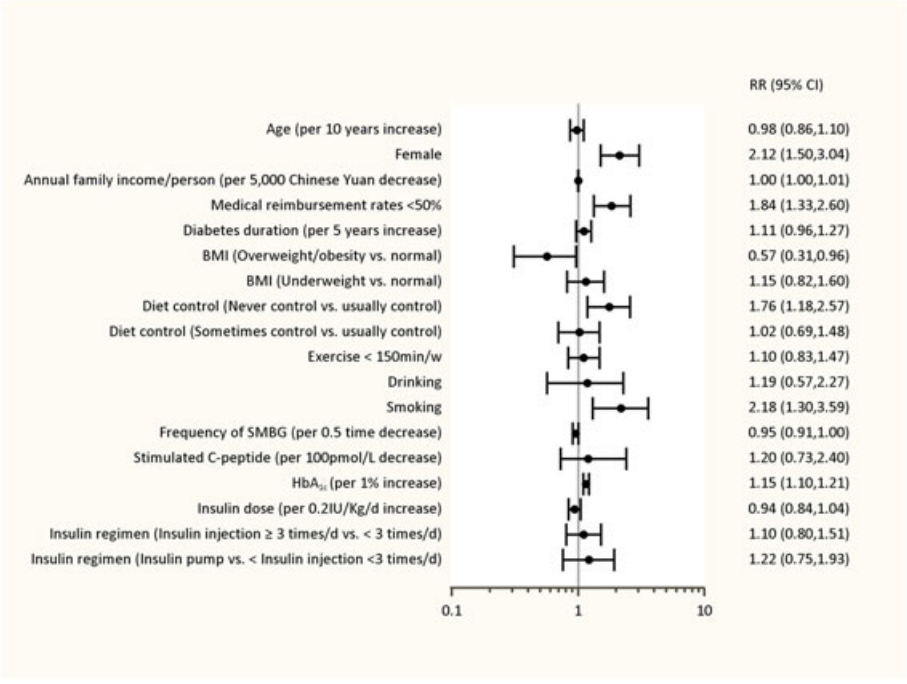


**Figure 1. Relative risk (RR) and 95% confidence intervals (CI) of the independent risk factors for secondary diabetic ketoacidosis (DKA) in patients with type 1 diabetes mellitus (T1DM). BMI, body mass index; CI, confidence interval; DKA, diabetic ketoacidosis; $HbA_{1c}$, glycated haemoglobin $A_{1c}$; RR, relative risk; SMBG, self-monitoring of blood glucose; T1DM, type 1 diabetes mellitus**



DOI: 10.1002/dmrr

**Table 2. Logistic regression analysis for secondary DKA recurrence in patients with type 1 diabetes mellitus (T1DM) ($n = 611$)**

| Independent variable | Coefficient | RR | 95% CI | $p$ |
|---|---|---|---|---|
| Female gender | 1.18 | 10.56 | 1.97, 56.72 | 0.01 |
| Per capita annual family income (per 5000 Chinese Yuan[a] decrease) | 0.11 | 1.12 | 0.99, 1.27 | 0.08 |
| Smoker | 0.97 | 6.99 | 1.02, 48.00 | 0.05 |
| Stimulated C-peptide (per 100 pmol/L decrease) | 1.09 | 4.22 | 1.20, 6.97 | 0.01 |
| $HbA_{1c}$ (per 1.0% increase) | 0.15 | 1.16 | 1.00, 1.34 | 0.05 |

DKA, diabetic ketoacidosis; T1DM, type 1 diabetes mellitus; RR, relative risk; CI, confidence intervals; $HbA_{1c}$, glycated haemoglobin $A_{1c}$.
[a]On 31 March 2012, 5000 Chinese Yuan = 793.65 USD.

