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Glycaemic control in type 2 diabetes patients and its predictors: a retrospective database study at a tertiary care Diabetes Centre in Ningbo, China

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Title

Glycaemic control in type 2 diabetes patients and its predictors: a retrospective database study at a tertiary care Diabetes Centre in Ningbo, China

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Abstract

Objectives: The aim of the study was to assess glycaemic control in type 2 diabetes (T2DM) patients at a tertiary care Diabetes Centre in Ningbo, China, and to determine factors that independently predict their glycaemic control.

Design: Retrospective cross-sectional study using an existing database, the Diabetes Information Management System.

Setting: Tertiary care Diabetes Centre in Ningbo, China.

Participants: The study included adult T2DM patients, registered and received treatment at the Diabetes Centre for at least six consecutive months. Those diagnosed with type 1 diabetes, gestational diabetes, secondary diabetes, unknown type of diabetes or endocrine diseases were excluded from the study. The study inclusion criteria were satisfied by 1387 patients, from 1 July 2012 to 30 June 2017.

Primary outcome measure: Glycaemic control (poor was defined as glycated haemoglobin (HbA1c) >=7% or fasting blood glucose (FBG) >7.0 mmol/L).

Results: In terms of HbA1c and FBG, the 5-year period prevalence of poor glycaemic control was 50.3% (n=698) and 57.3% (n=791), respectively. In terms of HbA1c and FBG, the odds of poor glycaemic control increased with the duration of T2DM ($p<0.001$), were lower in patients residing in urban areas ($p<0.001$ and $p=0.023$, respectively), only on diet and physical activity as part of their T2DM therapeutic regimen ($p<0.001$ and $p=0.003$, respectively), and without hyperlipidemia ($p=0.013$ and $p=0.004$, respectively).

Conclusions: More than half of T2DM patients at the Diabetes Centre in Ningbo, China have poor glycaemic control, and the predictors of glycaemic control were identified. The study findings could be taken into consideration in future interventional studies aimed at improving glycaemic control in these patients.

Keywords

Type 2 diabetes; poor glycaemic control; China

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Strengths and limitations of this study

- This is the first study to explore glycaemic control in type 2 diabetes patients at the tertiary care Diabetes Centre in Ningbo, China and, as far as we are aware, in the Zhejiang province of China.
- Glycated haemoglobin (which reflects the average blood glucose level over the past three months) and fasting blood glucose (a short-term index) were used to determine glycaemic control, which in turn provided a complete picture.
- Missing data could lead to bias but were generally low in this study. Multiple regression analyses included a sample with missing values for the adjusted variables.
- This retrospective study was conducted using an existing database, which is primarily developed for the clinical purpose and not for research (i.e., issues with routinely collected data were present).
- As this was a cross-sectional study, it was not possible to determine the causal association between different variables and glycaemic control.

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Introduction

China has the world's largest type 2 diabetes (T2DM) epidemic, a complex metabolic disorder which has major health, social and economic consequences. Almost 11% of all adults (about 110 million) are currently living with T2DM i.e., one in nine adults has T2DM. This number is expected to increase to 151 million by 2040 [1]. Its chronic hyperglycaemia is associated with long-term complications (e.g., cardiovascular disease) and even death [2]. In China, T2DM and its complications contribute to almost one million deaths each year. Alarmingly, nearly 40% of these deaths are premature (i.e., in people below the age of 70) [3]. China spends upwards of US $25 billion a year on the management of T2DM and 13% of its medical expenditures are directly caused by T2DM [4]. In spite of this, many T2DM patients have poor glycaemic control (51-68%) [5-9]. Unfortunately, these figures are much higher as compared to many developed countries [10, 11].

Ningbo is one of the most economically developed Chinese cities, located in the northeast Zhejiang province. In 2015, the prevalence of T2DM in people over 40 years of age in Ningbo city area was around 21% [12]. Ningbo First Hospital, with 1600 beds, is a general teaching hospital and one of the largest healthcare providers in the province. Annually, around two million patients visit this hospital, from local as well as from surrounding areas [13]. The hospital has a tertiary care Diabetes Centre. A team of qualified and experienced diabetes experts is working at the Diabetes Centre. Till date, no research has been conducted to explore glycaemic control in T2DM patients at the Diabetes Centre. The aim of the study was to assess their glycaemic control and to determine factors that independently predict their glycaemic control. Knowledge of factors associated with the poor glycaemic control in these patients would provide valuable information about strategies that healthcare professionals and providers can address to improve their glycaemic control.

Methods

Study design, data source and period

A retrospective cross-sectional study was conducted using an existing computerised medical records database, the Diabetes Information Management System. This

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database was developed by the Yinal Software Corporation, China for the Diabetes Centre. The study period was from 1st July 2012 to 30 June 2017 (5 years) and the database included 6699 patients.

Study population, inclusion and exclusion criteria

The study included adult (18 years of age or older) patients, diagnosed with T2DM, and registered and received treatment at the Diabetes Centre for at least six consecutive months. Those diagnosed with type 1 diabetes, gestational diabetes, secondary diabetes, unknown type of diabetes or endocrine diseases (such as Cushing syndrome and hyperthyroidism which may increase their blood glucose levels) were excluded from the study. The study inclusion criteria were satisfied by 1387 patients.

Study variables

The following variables were extracted from the database: age (in years), sex (male or female), education (university/college, class 7 to 12, class 1 to 6, or no qualifications), occupation (manual workers (i.e., more physical than mental work), non-manual workers (i.e., more mental than physical work) or never worked/retired), marital status (married or single/divorced/widowed), residence (urban or rural based on the “hukou” system (i.e., residence registration system in China)) [14], health insurance, smoking (current status), alcohol drinking (current status), family history of T2DM (any parent or sibling), duration of T2DM (in years), number of visits to the Diabetes Centre for T2DM since registration, T2DM therapeutic regimen (only diet and physical activity; diet and physical activity and oral hypoglycaemic drugs (OHD - metformin, acarbose, sulfonylureas, meglitinides and/or thiazo-lidinediones); diet and physical activity and insulin (long-term insulin, intermediate insulin, rapid-acting insulin and/or premix insulin); or diet and physical activity, OHD and insulin), comorbidities ((overweight or obese (diagnosis based on body mass index (BMI) >=24 kg/m^2) [15], hypertension (diagnosis based on blood pressure >=140/90 mm Hg), and hyperlipidemia (diagnosis based on serum lipids- total cholesterol ≥4.5 mmol/L or triglycerides ≥1.7 mmol/L), and blood glucose levels. Poor glycaemic control was defined as glycated haemoglobin (HbA1c) >=7% or fasting blood

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glucose (FBG) >7.0 mmol/L [16]. The HbA1c was estimated using the high-performance liquid chromatographic (HPLC) method, using the D-10 Hemoglobin Analyzer (Bio-Rad, USA). The FBG was estimated using the glucose oxidase method. It should be noted that data on dipeptidyl peptidase-4 (DPP-4) inhibitors and glucagon-like peptide 1 (GLP-1) receptor agonists were not available in the database. These drugs are not covered by the existing health insurance system in China and thus, these drugs are not sold in this hospital [17].

Ethics

The study was ethically approved by the Research Ethics Committee at the Ningbo First Hospital, China.

Statistical analyses

The 5-year period prevalence of poor glycaemic control in T2DM patients at the Diabetes Centre was calculated. Simple logistic regression methods were used to investigate the association between glycaemic control and other variables. To identify any independent association, multiple logistic regression models were developed using backward stepwise regression analyses and all the other variables were included. Sensitivity analyses were carried out – only those variables with a P value of ≤0.20 in simple logistic regressions were included in multiple logistic regression models. Multiple regression models included a sample with unknown values for these adjusted variables. Odds ratios (ORs) and their respective 95% confidence intervals (CIs) were calculated. The results were considered significant when P values were ≤0.05. All data were analysed using IBM SPSS Statistics Version 20.0 for Windows.

Results

57% of T2DM patients were male and the mean age was 54.1 years. In terms of HbA1c and FBG, the 5-year period prevalence of poor glycaemic control was 50.3% (n=698) and 57.3% (n=791), respectively. Table 1 reports the characteristics of T2DM patients with good and poor glycaemic control. In terms of HbA1c and FBG,

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glycaemic control was found to be associated with age (p<0.001), education (p<0.001), residence (p=0.012 and p=0.042, respectively), duration of T2DM (p<0.001) and T2DM therapeutic regimen (p<0.001). The additional associated factors were hypertension (p=0.005) in the case of HbA1c, and alcohol drinking (p=0.04) and hyperlipidemia (p=0.025) in the case of FBG.

Table 2 shows the multiple backward stepwise logistic regression analyses to determine factors independently associated with the poor glycaemic control. In terms of HbA1c and FBG, the odds of poor glycaemic control increased with the duration of T2DM (p<0.001), were lower in patients residing in urban areas (p<0.001 and p=0.023, respectively), only on diet and physical activity as part of their T2DM therapeutic regimen (p<0.001 and p=0.003, respectively), and without hyperlipidemia (p=0.013 and p=0.004, respectively). Table 3 reports the sensitivity analyses - multiple logistic regression models included only those variables with a P value of ≤0.20 in simple logistic regressions. Similar results were found in the sensitivity analyses. In terms of HbA1c and FBG, the odds of poor glycaemic control increased with the duration of T2DM (p<0.001), were lower in patients residing in urban areas (p<0.001 and p=0.046, respectively), only on diet and physical activity as part of their T2DM therapeutic regimen (p<0.001 and p=0.002, respectively), and without hyperlipidemia (p=0.013 and p=0.038, respectively).

Discussion

In terms of HbA1c and FBG, the 5-year period prevalence of poor glycaemic control in T2DM patients at the tertiary care Diabetes Centre in Ningbo, China was 50% and 57%, respectively. In other words, less than half of T2DM patients at the Diabetes Centre have adequate glycaemic control. The finding is consistent with a recent nationwide population-based study (51%) and a recent nationwide hospital-based study (52%) [5,6]. However, two other recent nationwide hospital-based studies reported much higher figures (65% and 68%) [7,8]. These hospital-based studies included a range of hospitals with different tier levels. In terms of glycaemic control in T2DM patients, tertiary care hospitals usually perform better as compared to primary or secondary care hospitals [18], and this could be the case in our study. Another reason could be different population characteristics in these studies. For example,

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the study which reported 68% included only those T2DM patients who were on OHDs alone or in combination with either insulin or GLP-1 receptor agonists, indicating poor glycaemic control with the disease progression. In spite of the availability of diabetes experts at this tertiary care Diabetes Centre and of effective and safe glucose-lowering therapies, the prevalence of poor glycaemic control in T2DM patients was high in our study as compared to other studies conducted in various developed countries [10,11]. This indicates that there is still a room for improvement at this Diabetes Centre.

