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Prevalence of diabetes mellitus in outpatients with essential hypertension in China: a cross-sectional study

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ABSTRACT

Objectives: To investigate the prevalence of diabetes mellitus (DM) and new detection of DM using fasting plasma glucose (FPG) and 2 h plasma glucose (2-hPG) in hypertensive outpatients in China.

Design: Multicenter cross-sectional study.

Setting: 46 hospitals in China.

Participants: Study patients were consecutively recruited from June to December 2009 from hypertension outpatient clinics in 46 hospitals in 22 provinces, autonomous regions and municipalities in China. At least 100 consecutive patients were recruited in each hospital. FPG was measured for all patients and 2-hPG was measured in those without a history of DM. A total of 4942 hypertensive outpatients aged ≥20 years were included.

Results: Prevalence of DM was 24.3% (which included both previously and newly diagnosed cases). Among the 1202 patients with DM, 417 (34.7%) were newly detected. In patients aged <45 years, 52.6% of cases of DM were newly detected. Of the 417 cases of newly detected diabetes, 54.9% were identified using FPG tests and the remaining 45.1% by 2-hPG tests; 27.1% of patients with newly detected DM had FPG <6.1 mmol/L and 16.5% had FPG <5.6 mmol/L.

Conclusions: Our findings showed a high prevalence of DM and newly detected DM among Chinese hypertensive outpatients. Application of additional 2-hPG testing to FPG assay can improve the detection rate of DM, especially in elderly patients.

INTRODUCTION

The prevalence of hypertension in China has escalated markedly in the past few decades, possibly because of epidemics of unhealthy lifestyle among the Chinese population. According to a recent national survey, the prevalence of hypertension is 18.8% in the general population, which means there are >200 million people with hypertension in China. Hypertension is often accompanied by diabetes mellitus (DM), and their coexistence can markedly increase the risk of cardiovascular disease (CVD). CVD is at least two times more frequent in hypertensive patients with DM than in those with hypertension alone. Early detection and treatment of DM in hypertensive patients may be particularly important to help reduce the risk of developing cardiovascular complications.

DM can be detected by various methods. Among these, the fasting plasma glucose (FPG) assay has been routinely used in China because of its technical convenience and low cost. The China National Diabetes and Metabolic Disorders Study group reported that 46.6% of newly detected DM patients had normal FPG and were diagnosed by increased 2 h plasma glucose (2-hPG) levels in an oral glucose-tolerance test (OGTT). This demonstrates that use of only routine FPG testing may result in a relatively high rate of false-negative diagnosis. The 2010 Chinese Guidelines for the Management of Diabetes recommends that OGTT (FPG and 2-hPG) should be considered for screening DM in hypertensive patients. However, application of OGTT for screening DM is more time-consuming, laborious and costly compared with an FPG assay. Given the large number (~200 million) of hypertensive patients in China,
nationwide application of additional OGTT to the routine FPG assay for screening DM in all hypertensive patients will carry an economic burden, especially for economically undeveloped regions. Therefore, the FPG assay is still the routine test in most hospitals in China.

Whether adding 2-hPG to the routine FPG test in Chinese hypertensive patients increases the detection rate of DM is still an important research question and lacks evidence from large samples and nationwide studies of hypertension patients. Therefore, the present study investigated the effects of two tests (FPG assay and 2-hPG test) in screening for DM in hypertensive outpatients at 46 hospitals from 22 cities or provinces in China.

METHODS

Study subjects and design

This was a cross-sectional national survey of hypertensive outpatients in 46 hospitals across China. We used multi-stage non-randomised sampling. In the first stage, we recruited 32 tertiary and 14 secondary hospitals from 22 cities or provinces in China. In the second stage, at least 100 consecutive eligible cases, beginning from the same time point, were enrolled from each hospital. The inclusion criteria were (1) patients with definite essential hypertension that had undergone antihypertensive treatment and (2) age \( \geq 20 \) years. Patients were excluded if they had (1) acute CVD; (2) kidney insufficiency that required dialysis; (3) hospitalisation for any reason; (4) any life-threatening comorbidity or (5) participation in any clinical trial of any drug. A total of 5206 hypertensive patients were enrolled from June 2009 to December 2009. After exclusion of 246 patients with incomplete data for FPG or 2-hPG levels, 4942 patients were included in the final analysis.

