Initiating Characteristics of Early-onset Type 2 Diabetes Mellitus in Chinese Patients

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Abstract

Background: Type 2 diabetes mellitus (T2DM) has traditionally been considered to affect mainly the elderly; however, the age at diagnosis has gradually reduced in recent years. Although the incidence of young-onset T2DM is increasing, it is still not fully clear the onset characteristics and risk factors of early-onset T2DM. The aim of this study was to describe the initiating characteristics of early-onset T2DM in Chinese patients and evaluate the risk factors for diabetes mellitus.

Methods: This cross-sectional controlled study was performed using a questionnaire survey method in outpatients of multiple centers in China. A total of 1545 patients with T2DM with an age at onset of <40 years were included, and the control group consisted of subjects aged <40 years with normal blood glucose level.

Results: In patients with young-onset T2DM, the mean age and initial hemoglobin 1Ac at diagnosis were 32.96 ± 5.40 years and $9.59 \pm 2.71\%$, respectively. Most of the patients were obese, followed irregular diet pattern and sedentary lifestyle, had life or work pressure, and had a family history of diabetes mellitus. Compared with subjects with normal blood glucose level, logistic regression analysis showed that waist-to-hip ratio (odds ratio [*OR*] 446.99, 95% confidence interval [*CI*] 42.37–4714.87), family history of diabetes mellitus (*OR* 23.46, *CI* 14.47–38.03), dyslipidemia (*OR* 2.65, *CI* 1.54–4.56), diastolic blood pressure (*OR* 1.02, *CI* 1.00–1.04), and body mass index (*OR* 0.95, *CI* 0.92–0.99) are independent factors for early-onset T2DM.

Conclusions: We observed that abdominal obesity, family history of diabetes mellitus, and medical history of hypertension and dyslipidemia are independent risk factors for early-onset T2DM. It is, therefore, necessary to apply early lifestyle intervention in young people with risk of diabetes mellitus.

Key words: Obesity; Risk Factor; Type 2 Diabetes Mellitus; Young

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a progressive metabolic disease characterized by insulin resistance. The incidence of T2DM has been rising every year with aging population and prevalence of obesity.[1,2] The International Diabetes Federation estimated that patients with diabetes mellitus

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may reach 0.382 billion throughout the world in 2013[3] and may reach 0.552 billion in 2030; among these patients, 60% will be in Asia.[4,5] Although T2DM is traditionally considered as a disease mainly affecting the elderly, the age at diagnosis has gradually reduced in recent years. A rapid increase in the incidence of early-onset T2DM has become a new trend all over the world.[6] From 1990 to 2000, the number of patients with early-onset T2DM increased 9 times in New York.[7] From 2003 to 2006, among all patients with T2DM in England, patients with T2DM aged <30 years increased from 5% to 12%,[8] and patients with T2DM aged <40 years accounted for about 24%.[9] In the late 1980s and early 1990s, the incidence of T2DM in Japanese children increased twice, leading to increased number of children with T2DM than type 1 diabetes mellitus in children with diabetes mellitus.[10] The incidence of obesity has also significantly increased (by 70%) in the younger population (age: 18–29 years), indicating that the younger population has the quickest increase in the incidence of obesity and T2DM.[11] Compared to the patients with type 1 diabetes mellitus after matching for age, the patients with early-onset T2DM still present a higher incidence of microvascular complications although the blood glucose level is well-controlled.[12-14] Hillier and Pedula confirmed that patients with early-onset T2DM present a higher risk of cardiovascular disease compared with patients with normal-onset T2DM (age at diagnosis ≥45 years).[15] Therefore, obesity and T2DM in younger population have become crucial in current medical economies and health.

The occurrence of early-onset T2DM may be associated with complex interaction between genes and environment. Previous studies have found that people with obesity, sedentary lifestyle, family history of diabetes mellitus, and lack of funds are the major reasons for the increase in early-onset T2DM.[16,17] Although the incidence of young-onset T2DM is increasing, it is still not fully clear whether T2DM is more likely to occur in the younger population. There is lack of studies on baseline metabolic characteristics in patients with T2DM aged <40 years and comparison of risk factors in patients aged <40 years with normal blood glucose level. The objective of this study was to describe the baseline characteristics in patients with T2DM with an age at onset of <40 years and evaluate risk factors related to early-onset T2DM.