In the unadjusted models (HbA1c and FBG), glycaemic control was found to be associated with age, education, residence, duration of T2DM and T2DM therapeutic regimen. The additional associated factors were hypertension in the case of HbA1c, and alcohol drinking and hyperlipidemia in the case of FBG. Previous studies conducted among T2DM patients in various countries reported similar and other factors associated with glycaemic control (such as age, sex, education, alcohol drinking, duration of T2DM, T2DM therapeutic regimen, overweight or obese, hypertension and hyperlipidemia) [7,18-24].

In terms of HbA1c and FBG, the odds of poor glycaemic control increased with the duration of T2DM, were lower in patients residing in urban areas, only on diet and physical activity as part of their T2DM therapeutic regimen, and without hyperlipidemia. Similar results were found in the sensitivity analyses. The association found between poor glycaemic control and longer duration of T2DM is consistent with previous studies [8,19,24-26]. Since T2DM is a progressive disease, the function and mass of β-cells gradually decline with the disease progression [27]. In order to attain glycaemic control, a stepwise approach has been recommended in the national T2DM management guideline [16]. The first and foremost step should be lifestyle modification (i.e., diet and physical activity), followed by addition of OHD(s) and/or insulin(s) with the disease progression. An association was found between poor glycaemic control and addition of OHD(s) and/or insulin(s), and the finding is consistent with previous studies [24,28]. This relationship more likely represents a marker of T2DM chronicity and severity than of medication effects themselves. Another reason could be the failure of clinicians to intensify therapy in a timely manner [29,30]. The uptake and adherence to the T2DM therapeutic regimen among

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patients could also be different from what was prescribed [23,30]. A recent study showed that only 43% of T2DM patients adhered to their therapeutic regimen (OHD(s) and/or insulin(s)) in China [31]. Thus, these issues should be explored and be taken into consideration in future studies.

The “hukou” system was used to classify T2DM patients into urban or rural residents. An association was found between poor glycaemic control and rural residents, which indicates health inequalities in T2DM management. This finding is consistent with another recently conducted study in China [5]. In addition to poor socioeconomic conditions of rural residents in China, no or delayed access to healthcare is a major issue in rural areas [32]. Even the health insurance system is different in rural and urban areas [33-35]. There are discrepancies in resource allocation between rural and urban areas. All these could explain the association found between poor glycaemic control and rural residents.

Like T2DM, hyperlipidemia is a risk factor for cardiovascular disease [36]. The association found between poor glycaemic control and hyperlipidemia is consistent with previous studies [24,37]. Glycaemic control mainly depends on the degree of residual pancreatic β-cells function and insulin sensitivity [38,39]. Abnormalities in lipid metabolism, characterised by an increase in serum lipids (total cholesterol and triglycerides), may result in lipid spill over to non-adipose tissues, such as pancreatic β-cells. This may lead to cellular dysfunction and lipoapoptosis [40,41]. It is also accepted that high serum triglyceride level is associated with insulin resistance [42]. These mechanisms may partly explain the association found between poor glycaemic control and hyperlipidemia. Further research needs to be conducted to confirm the role of hyperlipidemia in long-term glycaemic control. In continuation, early initiation of lipid-lowing therapy in T2DM patients may reduce the risk for cardiovascular disease and may have benefits in terms of their long-term glycaemic control.

The study has a number of strengths and weaknesses. This is the first study to explore glycaemic control in T2DM patients at the tertiary care Diabetes Centre in Ningbo, China. In addition, as far as we are aware, this is the first study on this issue in the Zhejiang province of China. HbA1c and FBG were used to determine

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glycaemic control, which in turn provided a complete picture. HbA1c reflects the average blood glucose level over the past three months. On the other hand, FBG is a short-term index. In terms of generalisability, the study findings could be valid in settings with similar populations and healthcare systems. Missing data could lead to bias but were generally low in this study. Multiple regression analyses included a sample with missing values for the adjusted variables. This retrospective study was conducted using an existing database, which is primarily developed for the clinical purpose and not for research. It is possible that our findings were the result of other factors not present in the database and thus, not adjusted for in the models, such as self-monitoring of blood glucose, uptake and adherence to the T2DM therapeutic regimen, and depression, anxiety and stress levels of patients [23,43,44]. Although the data were available on time, however, the other data quality issues of routinely collected data cannot be ignored, such as accuracy and reliability. Some of the data were self-reported and this could have been an issue. As this was a cross-sectional study, it was not possible to determine the causal association between different variables and glycaemic control. A long-term, longitudinal study should be conducted among these patients to assess the impact of various factors (these as well as other potential factors) on their glycaemic control. Ours was a hospital-based study and a population-based study should be conducted, which might give a different picture. This could be because of different population characteristics, including their healthcare-seeking behavior.

In conclusion, more than half of T2DM patients at the Diabetes Centre in Ningbo, China have poor glycaemic control, and the predictors of glycaemic control were identified. The study findings could be taken into consideration in future interventional studies aimed at improving glycaemic control in these patients.

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Authors' contributions

JL and KC designed the study, analysed the data and wrote the first draft of the manuscript. All the authors revised this for important intellectual content and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Ethics approval and consent to participate

The study used an existing computerised medical records database, the Diabetes Information Management System. The study was ethically approved by the Research Ethics Committee at the Ningbo First Hospital, China.

Data sharing

The study is part of a bigger project and further publications are expected from the dataset which prevents us from making it public right now.

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Table 1 Characteristics of T2DM patients with good and poor glycaemic control

	Good glycaemic control HbA1c<7% (n=689)	Poor glycaemic control HbA1c>=7% (n=698)	P value	Good glycaemic control FBG≤7.0 mmol/L (n=596)	Poor glycaemic control FBG>7.0 mmol/L (n=791)	P value
Age	51.1±14.4*	57.2±14.3*	<0.001	52.5±15.2*	55.4±14.1*	<0.001
Sex			0.157			0.83
Male	405 (58.8)	384 (55.0)		341 (57.2)	448 (56.6)	
Female	284 (41.2)	314 (45.0)		255 (42.8)	343 (43.4)	
Education			<0.001			<0.001
University/college	166 (24.1)	102 (14.6)		145 (24.3)	123 (15.5)	
Class 7-12	333 (48.3)	310 (44.4)		268 (45.0)	375 (47.4)	
Class 1-6	122 (17.7)	204 (29.2)		117 (19.6)	209 (26.4)	
No qualifications	35 (5.1)	67 (9.6)		45 (7.6)	57 (7.2)	
Unknown	33 (4.8)	15 (2.1)		21 (3.5)	27 (3.4)	
Occupation			0.064			0.231
Manual workers	94 (13.6)	121 (17.3)		87 (14.6)	128 (16.2)	
Non-manual workers	138 (20.0)	141 (20.2)		127 (21.3)	152 (19.2)	
Never worked/Retired	219 (31.8)	317 (45.4)		211 (35.4)	325 (41.1)	
Unknown	238 (34.5)	119 (17.0)		171 (28.7)	186 (23.5)	
Marital status			0.2			0.312
Married	510 (74.0)	562 (80.5)		446 (74.8)	626 (79.1)	
Single/divorced/widowed	55 (8.0)	77 (11.0)		61 (10.2)	71 (9.0)	
Unknown	124 (18.0)	59 (8.5)		89 (14.9)	94 (11.9)	
Residence			0.012			0.042
Urban	449 (65.2)	412 (59.0)		388 (65.1)	473 (59.8)	
Rural	231 (33.5)	281 (40.3)		202 (33.9)	310 (39.2)	
Unknown	9 (1.3)	5 (0.7)		6 (1.0)	8 (1.0)	

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Health insurance			0.583			0.704
	Yes	641 (93.0)	644 (92.3)	554 (93.0)	731 (92.4)	
	No	48 (7.0)	54 (7.7)	42 (7.0)	60 (7.6)	
Smoking			0.076			0.505
	No	567 (82.3)	548 (78.5)	484 (81.2)	631 (79.8)	
	Yes	122 (17.7)	150 (21.5)	112 (18.8)	160 (20.2)	
Alcohol drinking			0.182			0.04
	No	617 (89.6)	609 (87.2)	539 (90.4)	687 (86.9)	
	Yes	72 (10.4)	89 (12.8)	57 (9.6)	104 (13.1)	
Family history of T2DM			0.604			0.095
	No	429 (62.3)	444 (63.6)	390 (65.4)	483 (61.1)	
	Yes	260 (37.7)	254 (36.4)	206 (34.6)	308 (38.9)	
Duration of T2DM		4 (1,8)**	9 (4,14)**	<0.001	4 (1,10)**	7 (3,12)**	<0.001
	Unknown	42 (6.1)	14 (2.0)	40 (6.7)	16 (2.0)	
Number of visits to the Diabetes Centre for T2DM since registration		8 (4,13)**	8 (5,13)**	0.335	8 (4,13)**	8 (5,13)**	0.214
T2DM therapeutic regimen			<0.001			<0.001
Only diet and physical activity		99 (14.4)	45 (6.4)	92 (15.4)	52 (6.6)	
Diet and physical activity + OHD		335 (48.6)	296 (42.4)	267 (44.8)	364 (46.0)	
Diet and physical activity + insulin		38 (5.5)	27 (3.9)	31 (5.2)	34 (4.3)	
Diet and physical activity + OHD + insulin		217 (31.5)	330 (47.3)	206 (34.6)	341 (43.1)	
Overweight or obese			0.357			0.705
	No	311 (45.1)	303 (43.4)	260 (43.6)	354 (44.8)	
	Yes	345 (50.1)	372 (53.3)	311 (52.2)	406 (51.3)	
	Unknown	33 (4.8)	23 (3.3)	25 (4.2)	31 (3.9)	
Hypertension			0.005			0.847
	No	321 (46.6)	273 (39.1)	257 (43.1)	337 (42.6)	

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	Yes	368 (53.4)	425 (60.9)		339 (56.9)	454 (57.4)	
Hyperlipidemia				0.051			0.025
	No	164 (23.8)	136 (19.5)		146 (24.5)	154 (19.5)	
	Yes	525 (76.2)	562 (80.5)		450 (75.5)	637 (80.5)	

n(%), P value excludes unknown.
*Mean (standard deviation (SD)).
**Median (interquartile range (IQR)).