RR = 1.22), underweight BMI category (RR = 1.44), uncontrolled diet ('never controlled' or 'sometimes controlled' vs. 'usually controlled', RR = 2.09 or 2.02, respectively), exercising <150 min/week (RR = 1.66), presence of neuropathy (RR = 1.89), smoking (RR = 1.48) and low $HbA_{1c}$ values (per 1.0% decrease, RR = 1.46). Overweight/obesity was a protective factor (RR = 0.62). Moreover, 81.1% of the severe hypoglycaemia episodes occurred in the 16.2% of the T1DM patients who had recurrent events (≥ two episodes). The recurrence of severe hypoglycaemia was significantly associated with male gender (RR = 2.03), underweight (RR = 2.02), uncontrolled diet (RR = 3.11 for 'never controlled' vs. 'usually controlled', RR = 4.02 for 'sometimes controlled' vs. 'usually controlled'), exercising <150 min/week (RR = 2.87) and low $HbA_{1c}$ values (per 1.0% decrease, RR = 1.73). Overweight/obesity was again a protective factor (RR = 0.28) (Table 3).

## Discussion

The results of the current study indicate that acute complications of T1DM, including secondary DKA and severe hypoglycaemia, are common in Chinese patients with established T1DM. Although the difference could be attributable to methodological discrepancies between studies or heterogeneities of patients in terms of diet habit, SMBG, insulin-therapy regimens and so on, the crude incidence of secondary DKA reported here is higher than the incidence reported in studies from other countries [15–24], which varies from 1.5/100 patient–years

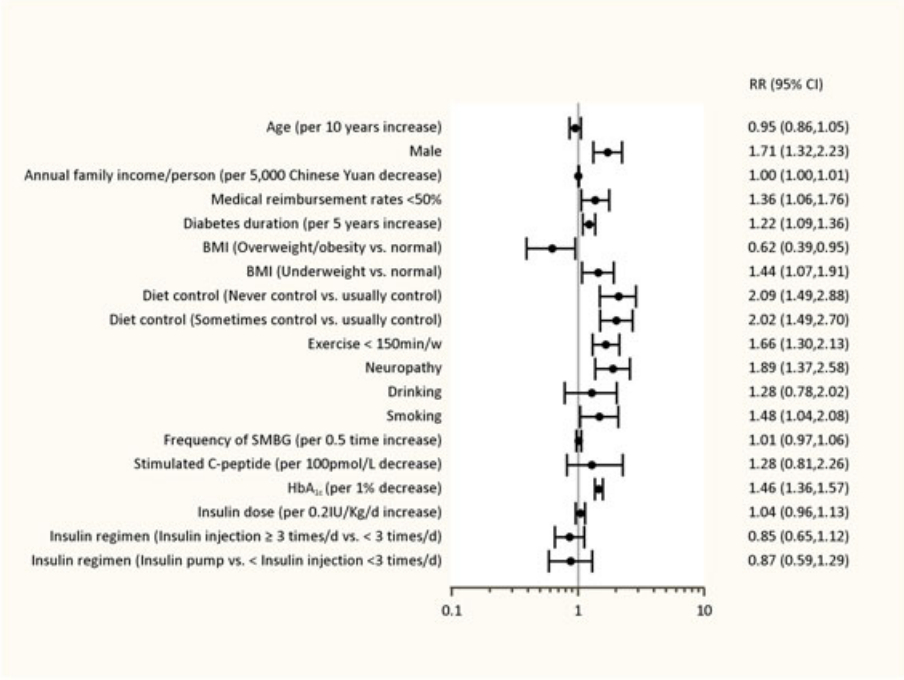


**Figure 2. Relative risk (RR) and 95% confidence intervals (CI) of the independent risk factors for severe hypoglycaemia in patients with type 1 diabetes mellitus (T1DM). BMI, body mass index; CI, confidence interval; $HbA_{1c}$, glycated haemoglobin $A_{1c}$; RR, relative risk; SMBG, self-monitoring of blood glucose; T1DM, type 1 diabetes mellitus**