METHODS

This study was approved by the Human Ethics Committee of General Hospital of Chinese People's Liberation Army, Beijing, China. Written informed consent was obtained from each patient.

This cross-sectional controlled study was performed using a questionnaire survey method in outpatients of 11 Grade A, Class III hospitals in six provinces and cities (Beijing, Chongqing, Shanxi Province, Shandong Province, Liaoning Province, and Gansu Province). The survey was conducted

by endocrine specialists using questionnaires that were filled after face-to-face interaction with patients when the patients were diagnosed with T2DM. The questionnaire included four parts such as evaluation of social and demographic characteristics, health-related living habits, health-related self-evaluation, and health-related problems. Data from 1581 patients with T2DM with age at onset <40 years were collected, and ultimately 1545 patients were included in this study after excluding patients with incomplete information. Inclusion criteria were (1) patients should be aged <40 years when they were diagnosed with T2DM and (2) the type of diabetes should be T2DM. Exclusion criteria were (1) patients aged >40 years when they were diagnosed with T2DM; (2) patients with type 1 diabetes mellitus and other special types of diabetes mellitus; and (3) patients with unclear types of diabetes. The control group consisted of subjects aged <40 years with normal blood glucose level from the epidemiological investigation of diabetes in Beijing community, and 482 subjects were included after matching for age and gender.

This study adopted the diagnostic criteria for T2DM of the World Health Organization issued in 1999.[18] Type 1 diabetes mellitus was defined as patients with a medical history of acute ketoacidosis when they were diagnosed with diabetes mellitus, with a large amount of ketonuria, and required persistent insulin therapy within the 1st year after diagnosed with diabetes mellitus. Hypertension was defined as systolic blood pressure (SBP) >140 mmHg or diastolic blood pressure (DBP) >90 mmHg. Obesity was defined using the body mass index (BMI, kg/m^2) for Chinese adults – normal (18.5–24.0), overweight (24.0–28.0), and obese (≥28.0).

The cutoff age of 40 years was chosen because the International Diabetes Association stratified the patients with diabetes mellitus as 20–39, 40–59, and 60–79 years for estimating the prevalence of diabetes mellitus in the world;[5] this criteria was also adopted in the previous studies on young-onset T2DM.[9]

Statistical analysis

Statistical analyses were performed using SPSS 17.0 software (IBM Corp., USA). Data in-line with normal distribution were analyzed using t-test and Chi-square test while those with nonnormal distribution were analyzed using Mann–Whitney U-test or Kruskal–Wallis test. The results were expressed as mean ± standard deviation (SD), ratio, and range. Multivariate analyses were performed using binary logistic regression, and a $P < 0.05$ was considered statistically significant.

RESULTS

Epidemiological characteristic of diabetes mellitus

Demographic characteristics of patients with early-onset type 2 diabetes mellitus

As shown in Table 1, among the 1545 patients with T2DM with age at onset <40 years, men and women accounted for