Table 2 Logistic regression analyses to determine factors independently associated with poor glycaemic control

		OR (95% CI)	P value
HbA1c≥7%			
Residence			<0.001
	Urban	1	
	Rural	1.66 (1.23 to 2.25)	
Duration of T2DM		1.13 (1.10 to 1.16)	<0.001
Number of visits to the Diabetes Centre for T2DM since registration		0.98 (0.97 to 1.00)	0.087
T2DM therapeutic regimen			<0.001
	Only diet and physical activity	1	
	Diet and physical activity + OHD	2.07 (1.14 to 3.77)	
	Diet and physical activity + insulin	1.08 (0.46 to 2.54)	
	Diet and physical activity + OHD + insulin	2.67 (1.47 to 4.85)	
Hyperlipidemia			0.013
	No	1	
	Yes	1.53 (1.10 to 2.14)	
FBG>7mmol/L			
Residence			0.023
	Urban	1	
	Rural	1.40 (1.05 to 1.87)	
Duration of T2DM		1.05 (1.03 to 1.07)	<0.001

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T2DM therapeutic regimen		0.003
Only diet and physical activity	1	
Diet and physical activity + OHD	2.64 (1.50 to 4.66)	
Diet and physical activity + insulin	2.11 (0.94 to 4.76)	
Diet and physical activity + OHD + insulin	2.90 (1.65 to 5.10)	
Hyperlipidemia		0.004
No	1	
Yes	1.60 (1.16 to 2.20)	
Hypertension		0.08
No	1	
Yes	0.77 (0.57 to 1.03)	

Table 3 Sensitivity analyses: multiple logistic regression models included those variables with *P*≤0.20 in simple logistic regressions

	OR (95% CI)	P value
HbA1c≥7%		
Residence		<0.001
Urban	1	
Rural	1.68 (1.24 to 2.27)	
Duration of T2DM	1.13 (1.10 to 1.15)	<0.001
T2DM therapeutic regimen		<0.001
Only diet and physical activity	1	
Diet and physical activity + OHD	2.09 (1.16 to 3.76)	
Diet and physical activity + insulin	1.07 (0.46 to 2.49)	
Diet and physical activity + OHD + insulin	2.61 (1.46 to 4.68)	
Hyperlipidemia		0.013
No	1	
Yes	1.53 (1.09 to 2.14)	
FBG>7mmol/L		
Residence		0.046
Urban	1	

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Rural	1.27 (1.01 to 1.61)	
Duration of T2DM	1.05 (1.03 to 1.06)	<0.001
T2DM therapeutic regimen		0.002
Only diet and physical activity	1	
Diet and physical activity + OHD	1.98 (1.31 to 3.00)	
Diet and physical activity + insulin	1.70 (0.89 to 3.24)	
Diet and physical activity + OHD + insulin	2.29 (1.50 to 3.49)	
Hyperlipidemia		0.038
No	1	
Yes	1.34 (1.02 to 1.76)	
Alcohol drinking		0.098
No	1	
Yes	1.35 (0.95 to1.91)	

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4,5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4,5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4,5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5,6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5,6
Bias	9	Describe any efforts to address potential sources of bias	5,6
Study size	10	Explain how the study size was arrived at	4,5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5,6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	n/a
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	n/a
		(*e*) Describe any sensitivity analyses	6
Results			

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Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5,6
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6, table 1
		(b) Indicate number of participants with missing data for each variable of interest	table 1
Outcome data	15*	Report numbers of outcome events or summary measures	6, table 1
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6,7, table 1,2
		(*b*) Report category boundaries when continuous variables were categorized	6,7, table 1,2,3
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7, table 3
Discussion			
Key results	18	Summarise key results with reference to study objectives	7,8,9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7,8,9
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Glycaemic control in type 2 diabetes patients and its predictors: a retrospective database study at a tertiary care Diabetes Centre in Ningbo, China

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Title

Glycaemic control in type 2 diabetes patients and its predictors: a retrospective database study at a tertiary care Diabetes Centre in Ningbo, China

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Abstract

Objectives: The aim of the study was to assess glycaemic control in type 2 diabetes (T2DM) patients at a tertiary care Diabetes Centre in Ningbo, China, and to determine factors that independently predict their glycaemic control.

Design: Retrospective cross-sectional study using an existing database, the Diabetes Information Management System.

Setting: Tertiary care Diabetes Centre in Ningbo, China.

Participants: The study included adult T2DM patients, registered and receiving treatment at the Diabetes Centre for at least six consecutive months. The study inclusion criteria were satisfied by 1387 patients, from 1 July 2012 to 30 June 2017.

Primary outcome measure: Glycaemic control (poor was defined as glycated haemoglobin (HbA1c) >=7% or fasting blood glucose (FBG) >7.0 mmol/L).

Results: In terms of HbA1c and FBG, the 5-year period prevalence of poor glycaemic control was 50.3% (n=698) and 57.3% (n=791), respectively. In terms of HbA1c and FBG, the odds of poor glycaemic control increased with the duration of T2DM (>1 to 2 years: OR 1.84, 95% CI 1.06 to 3.19; >2 to 4 years: 3.32, 1.88 to 5.85; and >4 years: 5.98, 4.09 to 8.75; and >1 to 2 years: 2.10, 1.22 to 3.62; >2 to 4 years: 2.48, 1.42 to 4.34; and >4 years: 3.34, 2.32 to 4.80) and were higher in patients residing in rural areas (1.68, 1.24 to 2.28; and 1.42, 1.06 to 1.91) and with hyperlipidaemia (1.57, 1.12 to 2.19; and 1.68, 1.21 to 2.33), respectively. In addition, in terms of HbA1c, the odds of poor glycaemic control were higher in patients on diet, physical activity, oral hypoglycaemic drug and insulin as part of their T2DM therapeutic regimen (1.37, 1.02 to 1.86). In terms of HbA1c and FBG, the odds of poor glycaemic control were lower in patients only on diet and physical activity as part of their T2DM therapeutic regimen (0.56, 0.31 to 0.99; and 0.42, 0.24 to 0.74), respectively.

Conclusions: More than half of T2DM patients at the Diabetes Centre in Ningbo, China have poor glycaemic control, and the predictors of glycaemic control were

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identified. The study findings could be taken into consideration in future interventional studies aimed at improving glycaemic control in these patients.

Keywords

Type 2 diabetes; poor glycaemic control; China

Strengths and limitations of this study

- This is the first study to explore glycaemic control in type 2 diabetes patients at the tertiary care Diabetes Centre in Ningbo, China and, as far as we are aware, in the Zhejiang province of China.
- Glycated haemoglobin (which reflects the average blood glucose level over the past three months) and fasting blood glucose (a short-term index) were used to determine glycaemic control, which in turn provided a complete picture.
- Missing data could lead to bias but were generally low in this study. Multiple regression analyses included a sample with missing values for the adjusted variables.
- This retrospective study was conducted using an existing database, which is primarily developed for the clinical purpose and not for research (i.e., issues with routinely collected data were present).
- As this was a cross-sectional study, it was not possible to determine the causal association between different variables and glycaemic control.

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Introduction

China has the world's largest type 2 diabetes (T2DM) epidemic, a complex metabolic disorder which has major health, social and economic consequences. Almost 11% of all adults are currently living with T2DM (around 114 million). This number is expected to increase to around 150 million by 2040 [1]. Its chronic hyperglycaemia is associated with long-term complications (e.g., cardiovascular disease) and even death [2]. In China, T2DM and its complications contribute to almost one million deaths each year. Alarmingly, nearly 40% of these deaths are premature (i.e., in people below the age of 70) [3]. China spends upwards of US $25 billion a year on the management of T2DM and 13% of its medical expenditures are directly caused by T2DM [4]. In spite of this, many T2DM patients have poor glycaemic control (51-68%) [5-9]. Unfortunately, these figures are much higher as compared to many developed countries [10,11].

In China, hospitals are categorised into three: primary care, secondary care and tertiary care. A primary care hospital (community hospital with general practitioners) usually has less than 100 beds, and are mainly responsible for providing preventive care and minimal health services. A secondary care hospital usually has 100 to 500 beds, and are mainly responsible for providing health services and for performing a role in medical education and research. A tertiary care hospital usually has more than 500 beds, and are mainly responsible for providing specialist health services and for performing a bigger role in medical education and research [12]. In China, people (including T2DM patients) can attend any hospital of their choice. In other words, it is not based on any referral system by the community hospital with general practitioners.

Ningbo is one of the most economically developed Chinese cities, located in the northeast Zhejiang province. In 2015, the prevalence of T2DM in people over 40 years of age in the city was around 21% [13]. There are 152 community hospitals with general practitioners, 21 secondary hospitals and 21 tertiary care hospitals in the city. Ningbo First Hospital, with 1600 beds, is a tertiary care hospital. Local patients, as well as those from surrounding areas, visit this hospital [14]. The hospital's Diabetes Centre has a team of qualified and experienced diabetes experts. Till date, no research has been conducted to explore glycaemic control in T2DM

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patients at the Diabetes Centre. The aim of the study was to assess their glycaemic control and to determine factors that independently predict their glycaemic control. Knowledge of factors associated with the poor glycaemic control in these patients would provide valuable information about strategies that healthcare professionals and providers can address to improve their glycaemic control.

Methods

Study design, data source and period

A retrospective cross-sectional study was conducted using an existing computerised medical records database, the Diabetes Information Management System. This database was developed by the Yinal Software Corporation, China for the Diabetes Centre. The study period was from 1st July 2012 to 30 June 2017 (5 years) and the database included 6699 patients.

Study population, inclusion and exclusion criteria

The study included adult (18 years of age or older) patients, diagnosed with T2DM, and registered and received treatment at the Diabetes Centre for at least six consecutive months. In China, T2DM patients are usually given at least six months' time to adjust to their T2DM therapeutic regimen and control their blood glucose levels. Those diagnosed with type 1 diabetes, gestational diabetes, secondary diabetes, unknown type of diabetes or endocrine diseases (such as Cushing syndrome and hyperthyroidism which may increase their blood glucose levels) were excluded from the study. The study inclusion criteria were satisfied by 1387 patients.