DOI: 10.1002/dmrr

**Table 3. Logistic regression analysis for recurrence of severe hypoglycemia in patients with type 1 diabetes mellitus (T1DM) ($n$ = 611)**

| Independent variable | Coefficient | RR | 95% CI | $p$ |
|---|---|---|---|---|
| Male gender | 0.71 | 2.03 | 1.18, 3.50 | 0.01 |
| T1DM duration (per 5-year increase) | 0.21 | 1.23 | 0.97, 1.57 | 0.09 |
| BMI categories | | | | <0.01 |
| Underweight versus normal | 0.70 | 2.02 | 1.08, 3.80 | |
| Overweight/obese versus normal | −1.29 | 0.28 | 0.10, 0.73 | |
| Diet control | | | | <0.01 |
| Never controlled versus usually controlled | 1.13 | 3.11 | 1.46, 6.63 | |
| Sometimes controlled versus usually controlled | 1.39 | 4.02 | 2.20, 7.36 | |
| Exercise <150 min/week | 1.05 | 2.87 | 1.72, 4.78 | <0.01 |
| Presence of neuropathy | 0.64 | 1.90 | 0.93, 3.88 | 0.08 |
| Smoker | 0.68 | 1.97 | 0.95, 4.08 | 0.07 |
| $HbA_{1c}$ (per 1.0% decrease) | 0.55 | 1.73 | 1.48, 2.02 | <0.01 |

T1DM, type 1 diabetes mellitus; RR, relative risk; CI, confidence interval; BMI, body mass index; $HbA_{1c}$, glycated haemoglobin $A_{1c}$.

in Sweden [17] to 26.3/100 patient–years in Malaysia [21]. The same is also true for severe hypoglycaemia, with most studies reporting a lower crude incidence than that in the present study [20,21,23–28]. Interestingly, reports of secondary DKA and severe hypoglycaemia are relatively rare in countries that have a high incidence of T1DM, such as Sweden [17,25], Australia [18,21], Austria [24], Germany [24], Italy [28,29] and the USA [19,20,23]. In contrast, areas in East and Southeast Asia [21], which have a relatively low incidence of T1DM, report higher rates of occurrence of secondary DKA and severe hypoglycaemia. Most previous studies showed that the incidence of secondary DKA or severe hypoglycaemia was higher among patients younger than 18 years than among patients aged ≥18 years. On the contrary, the present study did not observed similar results, and this may be due to a relatively short follow-up duration.

The present study also identified risk factors for secondary DKA and severe hypoglycaemia. Similar to other studies [19–21,23,29,30], T1DM patients with poor glycaemic control were more likely to experience secondary DKA, whereas those with low $HbA_{1c}$ values were at a high risk of severe hypoglycaemia. Women experienced more episodes of secondary DKA, whereas men were more likely to experience severe hypoglycaemia, which is also consistent with reports from previous studies [16,20,30]. These studies have suggested that young women with T1DM may skip insulin injections in order to lose weight [20,31], and men may be likely to exercise more than women [20,30]. However, our results indicate that patients with T1DM who exercise infrequently may also be at risk of severe hypoglycaemia, which is not in accord with the findings of current reports. A recent large-scale study conducted with T1DM patients in Germany and Austria indicated that no association existed between regular exercise and severe hypoglycaemia [32]. They hypothesized that T1DM patients who were well educated in blood glucose management were able to prevent hypoglycaemia during exercise. Our further analysis showed that patients who exercised more than 150 min/week were also better educated, had higher incomes and were more concerned about their diet. All of these factors might contribute to a lower risk of severe hypoglycaemia. Other lifestyle risk factors associated with secondary DKA and severe hypoglycaemia included uncontrolled diet and smoking, which have previously been well elucidated in cardiovascular complications [33]. However, there is little evidence about their role in acute complications of T1DM.