Table 1: Demographic characteristics of early-onset diabetes mellitus group

Characteristics	n	Mean ± SD/%
Men/women	1047/497	67.8/32.2
Age at diagnosis of new-onset diabetes (years)	1535	32.96 ± 5.40
Fasting blood glucose level at diagnosis (mmol/L)	1348	12.41 ± 5.11
2-h postprandial glucose level at diagnosis (mmol/L)	886	16.23 ± 5.68
Hb1Ac at first visit	754	9.59 ± 2.71
Hb1Ac within 3 months	754	8.48 ± 2.34
BMI at diagnosis (kg/m^2)	1504	27.39 ± 5.98
WHR at diagnosis	790	0.91 ± 0.10
Occupation		
Cadre	322	21.0
Commercial and service personnel	222	14.5
Professionals	184	12.0
Others	189	12.3
Worker	138	9
Peasant	47	3.1
Smoking at diagnosis		
Often	543	35.2
Sometimes	222	14.4
Never	776	50.4
Easily wake up at night or wake up early		
Yes	547	35.6
No	987	64.3
Sleep quality		
Very good	623	40.5
Normal	777	50.5
Very poor	139	9.0
Income (Yuan)		
<3000	392	27.5
3000–5000	559	39.1
>5000–10,000	288	20.2
>10,000	189	13.2
Whether received hypoglycemic therapy		
Yes	11402	90.7
No	142	9.2
Complications of diabetes mellitus		
Coronary heart disease	63	4.08
Diabetic retinopathy	192	12.42
Diabetic neuropathy	257	16.63
Carotid or lower limb atherosclerosis	150	9.71
Diabetic nephropathy	131	8.48
None	752	48.6
Drinking alcohol at diagnosis		
Often	391	25.4
Sometimes	513	33.3
Never	637	41.3
Gluttony before diagnosis		
Always	776	50.8
Sometimes	375	24.6
Never	376	24.6
Have meals on time or not at diagnosis		
Yes	894	58.2
No	641	41.8
Use of drugs aiding sleep		
Yes	82	5.3
No	1453	94.7
Have afternoon nap or not at diagnosis		
Yes	546	35.7
No	983	64.3
Feel sleepy during the day and lack of energy		
Often	284	18.5
Sometimes	846	57.1
Never	405	26.4
Job intensity at diagnosis		
Not much activity (office, etc.)	847	55.3
Light activity (pile line operation, etc.)	485	31.6
Moderate activity (erecting personnel, porter, etc.)	167	10.9
Heavy labor (steel making, farming, and casting)	34	2.2
Work overtime or not at diagnosis		
Often	476	31.2
Sometimes	455	29.8
Rare	597	39.1
Presence of pollution in the working environment at diagnosis		
Sound pollution	336	22.0
Air pollution	474	31.1
None	716	46.9
Favor the following foods or not at diagnosis		
Sweetmeats (including sweetened beverages)	835	54.0
High-fat diet	716	46.3
Savory snacks	440	28.4
Starchy foods	381	24.6
None	184	11.9
Stress in work or life before diagnosis		
Yes	786	51.0
No	753	49.0
Physical activity during spare time at diagnosis		
Often (every week)	186	12.2
Sometimes (1–2 times/month)	426	28.0
Rare (<1 time/month)	912	59.8
Had subdued mood at diagnosis		
Yes	524	34.2
No	1005	65.8
On night duty at diagnosis		
Often	284	18.7
Sometimes	346	22.8
Rare	886	58.4

Contd...

Hb1Ac: Hemoglobin 1Ac; BMI: Body mass index; WHR: Waist-to-hip ratio.

67.8% (1047) and 32.2% (497), respectively, with a higher ratio of men. Of these, cadre accounted for the largest proportion of 21.0% (322), and patients with monthly income between 3000 and 5000 Yuan accounted for 39.1% (559). The mean age at diagnosis was 32.96 ± 5.40 years, the mean fasting blood glucose level at initial diagnosis was 12.41 ± 5.10 mmol/L, and hemoglobin 1Ac (Hb1Ac) level at first visit was 9.59 ± 2.71%. BMI at diagnosis of T2DM was 27.39 ± 5.98 kg/m^2 and waist-to-hip ratio (WHR) was 0.91 ± 0.10%, indicating that overweight is a significant feature of these patients. The mean duration of T2DM from diagnosis was 5.89 years, and 90.7% of patients received hypoglycemic therapy, mainly oral administration of hypoglycemic drugs (43.4%). The mean Hb1Ac level at 3 months before the survey was 8.48 ± 2.34%, indicating poor blood glucose control. Overall, 38.2% of the patients experienced complications due to diabetes mellitus, among which the highest proportion was due to diabetic neuropathy, accounting for 16.6% (257/1545).