Study variables

The following variables (measured after six months of treatment at the Diabetes Centre) were extracted from the database: age (18-39 years, 40-59 years, or ≥60 years), sex (male or female), education (university/college, class 7 to 12, class 1 to 6, or no qualifications), occupation (manual workers (i.e., more physical than mental work), non-manual workers (i.e., more mental than physical work) or never worked/retired), marital status (married or single/divorced/widowed), residence (urban or rural based on the "hukou" system (i.e., residence registration system in

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China)) [15], health insurance, smoking (current status), alcohol drinking (current status), family history of T2DM (any parent or sibling), duration of T2DM (≤1 year, >1 to 2 years, >2 to 4 years, or >4 years), number of visits to the Diabetes Centre for T2DM since registration, T2DM therapeutic regimen (only diet and physical activity; diet and physical activity and oral hypoglycaemic drug (OHD - metformin, acarbose, sulfonylureas, meglitinides and/or thiazo-lidinediones); diet and physical activity and insulin (long-term insulin, intermediate insulin, rapid-acting insulin and/or premix insulin); or diet and physical activity, OHD and insulin)[16], comorbidities (overweight or obese (diagnosis based on body mass index (BMI) ≥24 kg/m^2) [17], hypertension (diagnosis based on blood pressure ≥140/90 mm Hg), and hyperlipidaemia (diagnosis based on serum lipids- total cholesterol ≥4.5 mmol/L or triglycerides ≥1.7 mmol/L)), and blood glucose levels. Following the current guideline for the prevention and management of T2DM in China, poor glycaemic control was defined as glycated haemoglobin (HbA1c) ≥7% or fasting blood glucose (FBG) >7.0 mmol/L [16]. The HbA1c was estimated using the high-performance liquid chromatographic (HPLC) method, using the D-10 Hemoglobin Analyzer (Bio-Rad, USA). The FBG was estimated using the glucose oxidase method. It should be noted that data on dipeptidyl peptidase-4 (DPP-4) inhibitors and glucagon-like peptide 1 (GLP-1) receptor agonists were not available in the database. These drugs are not covered by the existing health insurance system in China and thus, these drugs are not sold in this hospital [18].

Ethics

The study was ethically approved by the Research Ethics Committee at the Ningbo First Hospital, China.

Statistical analyses

The 5-year period prevalence of poor glycaemic control in T2DM patients at the Diabetes Centre was calculated. Simple logistic regression methods were used to investigate the association between glycaemic control and other variables. To identify any independent association, multiple logistic regression models were developed using backward stepwise regression analyses and all the other variables were included. Sensitivity analyses were carried out – only those variables with a

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P value of ≤0.20 in simple logistic regressions were included in multiple logistic regression models. Multiple regression models included a sample with unknown values for these adjusted variables. Odds ratios (ORs) and their respective 95% confidence intervals (CIs) were calculated. The results were considered significant when P values were ≤0.05. All data were analysed using IBM SPSS Statistics Version 20.0 for Windows.

Results

57% of T2DM patients were male and the mean age was 54.1 years. In terms of HbA1c and FBG, the 5-year period prevalence of poor glycaemic control was 50.3% (n=698) and 57.3% (n=791), respectively. Table 1 reports the characteristics of T2DM patients with good and poor glycaemic control. In terms of HbA1c and FBG, glycaemic control was found to be associated with age (p<0.001), education (<0.001), residence (0.012 and 0.042, respectively), duration of T2DM (<0.001) and T2DM therapeutic regimen (<0.001). The additional associated factors were hypertension (0.005) in the case of HbA1c, and alcohol drinking (0.040) and hyperlipidaemia (0.025) in the case of FBG.

Table 2 shows the multiple backward stepwise logistic regression analyses to determine factors independently associated with the poor glycaemic control. In terms of HbA1c and FBG, the odds of poor glycaemic control increased with the duration of T2DM (>1 to 2 years: OR 1.84, 95% CI 1.06 to 3.19; >2 to 4 years: 3.32, 1.88 to 5.85; and >4 years: 5.98, 4.09 to 8.75; and >1 to 2 years: 2.10, 1.22 to 3.62; >2 to 4 years: 2.48, 1.42 to 4.34; and >4 years: 3.34, 2.32 to 4.80) and were higher in patients residing in rural areas (1.68, 1.24 to 2.28; and 1.42, 1.06 to 1.91) and with hyperlipidaemia (1.57, 1.12 to 2.19; and 1.68, 1.21 to 2.33), respectively. In addition, in terms of HbA1c, the odds of poor glycaemic control were higher in patients on diet, physical activity, OHD and insulin as part of their T2DM therapeutic regimen (1.37, 1.02 to 1.86). In terms of HbA1c and FBG, the odds of poor glycaemic control were lower in patients only on diet and physical activity as part of their T2DM therapeutic regimen (0.56, 0.31 to 0.99; and 0.42, 0.24 to 0.74), respectively, and in terms of FBG, the odds were lower in patients with hypertension (0.73, 0.54 to 0.99).

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Table 3 reports the sensitivity analyses - multiple logistic regression models included only those variables with a P value of ≤0.20 in simple logistic regressions. Similar results were found in the sensitivity analyses except for the association between glycaemic control (in terms of FBG) and hypertension. In terms of HbA1c and FBG, the odds of poor glycaemic control increased with the duration of T2DM (>1 to 2 years: 1.83, 1.05 to 3.18; >2 to 4 years: 3.29, 1.88 to 5.77; and >4 years: 5.99, 4.09 to 8.76; and >1 to 2 years: 1.67, 1.08 to 2.60; >2 to 4 years: 2.16, 1.40 to 3.33; and >4 years: 2.51, 1.89 to 3.32) and were higher in patients residing in rural areas (1.68, 1.24 to 2.29; and 1.28, 1.01 to 1.62) and with hyperlipidaemia (1.58, 1.13 to 2.20; and 1.39, 1.05 to 1.83), respectively. In addition, in terms of HbA1c, the odds of poor glycaemic control were higher in patients on diet, physical activity, OHD and insulin as part of their T2DM therapeutic regimen (1.37, 1.02 to 1.85). In terms of HbA1c and FBG, the odds of poor glycaemic control were lower in patients only on diet and physical activity as part of their T2DM therapeutic regimen (0.52, 0.29 to 0.92; and 0.53, 0.35 to 0.80), respectively.

Discussion

In terms of HbA1c and FBG, the 5-year period prevalence of poor glycaemic control in T2DM patients at the tertiary care Diabetes Centre in Ningbo, China was 50.3% and 57.3%, respectively. In other words, less than half of T2DM patients at the Diabetes Centre have adequate glycaemic control. The finding is consistent with a recent nationwide population-based study (51%) and a recent nationwide hospital-based study (52%) [5,6]. However, two other recent nationwide hospital-based studies reported much higher figures (65% and 68%) [7,8]. These hospital-based studies included a range of hospitals with different tier levels. In terms of glycaemic control in T2DM patients, tertiary care hospitals usually perform better as compared to primary or secondary care hospitals [19], and this could be the case in our study. Another reason could be different population characteristics in these studies. For example, the study which reported 68% included only those T2DM patients who were on OHDs alone or in combination with either insulin or GLP-1 receptor agonists, indicating poor glycaemic control with the disease progression. In spite of the availability of diabetes experts at this tertiary care Diabetes Centre and of effective and safe glucose-lowering therapies, the prevalence of poor glycaemic control in

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T2DM patients was high in our study as compared to other studies conducted in various developed countries [10,11]. This indicates that there is still a room for improvement at this Diabetes Centre. It should be noted that Chinese people are more susceptible to T2DM as compared to Whites (e.g., they develop T2DM at a much younger age) [20]. It should also be noted that blood glucose levels of some patients could be relaxed, especially those who are old and frail. However, for the purpose of analysis, the glycaemic control was categorised into poor and good, based on the current guideline for the prevention and management of T2DM in China [16].

In the unadjusted models (HbA1c and FBG), glycaemic control was found to be associated with age, education, residence, duration of T2DM and T2DM therapeutic regimen. The additional associated factors were hypertension in the case of HbA1c, and alcohol drinking and hyperlipidaemia in the case of FBG. Previous studies conducted among T2DM patients in various countries reported similar and other factors associated with glycaemic control (such as age, sex, education, alcohol drinking, duration of T2DM, T2DM therapeutic regimen, overweight or obese, hypertension and hyperlipidaemia) [7,19,21-26].

In terms of HbA1c and FBG, the odds of poor glycaemic control increased with the duration of T2DM and were higher in patients residing in rural areas and with hyperlipidaemia. In addition, in terms of HbA1c, the odds of poor glycaemic control were higher in patients on diet, physical activity, OHD and insulin as part of their T2DM therapeutic regimen. In terms of HbA1c and FBG, the odds of poor glycaemic control were lower in patients only on diet and physical activity as part of their T2DM therapeutic regimen, and in terms of FBG, the odds were lower in patients with hypertension. Similar results were found in the sensitivity analyses except for the association between glycaemic control (in terms of FBG) and hypertension. The association found between poor glycaemic control and longer duration of T2DM is consistent with previous studies [8,21,26-28]. Since T2DM is a progressive disease, the function and mass of β-cells gradually decline with the disease progression [29]. In order to attain glycaemic control, a stepwise approach has been recommended in the national T2DM management guideline [16]. The first and foremost step should be lifestyle modification (i.e., diet and physical activity), followed by addition of OHD(s)

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and/or insulin(s) with the disease progression. An association was found between poor glycaemic control and addition of OHD(s) and insulin(s), and the finding is consistent with previous studies [26,30]. This relationship more likely represents a marker of T2DM chronicity and severity than of medication effects themselves. Another reason could be the failure of clinicians to intensify therapy in a timely manner [31,32]. The uptake and adherence to the T2DM therapeutic regimen among patients could also be different from what was prescribed [25,32]. A recent study showed that only 43% of T2DM patients adhered to their therapeutic regimen (OHD(s) and/or insulin(s)) in China [33]. In the database, data were available on prescription but not on uptake and adherence. Thus, these issues should be explored and be taken into consideration in future studies.