Data collection

A standard questionnaire was used for collecting information on demographic characteristics, smoking status, medical history of DM, hypertension and any other relevant disease. Anthropometric measurements and blood pressure (BP) were obtained by physical examination. The anthropometric indices of height and weight were measured while the patients were barefoot and in light clothing. Body mass index (BMI) was calculated as weight in kilograms divided by height squared in metres. Waist circumference (WC) was measured at a level midway between the lower rib margin and the iliac crest while participants were semiclothed. BP was measured in the right arm in the sitting position with a regular mercury sphygmomanometer after resting for at least 5 min. The mean of three consecutive BP readings was used.

Laboratory tests

Venous blood samples were collected after overnight fasting for laboratory measurements of serum lipid levels and FPG. After fasting venous blood samples were collected, each participant (except for those with a validated history of DM) received a 75 g OGTT. OGTT was performed by dissolving 75 g of glucose in 300 mL warm water, and then given to patients to drink within 5 min. A venous blood sample was taken 2 h later for measuring PG level. Total cholesterol (TC), triglyceride (TG) and FPG were determined by the enzymatic method. Low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) levels were measured by the homogeneous assay (Daiichi, Tokyo, Japan).

Definitions

Hypertension was defined according to the 2005 China Guidelines on the Management of Hypertension,

including mean systolic BP \( \geq 140 \) mm Hg and/or mean diastolic BP \( \geq 90 \) mm Hg when no antihypertensive agent was used; or systolic and diastolic BP \( < 140 \) and \( < 90 \) mm Hg, respectively, in patients with a history of hypertension and currently receiving antihypertensive treatment. DM was defined as FPG level \( \geq 7.0 \) mmol/L or 2hPG level \( \geq 11.1 \) mmol/L, or with a previous clinical diagnosis.\n
Obesity was defined as BMI \( \geq 28 \) kg/m\(^2\).\n
Central obesity was defined as WC \( \geq 90 \) cm in men and \( \geq 80 \) cm in women.\n
High triglycerides was defined as TG level \( \geq 1.7 \) mmol/L based on the criteria of the NCEP Adult Treatment Panel III report.\n
The educational level was divided into low (primary school), medium-low (junior high school), medium-high (high school) and high (college or university or higher). The medical insurance level was divided into low (reimbursement rate <30%), medium (reimbursement rate 30–79%) and high (reimbursement rate \( \geq 80\%\)).

Sample size estimation

There are a lack of national data for prevalence of DM among hypertensive patients, thus, we calculated sample size based on prevalence of 9.7% for DM for the Chinese general population.\n
The estimated sample size was 3365 if the prevalence of DM were 9.7%, under assumptions of \( \alpha \) (probability of type I error) 0.05 and power 90%. The actual sample size in the study was 4942.

Statistical analysis

Continuous variables are expressed as the mean (SD) in case of normal distribution, and are otherwise expressed as medians (IQRs). Categorical variables are expressed as number (percentage) and were compared by \( \chi^2 \) test. Linear trend was also calculated. A p value <0.05 was considered statistically significant. Data were managed and analysed using SPSS for Windows V.13.0 (SPSS Inc, Chicago, Illinois, USA).

RESULTS

A total of 4942 patients with complete FPG and 2-hPG data entered the final analysis, in which there were 2466...
men (49.9%) and 2476 women (50.1%), with an average age of 58.5±10.4 years. The baseline characteristics of the study patients are summarised in table 1.