Health-related living habits at diagnosis of type 2 diabetes mellitus

Among all the respondents, 59.9% (924/1545) had a family history of diabetes mellitus. With regard to sleep, 35.6% (547/1534) of patients easily woke up at night or woke up early, 5.3% (82/1535) took drugs that aid in sleep, and 35.7% (546/1529) used to take afternoon nap while 18.5% (284/1535) of patients often felt sleepy during the day and lacked energy. Regular smokers and regular drinkers accounted for 35.2% (543/1541) and 25.4% (391/1541), respectively. Overall, 58.2% (894/1537), 75.4% (1151/1527), and 54.4% (835/1545) of patients had meals on time, had the habit of gluttony, and liked sweetmeats (including sweetened beverages), respectively. Overall, 55.3% (847/1533) and 2.2% (34/1533) of patients were engaged in light physical activity and severe muscular work, respectively, and 12.2% (186/1524) of the patients exercised at least once a week. These results indicated that most of the patients with early-onset diabetes mellitus favored sweetmeats, gluttony, sedentary living, and light physical labor. Overall, 31.2% (476/1528) of patients often worked overtime, 18.7% (284/1516) of patients often were on night duty, 31.1% (474/1526) of patients experienced air pollution in their working environment, 22.0% (336/1526) of patients experienced noise pollution in their working environment, 51.0% (786/1539) of patients felt stressful in life and work, and 34.2% (524/1534) of patients had depression.

Age at onset among the different groups of various factors at diagnosis of type 2 diabetes mellitus

Table 2 presents the age at onset among the different groups of various factors in 1545 patients with T2DM. With regard to income, patients with a monthly income of <3000 Yuan had the earliest age at onset, and the difference was statistically significant ($P = 0.003$). Patients with BMI ≥28 kg/m^2 had the earliest age at onset, with a mean age of 32.35 ± 5.39 years, and the difference compared with patients with BMI <28 kg/m^2 was statistically significant ($P = 0.000$). Patients with a family

Table 2: Age at onset among the different groups of various factors in patients with T2DM

Variables	Group	n	Age at initial diagnosis of T2DM (years)	P
Birth weight (kg)	<2.5	82	32.32 ± 5.30	0.006
	2.5–4	780	32.56 ± 5.78	
	>4	91	32.25 ± 5.90	
	Not sure	542	33.71 ± 5.10	
Medical history of dystocia	Yes	79	31.63 ± 4.60	0.017
	No	1032	32.84 ± 5.61	
	Not sure	380	33.39 ± 5.60	
Stratification of BMI (kg/m^2)	<24	371	32.76 ± 6.37	0.000
	24–27.9	555	33.86 ± 5.03	
	≥28	564	32.35 ± 5.39	
Time before falling asleep	Before 22:00	179	33.49 ± 7.07	0.026
	22:00–24:00	867	33.13 ± 5.56	
	After 24:00	186	31.67 ± 5.34	
Family history of diabetes	Yes	924	32.50 ± 5.56	0.000
	No	618	33.69 ± 5.46	
Income (Yuan)	<3000	392	31.56 ± 6.88	0.003
	3000–5000	559	33.14 ± 5.06	
	>5000–10,000	288	33.83 ± 4.39	
	>10,000	189	33.99 ± 3.98	

Data are expressed as mean ± SD. BMI: Body mass index; T2DM: Type 2 diabetes mellitus; SD: Standard deviation.

history of diabetes mellitus showed an earlier onset than patients without a family history of diabetes mellitus, and the difference was statistically significant ($P = 0.000$). Patients with a birth weight ≥4 kg showed the earliest age at onset of T2DM, with a mean age of 32.25 ± 5.90 years, followed by patients with a birth weight <2.5 kg ($P = 0.006$) while patients with a medical history of dystocia showed an earlier age at onset than those without a medical history of dystocia ($P = 0.017$). These results indicated that a family history of diabetes mellitus, macrosomia at birth, and a medical history of dystocia is associated with an early age at onset of diabetes mellitus. With regard to sleeping time at night, patients who went to bed after 24:00 showed an earlier age at onset of diabetes mellitus, with a mean age of 31.67 ± 5.34 years, and showed statistically significant difference compared with patients who went to bed before 24:00 ($P = 0.026$).

Demographic comparison of subjects with normal blood glucose level and patients with type 2 diabetes mellitus