The “hukou” system was used to classify T2DM patients into urban or rural residents. An association was found between poor glycaemic control and rural residents, which indicates health inequalities in T2DM management. This finding is consistent with another recently conducted study in China [5]. In addition to poor socioeconomic conditions of rural residents in China, no or delayed access to healthcare is a major issue in rural areas [34]. Even the health insurance system is different in rural and urban areas [35-37]. There are discrepancies in resource allocation between rural and urban areas. All these could explain the association found between poor glycaemic control and rural residents.

Like T2DM, hyperlipidaemia is a risk factor for cardiovascular disease [38]. The association found between poor glycaemic control and hyperlipidaemia is consistent with previous studies [26,39]. Glycaemic control mainly depends on the degree of residual pancreatic β-cells function and insulin sensitivity [40,41]. It should be noted that in Chinese T2DM patients, the defects in β-cells function are more pronounced than decreased insulin sensitivity [42,43]. Abnormalities in lipid metabolism, characterised by an increase in serum lipids (total cholesterol and triglycerides), may result in lipid spill over to non-adipose tissues, such as pancreatic β-cells. This may lead to cellular dysfunction and lipoapoptosis [44,45]. It is also accepted that high serum triglyceride level is associated with insulin resistance [46]. These mechanisms may partly explain the association found between poor glycaemic control and hyperlipidaemia. Further research needs to be conducted to confirm the role of

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hyperlipidaemia in long-term glycaemic control. In continuation, early initiation of lipid-lowing therapy in T2DM patients may reduce the risk for cardiovascular disease and may have benefits in terms of their long-term glycaemic control.

The study has a number of strengths and weaknesses. This is the first study to explore glycaemic control in T2DM patients at the tertiary care Diabetes Centre in Ningbo, China. In addition, as far as we are aware, this is the first study on this issue in the Zhejiang province of China. HbA1c and FBG were used to determine glycaemic control, which in turn provided a complete picture. HbA1c reflects the average blood glucose level over the past three months. On the other hand, FBG is a short-term index. In terms of generalisability, the study findings could be valid in settings with similar populations and healthcare systems. Missing data could lead to bias but were generally low in this study. Multiple regression analyses included a sample with missing values for the adjusted variables. This retrospective study was conducted using an existing database, which is primarily developed for the clinical purpose and not for research. It is possible that our findings were the result of other factors not present in the database and thus, not adjusted for in the models, such as self-monitoring of blood glucose, uptake and adherence to the T2DM therapeutic regimen, and depression, anxiety and stress levels of patients [25,47,48]. Although the data were available on time, however, the other data quality issues of routinely collected data cannot be ignored, such as accuracy and reliability. Some of the data were self-reported (e.g., duration of T2DM), and recall error could have been a problem. This inaccurate measurement of the variable could mean that individuals were assigned to the wrong category, and then resulted in an incorrect estimation of the association between duration of T2DM and poor glycaemic control. As this was a cross-sectional study, it was not possible to determine the causal association between different variables and glycaemic control. A long-term, longitudinal study should be conducted among these patients to assess the impact of various factors (these as well as other potential factors) on their glycaemic control. Ours was a hospital-based study and a population-based study should be conducted, which might give a different picture. This could be because of different population characteristics, including their healthcare-seeking behavior.

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In conclusion, more than half of T2DM patients at the Diabetes Centre in Ningbo, China have poor glycaemic control, and the predictors of glycaemic control were identified. The study findings could be taken into consideration in future interventional studies aimed at improving glycaemic control in these patients.

Authors' contributions

JL and KC designed the study, analysed the data and wrote the first draft of the manuscript. JL, KC, MX, YC, FH, JC and LL revised it critically for important intellectual content and approved the final version.

Competing interests

The authors declare that they have no competing interests.

Ethics approval and consent to participate

The study used an existing computerised medical records database, the Diabetes Information Management System. The study was ethically approved by the Research Ethics Committee at the Ningbo First Hospital, China.

Data sharing

The dataset will be available upon request unless there are legal or ethical reasons for not doing so.

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Table 1 Characteristics of T2DM patients with good and poor glycaemic control

	Good glycaemic control HbA1c<7% (n=689)	Poor glycaemic control HbA1c≥7% (n=698)	P value	Good glycaemic control FBG≤7.0 mmol/L (n=596)	Poor glycaemic control FBG>7.0 mmol/L (n=791)	P value
Age						
18-39 years	158 (22.9)	81 (11.6)	<0.001	135 (22.7)	104 (13.1)	<0.001
40-59 years	323 (46.9)	300 (43.0)		247 (41.4)	376 (47.5)	
≥60 years	208 (30.2)	317 (45.4)		214 (35.9)	311 (39.3)	
Sex			0.157			0.830
Male	405 (58.8)	384 (55.0)		341 (57.2)	448 (56.6)	
Female	284 (41.2)	314 (45.0)		255 (42.8)	343 (43.4)	
Education			<0.001			<0.001
University/college	166 (24.1)	102 (14.6)		145 (24.3)	123 (15.5)	
Class 7-12	333 (48.3)	310 (44.4)		268 (45.0)	375 (47.4)	
Class 1-6	122 (17.7)	204 (29.2)		117 (19.6)	209 (26.4)	
No qualifications	35 (5.1)	67 (9.6)		45 (7.6)	57 (7.2)	
Unknown	33 (4.8)	15 (2.1)		21 (3.5)	27 (3.4)	
Occupation			0.064			0.231
Manual workers	94 (13.6)	121 (17.3)		87 (14.6)	128 (16.2)	
Non-manual workers	138 (20.0)	141 (20.2)		127 (21.3)	152 (19.2)	
Never worked/Retired	219 (31.8)	317 (45.4)		211 (35.4)	325 (41.1)	
Unknown	238 (34.5)	119 (17.0)		171 (28.7)	186 (23.5)	
Marital status			0.200			0.312
Married	510 (74.0)	562 (80.5)		446 (74.8)	626 (79.1)	
Single/divorced/widowed	55 (8.0)	77 (11.0)		61 (10.2)	71 (9.0)	
Unknown	124 (18.0)	59 (8.5)		89 (14.9)	94 (11.9)	
Residence			0.012			0.042
Urban	449 (65.2)	412 (59.0)		388 (65.1)	473 (59.8)	

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Rural	231 (33.5)	281 (40.3)		202 (33.9)	310 (39.2)	
Unknown	9 (1.3)	5 (0.7)		6 (1.0)	8 (1.0)	
Health insurance			0.583			0.704
Yes	641 (93.0)	644 (92.3)		554 (93.0)	731 (92.4)	
No	48 (7.0)	54 (7.7)		42 (7.0)	60 (7.6)	
Smoking			0.076			0.505
No	567 (82.3)	548 (78.5)		484 (81.2)	631 (79.8)	
Yes	122 (17.7)	150 (21.5)		112 (18.8)	160 (20.2)	
Alcohol drinking			0.182			0.040
No	617 (89.6)	609 (87.2)		539 (90.4)	687 (86.9)	
Yes	72 (10.4)	89 (12.8)		57 (9.6)	104 (13.1)	
Family history of T2DM			0.604			0.095
No	429 (62.3)	444 (63.6)		390 (65.4)	483 (61.1)	
Yes	260 (37.7)	254 (36.4)		206 (34.6)	308 (38.9)	
Duration of T2DM						
≤1 year	207 (30.1)	93 (13.3)	<0.001	173 (29.0)	127 (16.1)	<0.001
>1 to 2 years	77 (11.2)	44 (6.3)		55 (9.2)	66 (8.3)	
>2 to 4 years	72 (10.4)	60 (8.6)		53 (8.9)	79 (10.0)	
>4 years	291 (42.2)	487 (69.8)		275 (46.2)	503 (63.6)	
Unknown	42 (6.1)	14 (2.0)		40 (6.7)	16 (2.0)	
Number of visits to the Diabetes Centre for T2DM since registration	8 (4,13)*	8 (5,13)*	0.335	8 (4,13)*	8 (5,13)*	0.214
T2DM therapeutic regimen			<0.001			<0.001
Diet and physical activity + OHD	335 (48.6)	296 (42.4)		267 (44.8)	364 (46.0)	
Only diet and physical activity	99 (14.4)	45 (6.4)		92 (15.4)	52 (6.6)	
Diet and physical activity + insulin	38 (5.5)	27 (3.9)		31 (5.2)	34 (4.3)	
Diet and physical activity + OHD + insulin	217 (31.5)	330 (47.3)		206 (34.6)	341 (43.1)	

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Overweight or obese			0.357			0.705
	No	311 (45.1)	303 (43.4)		260 (43.6)	354 (44.8)
	Yes	345 (50.1)	372 (53.3)		311 (52.2)	406 (51.3)
	Unknown	33 (4.8)	23 (3.3)		25 (4.2)	31 (3.9)
Hypertension			0.005			0.847
	No	321 (46.6)	273 (39.1)		257 (43.1)	337 (42.6)
	Yes	368 (53.4)	425 (60.9)		339 (56.9)	454 (57.4)
Hyperlipidaemia			0.051			0.025
	No	164 (23.8)	136 (19.5)		146 (24.5)	154 (19.5)
	Yes	525 (76.2)	562 (80.5)		450 (75.5)	637 (80.5)

n(%), P value excludes unknown.
*Median (interquartile range (IQR)).