The prevalence of DM in this survey was 24.3% in hypertensive outpatients (table 2), and 785 (15.9%) of the hypertensive patients had been previously diagnosed with DM. The prevalence increased with age, from 11.1% in those aged <45 years to 30.7% in those aged ≥65 years, and this trend was significant ($\chi^2=80.518$, p<0.01). Patients with higher TG levels or obesity had a higher prevalence of DM. Of the 1202 patients with DM, 417 (34.7%) were newly diagnosed, and the proportion of newly detected DM was higher in the <45 years age group (52.6%), and in those with a low educational level (42.3%) and low level of medical insurance (43.2%).

Of the 417 hypertensive patients without a history of DM, 417 (10%) were found to have DM. Only 5.5% (229/4137) were newly diagnosed based on FPG assay, 4.5% (188/4157) were DM patients with increased 2-hPG and normal FPG levels (table 3). More patients with diabetes could be identified by OGTT screening from the patients with hypertension aged >65 years without a history of DM compared with younger patients with hypertension, which means that OGTT screening is more efficient for DM among patients with hypertension aged >65 years.

Of the 417 patients with newly diagnosed DM, 101 (24.2%) had isolated increased FPG levels, 188 (45.1%) had isolated increased 2-hPG levels and 128 (30.7%) had increased FPG and 2-hPG levels (figure 1). In the ≥65 years age group, 73 (52.5%) patients had isolated increased 2-hPG levels, which means the rate of DM detection was underestimated if using only FPG in patients with hypertension with undetected DM.

Among the 417 patients with newly diagnosed DM, 115 (27.1%) had isolated increased 2-hPG levels but <6.1 mmol/L FPG levels, 69 (16.5%) had isolated increased 2-hPG levels but <5.6 mmol/L FPG levels. In the ≥65 years age group, the prevalence was 32.4% and 24.5%, respectively (figure 1).

### DISCUSSION

This was a cross-sectional nationally representative survey of 4942 outpatients with hypertension from 46 hospitals in 22 provinces across China. The survey identified a high prevalence of DM among outpatients with hypertension (24.3%). The prevalence of DM was similar to that reported in other studies. In the present study, the prevalence of previously diagnosed DM was 15.9% compared with 8.4% with newly diagnosed DM. The objective of this study was to investigate outpatients with hypertension undergoing treatment; therefore, the detection rate of newly diagnosed DM was lower than that reported in Spanish patients with essential hypertension (11.6%). The detection rate of newly diagnosed DM was higher in patients with low educational level, low level of medical insurance, obesity and high triglycerides. Epidemiological studies have shown that patients with DM often cannot be detected in a timely manner, and the prevalence of undiagnosed DM accounted for roughly half of all cases. Among the 1202 patients with DM in the present study, 34.7% were newly diagnosed. In the younger age subgroup (<45 years), the proportion (52.6%) was high compared with other age groups. These data suggest that the strengthening of DM screening among patients with hypertension is crucial, especially among younger patients or those with poor economic conditions and related metabolic abnormalities (such as obesity or high triglycerides).
In this study, 45.1% of cases of newly diagnosed DM were detected based on 2-hPG levels. This is consistent with the findings reported by other studies. Yang et al found that 46.6% of patients with newly diagnosed DM had isolated increased 2-hPG levels in the general Chinese population. Among middle-aged and elderly hypertensive patients, 54.4% of cases of newly diagnosed DM were detected based on 2-hPG assay. Gu et al found that 57.6% of cases of newly diagnosed DM had isolated increased 2-hPG levels among the new-onset hypertensive patients in the Chinese population. For patients with in Spain, 55.3% of newly diagnosed DM was detected based on 2-hPG assay. In addition, the present study showed that 52.5% of newly diagnosed DM detected by 2-hPG was in the elderly subgroup. Previous studies also found that 2-hPG tests were superior to FPG assays in screening for DM in elderly individuals. The Rancho Bernardo Study reported that among individuals aged $\geq 60$ years, 60% of patients with diabetes were identified by 2-hPG tests.