Since many metabolic characteristics are correlated with age and gender, subjects aged <40 years with normal blood glucose level were selected. A total of 482 subjects were enrolled in the control group after matching for age and gender. The results of single factor analysis are presented in Table 3. It can be observed that the mean BMI in the early-onset T2DM group is significantly higher than that in the control group (27.39 vs. 26.40 kg/m^2, $P < 0.001$). In addition, WHR is also significantly higher than that in the control group (0.91 vs. 0.87, $P < 0.001$). Most of the patients in the early-onset T2DM group had a family history of diabetes mellitus, which was significantly higher than the control group (59.9 vs. 6.2%, $P < 0.001$). Patients with a

medical history of hypertension at diagnosis in the early-onset T2DM group were significantly higher than that in the control group (12.3 vs. 7.7%, $P = 0.002$). Patients with a medical history of dyslipidemia and coronary heart disease at diagnosis in the early-onset T2DM group were significantly higher than those in the control group (20.7 vs. 6.4%, $P < 0.001$ and 1.89 vs. 0.4%, $P = 0.012$, respectively). Among the 1541 patients, 58.7% of the patients with early-onset T2DM had a habit of drinking alcohol before diagnosis, which was significantly elevated compared with the control group ($P < 0.001$). Although patients with early-onset T2DM with smoking before diagnosis accounted for a high proportion (49.6%) when compared to the control group (44.2%), the difference between these two groups was not statistically significant.

As the occurrence of diabetes mellitus is associated with many factors, multivariate logistic regression analysis was performed to evaluate the risk factors independently correlated to the patients with early-onset T2DM. The results are presented in Table 4. Variables in the multivariate logistic regression analysis included BMI, WHR, DBP, SBP, medical history of hypertension, family history of diabetes mellitus, medical history of dyslipidemia, medical history of coronary heart disease, and drinking alcohol. After correcting for all the other variables, it was observed that a unit increase in WHR in patients with early-onset T2DM leads to an increase in the risk of diabetes mellitus by 446.99 times (odds ratio [OR] 446.99, 95% confidence interval [CI] 42.37–4714.87]. The other variables that are independently correlated with early-onset T2DM include family history of diabetes mellitus (OR 23.46, CI 14.47–38.03), dyslipidemia (OR 2.65, CI 1.54–4.56), DBP (OR 1.02, CI 1.00–1.04), and BMI (OR 0.95, CI 0.92–0.99). History of hypertension and coronary heart disease, drinking alcohol, and SBP is not independently correlated with the occurrence of early-onset T2DM.

DISCUSSION

This study described the baseline characteristics of patients with T2DM with an age at diagnosis of <40 years and evaluated the correlated risk factors. The results found that abdominal obesity, family history of diabetes mellitus, and medical of hypertension and dyslipidemia are independent risk factors for early-onset T2DM.

In the 1545 patients with T2DM with age at diagnosis of <40 years, most of the patients were obese, followed a sedentary lifestyle, indulged in gluttony, and felt stressful in life or work when they were diagnosed with diabetes mellitus. Only a small proportion of patients performed physical exercise every week. Patients who were obese and patients with low income had the earliest age at onset. Patients with a medical history of dystocia or macrosomia or family history of diabetes mellitus had earlier age at onset than patients without a medical history of these diseases. The mean age at diagnosis was 32.96 ± 5.40 years, which was similar to the results of a previous study;[19] however, Hb1Ac level was 9.59% which was higher than the previous study.[15]

Table 3: Baseline characteristics in the early-onset T2DM and the control groups

Characteristics	Early-onset T2DM group (n = 1545)	Control group (n = 482)	P
Age (years)	32.96 (5.40)	32.78 (5.63)	
Men	67.8	67.6	
Women	32.2	32.4	
BMI (kg/m²)	27.39 (5.98)	26.40 (4.89)	0.000
WHR	0.91 (0.10)	0.87 (0.08)	0.000
SBP (mmHg)	125.70 (15.61)	123.48 (15.38)	0.010
DBP (mmHg)	80.62 (11.13)	77.38 (14.34)	0.000
Family history of diabetes mellitus	59.9	6.2	0.000
Medical history of hypertension	12.3	7.7	0.002
Medical history of dyslipidemia	20.7	6.4	0.000
Medical history of coronary disease	1.89	0.4	0.012
Smoker	49.6	44.2	0.075
Drinker	58.7	41.5	0.000

Data are presented as % or mean (SD). BMI: Body mass index; DBP: Diastolic blood pressure; SBP: Systolic blood pressure; WHR: Waist-to-hip ratio; T2DM: Type 2 diabetes mellitus.