Table 2 Logistic regression analyses to determine factors independently associated with poor glycaemic control

	OR (95% CI)	P value
HbA1c≥7%		
Residence		<0.001
Urban	1	
Rural	1.68 (1.24 to 2.28)	
Duration of T2DM		<0.001
≤1 year	1	
>1 to 2 years	1.84 (1.06 to 3.19)	
>2 to 4 years	3.32 (1.88 to 5.85)	
>4 years	5.98 (4.09 to 8.75)	
Marital status		0.098
Married	1	
Single/divorced/widowed	1.45 (0.93 to 2.25)	
T2DM therapeutic regimen		0.001
Diet and physical activity + OHD	1	

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Only diet and physical activity	0.56 (0.31 to 0.99)	
Diet and physical activity + insulin	0.55 (0.28 to 1.10)	
Diet and physical activity + OHD + insulin	1.37 (1.02 to 1.86)	
Hyperlipidaemia		0.008
No	1	
Yes	1.57 (1.12 to 2.19)	
FBG>7mmol/L		
Residence		0.019
Urban	1	
Rural	1.42 (1.06 to 1.91)	
Duration of T2DM		<0.001
≤1 year	1	
>1 to 2 years	2.10 (1.22 to 3.62)	
>2 to 4 years	2.48 (1.42 to 4.34)	
>4 years	3.34 (2.32 to 4.80)	
T2DM therapeutic regimen		0.005
Diet and physical activity + OHD	1	
Only diet and physical activity	0.42 (0.24 to 0.74)	
Diet and physical activity + insulin	0.84 (0.43 to 1.64)	
Diet and physical activity + OHD + insulin	1.16 (0.86 to 1.56)	
Hyperlipidaemia		0.002
No	1	
Yes	1.68 (1.21 to 2.33)	
Hypertension		0.045
No	1	
Yes	0.73 (0.54 to 0.99)	

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Table 3 Sensitivity analyses: multiple logistic regression models included those variables with *P*≤0.20 in simple logistic regressions

	OR (95% CI)	P value
HbA1c≥7%		
Residence		<0.001
Urban	1	
Rural	1.68 (1.24 to 2.29)	
Duration of T2DM		<0.001
≤1 year	1	
>1 to 2 years	1.83 (1.05 to 3.18)	
>2 to 4 years	3.29 (1.88 to 5.77)	
>4 years	5.99 (4.09 to 8.76)	
Marital status		0.096
Married	1	
Single/divorced/widowed	1.45 (0.94 to 2.25)	
T2DM therapeutic regimen		<0.001
Diet and physical activity + OHD	1	
Only diet and physical activity	0.52 (0.29 to 0.92)	
Diet and physical activity + insulin	0.54 (0.27 to 1.06)	
Diet and physical activity + OHD + insulin	1.37 (1.02 to 1.85)	
Hyperlipidaemia		0.007
No	1	
Yes	1.58 (1.13 to 2.20)	
FBG>7mmol/L		
Residence		0.044
Urban	1	
Rural	1.28 (1.01 to 1.62)	
Duration of T2DM		<0.001
≤1 year	1	
>1 to 2 years	1.67 (1.08 to 2.60)	
>2 to 4 years	2.16 (1.40 to 3.33)	
>4 years	2.51 (1.89 to 3.32)	

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T2DM therapeutic regimen		0.002
Diet and physical activity + OHD	1	
Only diet and physical activity	0.53 (0.35 to 0.80)	
Diet and physical activity + insulin	0.88 (0.50 to 1.52)	
Diet and physical activity + OHD + insulin	1.21 (0.94 to 1.55)	
Hyperlipidaemia		0.020
No	1	
Yes	1.39 (1.05 to 1.83)	

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4,5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4,5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4,5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5,6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5,6
Bias	9	Describe any efforts to address potential sources of bias	5,6
Study size	10	Explain how the study size was arrived at	4,5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5,6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	n/a
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	n/a
		(*e*) Describe any sensitivity analyses	6
Results			

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Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5,6
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6, table 1
		(b) Indicate number of participants with missing data for each variable of interest	table 1
Outcome data	15*	Report numbers of outcome events or summary measures	6, table 1
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6,7, table 1,2
		(*b*) Report category boundaries when continuous variables were categorized	6,7, table 1,2,3
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7, table 3
Discussion			
Key results	18	Summarise key results with reference to study objectives	7,8,9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7,8,9
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Glycaemic control in type 2 diabetes patients and its predictors: a retrospective database study at a tertiary care Diabetes Centre in Ningbo, China

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Title

Glycaemic control in type 2 diabetes patients and its predictors: a retrospective database study at a tertiary care Diabetes Centre in Ningbo, China

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Abstract

Objectives: The aim of the study was to assess glycaemic control in type 2 diabetes (T2DM) patients at a tertiary care Diabetes Centre in Ningbo, China, and to determine factors that independently predict their glycaemic control.

Design: Retrospective cross-sectional study using an existing database, the Diabetes Information Management System.

Setting: Tertiary care Diabetes Centre in Ningbo, China.

Participants: The study included adult T2DM patients, registered and receiving treatment at the Diabetes Centre for at least six consecutive months. The study inclusion criteria were satisfied by 1387 patients, from 1 July 2012 to 30 June 2017.

Primary outcome measure: Glycaemic control (poor was defined as glycated haemoglobin (HbA1c) >=7% or fasting blood glucose (FBG) >7.0 mmol/L).

Results: In terms of HbA1c and FBG, the 5-year period prevalence of poor glycaemic control was 50.3% and 57.3%, respectively. In terms of HbA1c and FBG, the odds of poor glycaemic control increased with the duration of T2DM (>1 to 2 years: OR 1.84, 95% CI 1.06-3.19; >2 to 4 years: 3.32, 1.88-5.85; and >4 years: 5.98, 4.09-8.75; and >1 to 2 years: 2.10, 1.22-3.62; >2 to 4 years: 2.48, 1.42-4.34; and >4 years: 3.34, 2.32-4.80) and were higher in patients residing in rural areas (1.68, 1.24-2.28; and 1.42, 1.06-1.91), with hyperlipidaemia (1.57, 1.12-2.19; and 1.68, 1.21-2.33), on diet, physical activity and oral hypoglycaemic drug (OHD) as part of their T2DM therapeutic regimen (1.80, 1.01-3.23; and 2.40, 1.36-4.26), and on diet, physical activity, OHD and insulin (2.47, 1.38-4.41; and 2.78, 1.58-4.92), respectively.

Conclusions: More than half of T2DM patients at the Diabetes Centre in Ningbo, China have poor glycaemic control, and the predictors of glycaemic control were identified. The study findings could be taken into consideration in future interventional studies aimed at improving glycaemic control in these patients.

Keywords

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Type 2 diabetes; poor glycaemic control; China

Strengths and limitations of this study

- This is the first study to explore glycaemic control in type 2 diabetes patients at the tertiary care Diabetes Centre in Ningbo, China and, as far as we are aware, in the Zhejiang province of China.
- Glycated haemoglobin (which reflects the average blood glucose level over the past three months) and fasting blood glucose (a short-term index) were used to determine glycaemic control, which in turn provided a complete picture.
- Missing data could lead to bias but were generally low in this study. Multiple regression analyses included a sample with missing values for the adjusted variables.
- This retrospective study was conducted using an existing database, which is primarily developed for the clinical purpose and not for research (i.e., issues with routinely collected data were present).
- As this was a cross-sectional study, it was not possible to determine the causal association between different variables and glycaemic control.

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Introduction

China has the world's largest type 2 diabetes (T2DM) epidemic, a complex metabolic disorder which has major health, social and economic consequences. Almost 11% of all adults are currently living with T2DM (around 114 million). This number is expected to increase to around 150 million by 2040 [1]. Its chronic hyperglycaemia is associated with long-term complications (e.g., cardiovascular disease) and even death [2]. In China, T2DM and its complications contribute to almost one million deaths each year. Alarmingly, nearly 40% of these deaths are premature (i.e., in people below the age of 70) [3]. China spends upwards of US $25 billion a year on the management of T2DM and 13% of its medical expenditures are directly caused by T2DM [4]. In spite of this, many T2DM patients have poor glycaemic control (51-68%) [5-9]. Unfortunately, these figures are much higher as compared to many developed countries [10,11].

In China, hospitals are categorised into three: primary care, secondary care and tertiary care. A primary care hospital (community hospital with general practitioners) usually has less than 100 beds, and are mainly responsible for providing preventive care and minimal health services. A secondary care hospital usually has 100 to 500 beds, and are mainly responsible for providing health services and for performing a role in medical education and research. A tertiary care hospital usually has more than 500 beds, and are mainly responsible for providing specialist health services and for performing a bigger role in medical education and research [12]. In China, people (including T2DM patients) can attend any hospital of their choice. In other words, it is not based on any referral system by the community hospital with general practitioners.

Ningbo is one of the most economically developed Chinese cities, located in the northeast Zhejiang province. In 2015, the prevalence of T2DM in people over 40 years of age in the city was around 21% [13]. There are 152 community hospitals with general practitioners, 21 secondary hospitals and 21 tertiary care hospitals in the city. Ningbo First Hospital, with 1600 beds, is a tertiary care hospital. Local patients, as well as those from surrounding areas, visit this hospital [14]. The hospital's Diabetes Centre has a team of qualified and experienced diabetes experts. Till date, no research has been conducted to explore glycaemic control in T2DM

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patients at the Diabetes Centre. The aim of the study was to assess their glycaemic control and to determine factors that independently predict their glycaemic control. Knowledge of factors associated with the poor glycaemic control in these patients would provide valuable information about strategies that healthcare professionals and providers can address to improve their glycaemic control.

Methods

Study design, data source and period

A retrospective cross-sectional study was conducted using an existing computerised medical records database, the Diabetes Information Management System. This database was developed by the Yinal Software Corporation, China for the Diabetes Centre. The study period was from 1st July 2012 to 30 June 2017 (5 years) and the database included 6699 patients.

Study population, inclusion and exclusion criteria

The study included adult (18 years of age or older) patients, diagnosed with T2DM, and registered and receiving treatment at the Diabetes Centre for at least six consecutive months. In China, T2DM patients are usually given at least six months' time to adjust to their T2DM therapeutic regimen and control their blood glucose levels. Those diagnosed with type 1 diabetes, gestational diabetes, secondary diabetes, unknown type of diabetes or endocrine diseases (such as Cushing syndrome and hyperthyroidism which may increase their blood glucose levels) were excluded from the study. The study inclusion criteria were satisfied by 1387 patients.