The present study reported that application of additional 2-hPG to the routine FPG assay can increase detection rate by 4.5%, especially in the elderly group (6.1%). At present, there are $\sim 200$ million patients with hypertension in China. According to published data from a national survey (treatment rate of hypertension was 24.7%), $\sim 49$ million patients underwent antihypertensive treatment. If using FPG assays alone, $\sim 2$ million patients with DM will be expected to be misdiagnosed. If using OGTT assay, 2-hPG test for DM screening will have an economic burden. This burden may be particularly heavy for some economically underdeveloped regions of China. The 2010 Chinese Guidelines for the Management of Hypertension recommend that 2-hPG testing should be considered for hypertensive patients with impaired glucose tolerance (FPG $\geq 6.1$ mmol/L). The present study found that 27.1% of patients had normal FPG ($<6.1$ mmol/L) among the patients with newly diagnosed DM. In 2003, the American Diabetes Association lowered the inferior threshold of FPG to 5.6 mmol/L for defining impaired FPG, assuming that

| Table 2 Detection rates for diabetes in hypertensive outpatient with different characteristics |
|----------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Number | Prevalence | Detection rates of diabetes (%) | Proportion of newly diagnosed | |
| Total   | 4942 | 1202 (24.3) | 785 (15.9) | 417 (8.4) | 34.7 |
| Gender  | | | | | |
| Male    | 2466 | 604 (24.5) | 409 (16.6) | 195 (7.9) | 32.3 |
| Female  | 2476 | 598 (24.2) | 376 (15.2) | 222 (9.0) | 37.1 |
| Age group (years)  | | | | | |
| <45     | 512 | 57 (11.1) | 27 (5.3) | 30 (5.9) | 52.6 |
| 45–54   | 1262 | 275 (21.8) | 157 (12.4) | 118 (9.4) | 42.9 |
| 55–64   | 1655 | 405 (24.5) | 275 (16.6) | 130 (7.9) | 32.1 |
| ≥65     | 1513 | 465 (30.7)**† | 326 (21.5)**† | 139 (9.2) | 29.9 |
| Education levels | | | | | |
| Low     | 791 | 222 (28.1) | 128 (16.2) | 94 (11.9) | 42.3 |
| Medium-low | 1326 | 336 (25.3) | 214 (16.1) | 122 (9.2) | 36.3 |
| Medium-high | 1484 | 363 (24.5) | 234 (15.8) | 129 (8.7) | 35.5 |
| High    | 1341 | 281 (21.0)**† | 209 (15.6) | 72 (5.4)**† | 25.6 |
| Medical insurance | | | | | |
| Low     | 1593 | 359 (22.5) | 204 (12.8) | 155 (9.7) | 43.2 |
| Medium  | 1916 | 494 (25.8) | 331 (17.3) | 163 (8.5) | 33.0 |
| High    | 1433 | 349 (24.4) | 250 (17.4)**† | 99 (6.9)**† | 28.4 |
| Obesity | | | | | |
| No      | 4059 | 941 (23.2) | 630 (15.5) | 311 (7.7) | 33.0 |
| Yes     | 883 | 261 (29.6)** | 155 (17.6) | 106 (12.0) | 40.6 |
| Central obesity | | | | | |
| No      | 1775 | 351 (19.8) | 243 (13.7) | 108 (6.1) | 30.8 |
| Yes     | 3167 | 851 (26.9)** | 542 (17.1) | 309 (9.8) | 36.3 |
| High triglycerides | | | | | |
| No      | 2568 | 570 (22.2) | 387 (15.1) | 183 (7.1) | 32.1 |
| Yes     | 2374 | 632 (26.6)** | 398 (16.8) | 234 (9.9)** | 37.0 |

Data are presented as number (per cent).
Data were compared by $\chi^2$ test.