Table 4: Results of multivariate logistic regression analysis

Variables	OR (95% CI)	P
Medical history of hypertension	0.68 (0.38–1.20)	0.188
Family history of diabetes mellitus	23.46 (14.47–38.03)	0.000
Drinker	1.24 (0.87–1.74)	0.206
Medical history of dyslipidemia	2.65 (1.54–4.56)	0.000
Medical history of coronary disease	2.93 (0.56–15.26)	0.201
SBP	0.99 (0.97–1.01)	0.449
DBP	1.02 (1.00–1.04)	0.044
WHR	446.96 (42.37–4714.87)	0.000
BMI	0.95 (0.92–0.99)	0.016

OR: Odds ratio; CI: Confidence interval; BMI: Body mass index; DBP: Diastolic blood pressure; SBP: Systolic blood pressure; WHR: Waist-to-hip ratio.

In this study, the mean BMI in the early-onset T2DM group is significantly higher than that in the control group. The patients in the early-onset T2DM group with a family history of diabetes mellitus, a medical history of hypertension and a medical history of dyslipidemia and coronary heart disease at diagnosis were significantly higher than those in the control group. Most of the patients with early-onset T2DM had the habits of smoking or drinking alcohol.

As known, obesity tends to increase the risk of T2DM.[20,21] Studies have found that compared with the patients with T2DM with older age at diagnosis, patients with age at diagnosis of <40 years show a higher level of obesity, blood glucose level, blood fat level, and a poor glucose control.[22] Compared with late-onset T2DM, the early-onset

T2DM shows a higher level of WHR and insulin resistance, and abdominal obesity is one of the important causes of young-onset T2DM.[23] In the present study, results of the multivariate logistic regression analysis showed that WHR is significantly independently correlated with the incidence of early-onset T2DM, and it is an independent risk factor for early-onset T2DM. Thus, WHR is a better indicator of body fat distribution and risk of diabetes mellitus.

In the present study, proportion of obese subjects as well as proportions of patients with high cholesterol and hypertension showed significant differences between the two groups. In the patients with early-onset T2DM, 12.3% had a medical history of hypertension and 20.7% had a medical history of dyslipidemia when they were diagnosed with diabetes mellitus, which was significantly higher than those in the control group were. Early-onset T2DM group showed a higher initial Hb1Ac (9.59%) level, indicating that most of the young patients had insulin resistance syndrome when they were diagnosed with diabetes mellitus. In addition, it has been reported that compared with elderly patients with T2DM, these young patients may have 2–3 times more risk of insulin resistance syndrome related to cardiovascular disease, and the incidence of macrovascular complications gradually increase with prolonged duration of diabetes mellitus.[24] It is worth noting that normally patients with clinical early-onset T2DM have a high level of DBP while diabetic patients with hypertension may present a double risk of cardiovascular diseases.[25] In this study, multivariate analysis showed that DBP and dyslipidemia at the time of diagnosis of T2DM are independent risk factors for the occurrence of diabetes mellitus in young patients. Therefore, early intervention against hypertension and hyperlipidemia is also very important for patients with early-onset T2DM.[26]

Genetic predisposition is an important risk factor of T2DM. The studies have revealed that patients with T2DM with a family history of diabetes mellitus may have a higher BMI, body weight, and WHR level than patients without a family history of diabetes mellitus.[27,28] Around 84% of teenaged US patients with T2DM have a family history of diabetes mellitus. These suggested that genetic predisposition tends to increase the risk of T2DM in young patients since family members often have similar living environments.[17,29] Studies have also found that aerobic exercise tends to prevent the occurrence of T2DM and improve abdominal obesity and BMI level.[30] Therefore, enhancing physical exercise is an effective way to reduce the risk of diabetes mellitus in young people who have a risk of developing diabetes mellitus.

To prevent the occurrence of T2DM and delay the progression of diabetes mellitus-related complications, it is very important to identify and screen young people with a risk of T2DM. An early effective lifestyle intervention may prevent weight gain, and delay progression and complications of T2DM in young people with a risk of diabetes mellitus.[31]

The limitation of this study is the relatively small sample size. The control subjects and patients with T2DM were enrolled from different research groups, which may result in geographic bias. A recall questionnaire mode may result in bias and loss of some information. Therefore, a study with a larger sample size is required to confirm the results of this study, and efforts should be directed at reducing the incidence of T2DM in young patients to help reduce the burden on the economy.

Conflicts of interest
There are no conflicts of interest.

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