Study variables

The following variables (measured after six months of treatment at the Diabetes Centre) were extracted from the database: age (18-39 years, 40-59 years, or ≥60 years); sex; education (university/college, class 7 to 12, class 1 to 6, or no qualifications); occupation: manual workers (i.e., more physical than mental work), non-manual workers (i.e., more mental than physical work) or never worked/retired; marital status (married or single/divorced/widowed); residence: urban or rural based on the "hukou" system (i.e., residence registration system in China)) [15]; health

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insurance; smoking (current status); alcohol drinking (current status); family history of T2DM (any parent or sibling); duration of T2DM (≤1 year, >1 to 2 years, >2 to 4 years, or >4 years); number of visits to the Diabetes Centre for T2DM since registration; T2DM therapeutic regimen: only diet and physical activity, diet and physical activity and oral hypoglycaemic drug (OHD - metformin, acarbose, sulfonylureas, meglitinides and/or thiazo-lidinediones), diet and physical activity and insulin (long-term insulin, intermediate insulin, rapid-acting insulin and/or premix insulin), or diet and physical activity, OHD and insulin [16]; body mass index (BMI): under (<18.5 kg/m^2), normal (18.5-23.9 kg/m^2), overweight (24.0-27.9 kg/m^2) or obese (≥28 kg/m^2) [17]; hypertension (diagnosis based on blood pressure ≥140/90 mm Hg); hyperlipidaemia (diagnosis based on serum lipids - total cholesterol ≥4.5 mmol/L or triglycerides ≥1.7 mmol/L)); and blood glucose levels. Following the current guideline for the prevention and management of T2DM in China, poor glycaemic control was defined as glycated haemoglobin (HbA1c) ≥7% or fasting blood glucose (FBG) >7.0 mmol/L [16]. The HbA1c was estimated using the high-performance liquid chromatographic (HPLC) method, using the D-10 Hemoglobin Analyzer (Bio-Rad, USA). The FBG was estimated using the glucose oxidase method. It should be noted that data on dipeptidyl peptidase-4 (DPP-4) inhibitors and glucagon-like peptide 1 (GLP-1) receptor agonists were not available in the database. These drugs are not covered by the existing health insurance system in China and thus, these drugs are not sold in this hospital [18].

Ethics

The study was ethically approved by the Research Ethics Committee at the Ningbo First Hospital, China.

Statistical analyses

The 5-year period prevalence of poor glycaemic control in T2DM patients at the Diabetes Centre was calculated. Simple logistic regression methods were used to investigate the association between glycaemic control and other variables. To identify any independent association, multiple logistic regression models were developed using backward stepwise regression analyses and all the other variables were included. Sensitivity analyses were carried out – only those variables with a

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P value of ≤0.20 in simple logistic regressions were included in multiple logistic regression models. Multiple regression models included a sample with unknown values for these adjusted variables. Odds ratios (ORs) and their respective 95% confidence intervals (CIs) were calculated. The results were considered significant when P values were ≤0.05. All data were analysed using IBM SPSS Statistics Version 20.0 for Windows.

Results

57% of T2DM patients were male and the mean age was 54.1 years. In terms of HbA1c and FBG, the 5-year period prevalence of poor glycaemic control was 50.3% (n=698) and 57.3% (n=791), respectively. Table 1 reports the characteristics of T2DM patients with good and poor glycaemic control. In terms of HbA1c and FBG, glycaemic control was found to be associated with age, education, residence, duration of T2DM and T2DM therapeutic regimen. The additional associated factors were hypertension in the case of HbA1c, and alcohol drinking and hyperlipidaemia in the case of FBG.

Table 2 shows the multiple backward stepwise logistic regression analyses to determine factors independently associated with the poor glycaemic control. In terms of both HbA1c and FBG, the odds of poor glycaemic control increased with the duration of T2DM and were higher in patients residing in rural areas, with hyperlipidaemia, on diet, physical activity and OHD as part of their T2DM therapeutic regimen, and on diet, physical activity, OHD and insulin. In addition, in terms of FBG, the odds of poor glycaemic control were lower in patients with hypertension.

Table 3 reports the sensitivity analyses - multiple logistic regression models included only those variables with a P value of ≤0.20 in simple logistic regressions. Similar results were found in the sensitivity analyses except for the association between glycaemic control (in terms of FBG) and hypertension.

Discussion

In terms of HbA1c and FBG, the 5-year period prevalence of poor glycaemic control in T2DM patients at the tertiary care Diabetes Centre in Ningbo, China was 50.3%

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and 57.3%, respectively. In other words, less than half of T2DM patients at the Diabetes Centre have adequate glycaemic control. The finding is consistent with a recent nationwide population-based study (51%) and a recent nationwide hospital-based study (52%) [5,6]. However, two other recent nationwide hospital-based studies reported much higher figures (65% and 68%) [7,8]. These hospital-based studies included a range of hospitals with different tier levels. In terms of glycaemic control in T2DM patients, tertiary care hospitals usually perform better as compared to primary or secondary care hospitals [19], and this could be the case in our study. Another reason could be different population characteristics in these studies. For example, the study which reported 68% included only those T2DM patients who were on OHDs alone or in combination with either insulin or GLP-1 receptor agonists, indicating poor glycaemic control with the disease progression. In spite of the availability of diabetes experts at this tertiary care Diabetes Centre, the prevalence of poor glycaemic control in T2DM patients was high in our study as compared to other studies conducted in various developed countries [10,11]. Some of the reasons could be non-usage of new hypoglycaemic drugs (such as DPP-IV inhibitors and GLP-1 receptor agonists) and inadequate self-management of T2DM in this population. This indicates that there is still a room for improvement at this Diabetes Centre. It should be noted that Chinese people are more susceptible to T2DM as compared to Whites (e.g., they develop T2DM at a much younger age) [20]. It should also be noted that blood glucose levels of some patients could be relaxed, especially those who are old and frail. However, for the purpose of analysis, the glycaemic control was categorised into poor and good, based on the current guideline for the prevention and management of T2DM in China [16].

In the unadjusted models (HbA1c and FBG), glycaemic control was found to be associated with age, education, residence, duration of T2DM and T2DM therapeutic regimen. The additional associated factors were hypertension in the case of HbA1c, and alcohol drinking and hyperlipidaemia in the case of FBG. Previous studies conducted among T2DM patients in various countries reported similar and other factors associated with glycaemic control (such as age, sex, education, alcohol drinking, duration of T2DM, T2DM therapeutic regimen, overweight or obese, hypertension and hyperlipidaemia) [7,19,21-26].

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The association found between poor glycaemic control and longer duration of T2DM is consistent with previous studies [8,21,26-28]. Since T2DM is a progressive disease, the function and mass of β-cells gradually decline with the disease progression [29]. In order to attain glycaemic control, a stepwise approach has been recommended in the national T2DM management guideline [16]. The first and foremost step should be lifestyle modification (i.e., diet and physical activity), followed by addition of OHD(s) and/or insulin(s) with the disease progression. An association was found between poor glycaemic control and addition of OHD(s) and insulin(s), and the finding is consistent with previous studies [26,30]. This relationship more likely represents a marker of T2DM chronicity and severity than of medication effects themselves. Another reason could be the failure of clinicians to intensify therapy in a timely manner [31,32]. The uptake and adherence to the T2DM therapeutic regimen among patients could also be different from what was prescribed [25,32]. A recent study showed that only 43% of T2DM patients adhered to their therapeutic regimen (OHD(s) and/or insulin(s)) in China [33]. In the database, data were available on prescription but not on uptake and adherence. Thus, these issues should be explored and be taken into consideration in future studies.

The “hukou” system was used to classify T2DM patients into urban or rural residents. An association was found between poor glycaemic control and rural residents, which indicates health inequalities in T2DM management. This finding is consistent with another recently conducted study in China [5]. In addition to poor socioeconomic conditions of rural residents in China, no or delayed access to healthcare is a major issue in rural areas [34]. Even the health insurance system is different in rural and urban areas [35-37]. There are discrepancies in resource allocation between rural and urban areas. All these could explain the association found between poor glycaemic control and rural residents.

Like T2DM, hyperlipidaemia is a risk factor for cardiovascular disease [38]. The association found between poor glycaemic control and hyperlipidaemia is consistent with previous studies [26,39]. Glycaemic control mainly depends on the degree of residual pancreatic β-cells function and insulin sensitivity [40,41]. It should be noted that in Chinese T2DM patients, the defects in β-cells function are more pronounced

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than decreased insulin sensitivity [42,43]. Abnormalities in lipid metabolism, characterised by an increase in serum lipids (total cholesterol and triglycerides), may result in lipid spill over to non-adipose tissues, such as pancreatic β-cells. This may lead to cellular dysfunction and lipoapoptosis [44,45]. It is also accepted that high serum triglyceride level is associated with insulin resistance [46]. These mechanisms may partly explain the association found between poor glycaemic control and hyperlipidaemia. Further research needs to be conducted to confirm the role of hyperlipidaemia in long-term glycaemic control. In continuation, early initiation of lipid-lowing therapy in T2DM patients may reduce the risk for cardiovascular disease.

The study has a number of strengths and weaknesses. This is the first study to explore glycaemic control in T2DM patients at the tertiary care Diabetes Centre in Ningbo, China. In addition, as far as we are aware, this is the first study on this issue in the Zhejiang province of China. HbA1c and FBG were used to determine glycaemic control, which in turn provided a complete picture. HbA1c reflects the average blood glucose level over the past three months. On the other hand, FBG is a short-term index. In terms of generalisability, the study findings could be valid in settings with similar populations and healthcare systems. Missing data could lead to bias but were generally low in this study. Multiple regression analyses included a sample with missing values for the adjusted variables. This retrospective study was conducted using an existing database, which is primarily developed for the clinical purpose and not for research. It is possible that our findings were the result of other factors not present in the database and thus, not adjusted for in the models, such as self-monitoring of blood glucose, uptake and adherence to the T2DM therapeutic regimen, and depression, anxiety and stress levels of patients [25,47,48]. Although the data were available on time, however, the other data quality issues of routinely collected data cannot be ignored, such as accuracy and reliability. Some of the data were self-reported (e.g., duration of T2DM), and recall error could have been a problem. This inaccurate measurement of the variable could mean that individuals were assigned to the wrong category, and then resulted in an incorrect estimation of the association between duration of T2DM and poor glycaemic control. As this was a cross-sectional study, it was not possible to determine the causal association between different variables and glycaemic control. A long-term, longitudinal study should be conducted among these patients to assess the impact of various factors

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(these as well as other potential factors) on their glycaemic control. Ours was a hospital-based study and a population-based study should be conducted, which might give a different picture. This could be because of different population characteristics, including their healthcare-seeking behavior.

In conclusion, more than half of T2DM patients at the Diabetes Centre in Ningbo, China have poor glycaemic control, and the predictors of glycaemic control were identified. The study findings could be taken into consideration in future interventional studies aimed at improving glycaemic control in these patients.

Authors' contributions

JL and KC designed the study, analysed the data and wrote the first draft of the manuscript. JL, KC, MX, YC, FH, JC and LL revised it critically for important intellectual content and approved the final version.