*p<0.05.
** p<0.01.
†Linear trend p<0.01.
individuals with an FPG level above this cut-off value have a markedly higher risk of developing DM, other metabolic abnormalities and complications. However, as shown in our study, when 5.6 mmol/L was used as a cut-off point, 16.5% of patients with DM had a normal FPG level (<5.6 mmol/L). Adam et al.24 also observed that 25.8% of patients with diabetes would have been missed if 2-hPG tests were only performed for patients with abnormal FPG results. These results demonstrate that application of 2-hPG tests may inevitably lead to misdiagnosis of DM if only undertaken in patients with abnormal FPG results. The present study further indicated that 32.4% (with FPG ≥6.1 mmol/L as the criterion) and 24.5% (with FPG ≥5.6 mmol/L as the criterion) of newly diagnosed patients with diabetes would have been misdiagnosed in the older (≥65 years) patients. This implies that 2-hPG assay should be performed in elderly patients in order to reduce misdiagnosis, regardless of the abnormal fasting glucose levels.

Potential limitations of this investigation merit consideration. First, our study sample consisted entirely of hypertensive outpatients enrolled from 46 hospitals (mainly secondary and tertiary hospitals) in 22 cities or provinces in China. This factor may limit the ability to generalise our findings, which cannot reflect the status of outpatients from primary hospitals and hypertension in the general population. Second, repeat assays should be conducted every other day for the diagnosis of DM, unless the patients have specific clinical symptoms.91 11 7

Our study was a large epidemiological investigation, we were not able to collect data for repeat OGTT measurement, which may underestimate or overestimate the prevalence of DM. The American Diabetes Association25 and other organisations26 recommended using glycated haemoglobin (HbA1c) for DM diagnosis. But in China, the HbA1c test is not widely available, especially in some secondary hospitals.

In conclusion, our findings demonstrate that 25% of hypertensive outpatients had concomitant DM, and approximately 35% of DM cases were newly detected. In newly diagnosed DM, 45.0% of cases were detected based on isolated increased 2-hPG level. Application of additional 2-hPG tests could increase the detection rates of DM by 4.5% among hypertensive outpatients in China, and especially by 6.1% in elderly patients.

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Contributors JL contributed to the conception and design, acquisition of data, analysis and interpretation of data, drafted and wrote the paper. DZ contributed to the conception and design, critical revision of this paper for

| Table 3 Detection rates for diabetes in hypertensive outpatients according to two methods* |
|---------------------------------|-------------|-------------|-------------|
|                                 | Number      | Only FPG    | Only 2-hPG  | FPG +2-hPG |
| Total                           | 4157        | 101 (2.4)   | 188 (4.5)   | 128 (3.1)  |
| Gender                          |             |             |             |             |
| Male                            | 2057        | 50 (2.4)    | 86 (4.2)    | 59 (2.9)   |
| Female                          | 2100        | 51 (2.4)    | 102 (4.9)   | 69 (3.3)   |
| Age group (years)               |             |             |             |             |
| <45                             | 485         | 7 (1.4)     | 13 (2.7)    | 10 (2.1)   |
| 45–54                           | 1105        | 29 (2.6)    | 50 (4.5)    | 39 (3.5)   |
| 55–64                           | 1380        | 32 (2.3)    | 52 (3.8)    | 46 (3.3)   |
| ≥65                             | 1187        | 33 (2.8)    | 73 (6.1)    | 33 (2.8)   |
| Obesity                         |             |             |             |             |
| No                              | 3429        | 76 (2.2)    | 145 (4.2)   | 90 (2.6)   |
| Yes                             | 728         | 25 (3.4)    | 43 (5.9)    | 38 (5.2)   |
| Central obesity                 |             |             |             |             |
| No                              | 1532        | 25 (1.6)    | 52 (3.4)    | 31 (2.0)   |
| Yes                             | 2625        | 76 (2.9)    | 136 (5.2)   | 97 (3.7)   |
| High triglycerides              |             |             |             |             |
| No                              | 2181        | 45 (2.1)    | 84 (3.9)    | 54 (2.5)   |
| Yes                             | 1976        | 56 (2.8)    | 104 (5.3)   | 74 (3.7)   |

Data are presented as number (per cent).

*Patients with a history of diabetes were excluding.

FPG, fasting plasma glucose; 2-hPG, 2 h plasma glucose.

Figure 1 Distribution of the level of fasting plasma glucose and 2 h plasma glucose in newly detected diabetes.
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