Our results indicated that patients with type 1 diabetes who were obese or overweight, as compared with patients who have normal weight or lean, had a lower risk of secondary DKA and severe hypoglycaemia. Nonetheless, patients should not be encouraged to gain weight because of the harmful effects of obesity/overweight on macrovascular complications. In addition, considering that nearly 20% of patients with T1DM were underweight, it is very important to help them maintain a healthy weight through appropriate medical nutrition therapy. We found that risk factors for severe hypoglycaemia included a longer duration of T1DM and the presence of neuropathy. These results were consistent with those of most previous studies. A lack of insurance, another risk factor in this study, may contribute to poor compliance to prescribed insulin treatment and therefore increase the risk of secondary DKA and severe hypoglycaemia episodes [20]. Previous studies showed that SMBG frequency played an important role in the risk of acute complications in T1DM, this relationship was not observed in the current study. This may be explained by the fact that the frequency of SMBG for the entire sample was much lower than that reported in other studies [21,34].

The effect of different modalities of insulin therapy (insulin pump, multiple daily injection or daily insulin injections less than three times per day) on acute complications including secondary DKA and severe hypoglycaemia was controversial. Diabetes Control and Complications Trial [35] and one Sweden study [36] demonstrated that



DOI: 10.1002/dmrr

patients treated with insulin pump had a higher risk of secondary DKA and severe hypoglycaemia compared with patients treated with subcutaneous insulin injections, whereas the present study found that there was no significant difference among various insulin regimens. Although our results differ from some published studies, they were consistent with those of recently published findings of T1D Exchange study [37] from the USA and one study from Germany and Austria [38]. However, only a small proportion of patients treated with insulin pump (13.4%) may contribute to our result as well. In the current studies, no significant difference was found in the incidence of severe hypoglycaemia between patients treated with insulin glargine and patients treated with NPH insulin, which was consistent with the previous study [39] and inconsistent with another study [29]. Our results also showed that use of insulin glargine compared with NPH insulin appeared no difference in the risk of secondary DKA. This was not in agreement with other research [40], which showed that insulin glargine was associated with higher risk of secondary DKA compared with NPH insulin.

High-risk patients with established T1DM were more likely to experience recurrent complications, which support results from previous studies [20,41]. The patient characteristics that predicted recurrence of both secondary DKA and severe hypoglycaemia included female gender, poor glycaemic control, poor $\beta$ cell function, low income and smoking. Lack of insurance also played a role in the repeated occurrence of severe hypoglycaemia. Therefore, these patients may need additional support from health care providers to prevent recurrence.

The strengths of this study include its large sample size, representing all types of T1DM and patients recruited from multiple centres. Nonetheless, as a pilot study, it has several limitations that must be considered. First, it lacks long-term follow-up data, with most patients only participating in a few visits over a period of less than a year. Furthermore, we did not analyse the severity and disease burden of secondary DKA or severe hypoglycaemia. Future prospective studies with these patients will provide further insights into these issues.

In conclusion, occurrence of secondary DKA and severe hypoglycaemia was more frequent in Chinese patients with established T1DM than that reported in studies conducted in other countries. Moreover, high-risk patients were more likely to experience recurrent episodes of secondary DKA and severe hypoglycaemia. Comprehensive management of T1DM should take into consideration appropriate control of metabolic risk factors to reduce the occurrence and potential consequences of secondary DKA and severe hypoglycaemia.

## Acknowledgements

This study was supported by the Guangdong Provincial Department of Science and Technology (Grant No. 2010B031500008), the Sun Yat-Sen University Clinical Research 5010 Programme (Grant No. 2007030), the National Science Fund for Distinguished Young Scholars (Grant No. 81025005), the 985 Project (Grant No. 82000–3281901), the New Drug Development, Construction and Management of Clinical Biobank for Major Disease (Grant No. 2011ZX0907-001-08), the Health Department of Fujian Province (Grant No. 2013-2-87) and the unrestricted research grants from Novo Nordisk, Sanofi–Aventis, Bayer, Johnson & Johnson and Medtronic. We thank all the doctors, nurses, technicians and patients in the 16 participating hospitals for their dedication to this study.

## Conflicts of interest

The authors have no conflicts of interest.

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