Competing interests

The authors declare that they have no competing interests.

Ethics approval and consent to participate

The study used an existing computerised medical records database, the Diabetes Information Management System. The study was ethically approved by the Research Ethics Committee at the Ningbo First Hospital, China.

Data sharing

The dataset will be available upon request unless there are legal or ethical reasons for not doing so.

Funding

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Table 1 Characteristics of T2DM patients with good and poor glycaemic control

	Good glycaemic control HbA1c<7% (n=689)	Poor glycaemic control HbA1c≥7% (n=698)	P value	Good glycaemic control FBG≤7.0 mmol/L (n=596)	Poor glycaemic control FBG>7.0 mmol/L (n=791)	P value
Age						
18-39 years	158 (22.9)	81 (11.6)	<0.001	135 (22.7)	104 (13.1)	<0.001
40-59 years	323 (46.9)	300 (43.0)		247 (41.4)	376 (47.5)	
≥60 years	208 (30.2)	317 (45.4)		214 (35.9)	311 (39.3)	
Sex			0.157			0.830
Male	405 (58.8)	384 (55.0)		341 (57.2)	448 (56.6)	
Female	284 (41.2)	314 (45.0)		255 (42.8)	343 (43.4)	
Education			<0.001			<0.001
University/college	166 (24.1)	102 (14.6)		145 (24.3)	123 (15.5)	
Class 7-12	333 (48.3)	310 (44.4)		268 (45.0)	375 (47.4)	
Class 1-6	122 (17.7)	204 (29.2)		117 (19.6)	209 (26.4)	
No qualifications	35 (5.1)	67 (9.6)		45 (7.6)	57 (7.2)	
Unknown	33 (4.8)	15 (2.1)		21 (3.5)	27 (3.4)	
Occupation			0.064			0.231
Manual workers	94 (13.6)	121 (17.3)		87 (14.6)	128 (16.2)	
Non-manual workers	138 (20.0)	141 (20.2)		127 (21.3)	152 (19.2)	
Never worked/Retired	219 (31.8)	317 (45.4)		211 (35.4)	325 (41.1)	
Unknown	238 (34.5)	119 (17.0)		171 (28.7)	186 (23.5)	
Marital status			0.200			0.312
Married	510 (74.0)	562 (80.5)		446 (74.8)	626 (79.1)	
Single/divorced/widowed	55 (8.0)	77 (11.0)		61 (10.2)	71 (9.0)	
Unknown	124 (18.0)	59 (8.5)		89 (14.9)	94 (11.9)	
Residence			0.012			0.042
Urban	449 (65.2)	412 (59.0)		388 (65.1)	473 (59.8)	

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	Rural	231 (33.5)	281 (40.3)		202 (33.9)	310 (39.2)	
	Unknown	9 (1.3)	5 (0.7)		6 (1.0)	8 (1.0)	
Health insurance				0.583			0.704
	Yes	641 (93.0)	644 (92.3)		554 (93.0)	731 (92.4)	
	No	48 (7.0)	54 (7.7)		42 (7.0)	60 (7.6)	
Smoking				0.076			0.505
	No	567 (82.3)	548 (78.5)		484 (81.2)	631 (79.8)	
	Yes	122 (17.7)	150 (21.5)		112 (18.8)	160 (20.2)	
Alcohol drinking				0.182			0.040
	No	617 (89.6)	609 (87.2)		539 (90.4)	687 (86.9)	
	Yes	72 (10.4)	89 (12.8)		57 (9.6)	104 (13.1)	
Family history of T2DM				0.604			0.095
	No	429 (62.3)	444 (63.6)		390 (65.4)	483 (61.1)	
	Yes	260 (37.7)	254 (36.4)		206 (34.6)	308 (38.9)	
Duration of T2DM							
	≤1 year	207 (30.1)	93 (13.3)	<0.001	173 (29.0)	127 (16.1)	<0.001
	>1 to 2 years	77 (11.2)	44 (6.3)		55 (9.2)	66 (8.3)	
	>2 to 4 years	72 (10.4)	60 (8.6)		53 (8.9)	79 (10.0)	
	>4 years	291 (42.2)	487 (69.8)		275 (46.2)	503 (63.6)	
	Unknown	42 (6.1)	14 (2.0)		40 (6.7)	16 (2.0)	
Number of visits to the Diabetes Centre for T2DM since registration		8 (4,13)*	8 (5,13)*	0.335	8 (4,13)*	8 (5,13)*	0.214
T2DM therapeutic regimen				<0.001			<0.001
	Only diet and physical activity	99 (14.4)	45 (6.4)		92 (15.4)	52 (6.6)	
	Diet and physical activity + OHD	335 (48.6)	296 (42.4)		267 (44.8)	364 (46.0)	
	Diet and physical activity + insulin	38 (5.5)	27 (3.9)		31 (5.2)	34 (4.3)	
	Diet and physical activity + OHD + insulin	217 (31.5)	330 (47.3)		206 (34.6)	341 (43.1)	

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BMI			0.817			0.907
	Under	22 (3.2)	23 (3.3)		21 (3.5)	24 (3.0)
	Normal	289 (41.9)	280 (40.1)		239 (40.1)	330 (41.7)
	Overweight	244 (35.4)	265 (38.0)		222 (37.3)	287 (36.3)
	Obese	101 (14.7)	107 (15.3)		89 (14.9)	119 (15.1)
	Unknown	33 (4.8)	23 (3.3)		25 (4.2)	31 (3.9)
Hypertension			0.005			0.847
	No	321 (46.6)	273 (39.1)		257 (43.1)	337 (42.6)
	Yes	368 (53.4)	425 (60.9)		339 (56.9)	454 (57.4)
Hyperlipidaemia			0.051			0.025
	No	164 (23.8)	136 (19.5)		146 (24.5)	154 (19.5)
	Yes	525 (76.2)	562 (80.5)		450 (75.5)	637 (80.5)

n(%), P value excludes unknown.
*Median (interquartile range (IQR)).

Table 2 Logistic regression analyses to determine factors independently associated with poor glycaemic control

		OR (95% CI)	P value
HbA1c≥7%			
Residence			<0.001
	Urban	1	
	Rural	1.68 (1.24 to 2.28)	
Duration of T2DM			<0.001
	≤1 year	1	
	>1 to 2 years	1.84 (1.06 to 3.19)	
	>2 to 4 years	3.32 (1.88 to 5.85)	
	>4 years	5.98 (4.09 to 8.75)	
Marital status			0.098
	Married	1	
	Single/divorced/widowed	1.45 (0.93 to 2.25)	

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T2DM therapeutic regimen		0.001
Only diet and physical activity	1	
Diet and physical activity + OHD	1.80 (1.01 to 3.23)	
Diet and physical activity + insulin	1.00 (0.43 to 2.33)	
Diet and physical activity + OHD + insulin	2.47 (1.38 to 4.41)	
Hyperlipidaemia		0.008
No	1	
Yes	1.57 (1.12 to 2.19)	
FBG>7mmol/L		
Residence		0.019
Urban	1	
Rural	1.42 (1.06 to 1.91)	
Duration of T2DM		<0.001
≤1 year	1	
>1 to 2 years	2.10 (1.22 to 3.62)	
>2 to 4 years	2.48 (1.42 to 4.34)	
>4 years	3.34 (2.32 to 4.80)	
T2DM therapeutic regimen		0.005
Only diet and physical activity	1	
Diet and physical activity + OHD	2.40 (1.36 to 4.26)	
Diet and physical activity + insulin	2.02 (0.88 to 4.62)	
Diet and physical activity + OHD + insulin	2.78 (1.58 to 4.92)	
Hyperlipidaemia		0.002
No	1	
Yes	1.68 (1.21 to 2.33)	
Hypertension		0.045
No	1	
Yes	0.73 (0.54 to 0.99)	

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Table 3 Sensitivity analyses: multiple logistic regression models included those variables with *P*≤0.20 in simple logistic regressions

	OR (95% CI)	P value
HbA1c≥7%		
Residence		<0.001
Urban	1	
Rural	1.68 (1.24 to 2.29)	
Duration of T2DM		<0.001
≤1 year	1	
>1 to 2 years	1.83 (1.05 to 3.18)	
>2 to 4 years	3.29 (1.88 to 5.77)	
>4 years	5.99 (4.09 to 8.76)	
Marital status		0.096
Married	1	
Single/divorced/widowed	1.45 (0.94 to 2.25)	
T2DM therapeutic regimen		<0.001
Only diet and physical activity	1	
Diet and physical activity + OHD	1.93 (1.08 to 3.45)	
Diet and physical activity + insulin	1.03 (0.45 to 2.39)	
Diet and physical activity + OHD + insulin	2.65 (1.49 to 4.72)	
Hyperlipidaemia		0.007
No	1	
Yes	1.58 (1.13 to 2.20)	
FBG>7mmol/L		
Residence		0.044
Urban	1	
Rural	1.28 (1.01 to 1.62)	
Duration of T2DM		<0.001
≤1 year	1	
>1 to 2 years	1.67 (1.08 to 2.60)	

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>2 to 4 years	2.16 (1.40 to 3.33)	
>4 years	2.51 (1.89 to 3.32)	
T2DM therapeutic regimen		0.002
Only diet and physical activity	1	
Diet and physical activity + OHD	1.90 (1.25 to 2.89)	
Diet and physical activity + insulin	1.66 (0.87 to 3.19)	
Diet and physical activity + OHD + insulin	2.30 (1.50 to 3.52)	
Hyperlipidaemia		0.020
No	1	
Yes	1.39 (1.05 to 1.83)	

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4,5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4,5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4,5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5,6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5,6
Bias	9	Describe any efforts to address potential sources of bias	5,6
Study size	10	Explain how the study size was arrived at	4,5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5,6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	n/a
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	n/a
		(*e*) Describe any sensitivity analyses	6
Results			

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Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5,6
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6, table 1
		(b) Indicate number of participants with missing data for each variable of interest	table 1
Outcome data	15*	Report numbers of outcome events or summary measures	6, table 1
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6,7, table 1,2
		(*b*) Report category boundaries when continuous variables were categorized	6,7, table 1,2,3
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7, table 3
Discussion			
Key results	18	Summarise key results with reference to study objectives	7,8,9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7,8,9
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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