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Effect of HbA_{1c} combined FPG on screening diabetes in health check-up

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ABSTRACT

Objective: To appraise the effectiveness of HbA_{1c} and fasting plasma glucose (FPG) on screening diabetes in health check-up. **Methods:** A total of 1 337 individuals (male 850, female 487), aged 27 to 91 years with HbA_{1c} test were included. Participates with HbA_{1c} ≥6.0% or FPG≥6.1 mmol/L underwent oral glucose tolerance test (OGTT). Diabetes mellitus was diagnosed according to the criteria of WHO in 1999, FPG≥7.0 mmol/L and/or OGTT 2 h-postload plasm glucose (2 h-PG) ≥11.1 mmol/L. The sensitivity and specificity of HbA_{1c} thresholds and FPG or combination test on screening of diabetes were analyzed. **Results:** A total of 842 subjects had HbA_{1c} <6.0%, in which 32 had isolated FPG≥6.1 mmol/L, of 495 had HbA_{1c}≥6.0%. Subjects with HbA_{1c}≥6.0% had significant increased disorder indexes than those with HbA_{1c}<6.0%. 527 subjects who had HbA_{1c}≥6.0% or FPG≥6.1 mmol/L underwent OGTT. A total of 234 subjects were newly diagnosed diabetes, including 123 (123/234, 52.56%) with FPG≥7.0 mmol/L, and 111 subjects (111/234, 47.43%) with isolated 2 h-PG≥11.1 mmol/L. Among 234 new diabetes, 91.88% (215 subjects) had HbA_{1c}≥6.3%, and 77.40% (181 subjects) had HbA_{1c}≥6.5%. HbA_{1c}≥6.3% combined FPG ≥7.0 mmol/L increased the positive rate of newly diagnosed diabetes from 91.88% to 96.58%. **Conclusions:** HbA_{1c} is a practical and convenient tool for screening undiagnosed diabetes in routine health check-up of a large population. Combined use of HbA_{1c}≥6.3% and/or FPG≥7.0 mmol/L is efficient for early detection of diabetes.

1. Introduction

Type 2 diabetes (T2DM) and its long-term complications have become a medical and social burden in China[1]. T2DM often shows concealed progress in early stages and remains asymptomatically for near 10 years[2]. It is reported in a Chinese investigation that near half of people with T2DM are undiagnosed[1]. Several clinical trials have demonstrated that early detection of subjects with diabetes and at high risk is essential for prevention and treatment[3-5]. Till now, the most widely used screening test is fasting plasma glucose (FPG) in health check up in most part of China. Almost half diabetes patients with higher 2 h-postload plasm glucose (2 h-PG) are missed by FPG[1,6-8]. OGTT is the gold standard test for the diagnosis of diabetes according to WHO. But it is time-consuming and inconvenient, and not used routinely in clinical, especially in health check up of large population. In 2009, International Expert Committee defined glycated haemoglobin (HbA_{1c}) cut point ≥6.5% as new criteria for the diagnosis of diabetes[8]. A Chinese investigation reported that HbA_{1c} threshold of 6.3%

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was highly specific for detecting undiagnosed diabetes in Chinese adults[9].

This study applied HbA_{1c} thresholds test for screening diabetes in health check up in Hainan Island, China. We assessed the validity of $HbA_{1c} \geqslant 6.3\%$ as a screening threshold for undiagnosed diabetes, and the validity of combined $HbA_{1c} \geqslant 6.3\%$ and/or FPG$\geqslant$7.0 mmol/L.

2. Materials and methods

2.1. Participants

A total of 1 389 individuals (male 880, female 509), aged 27-91 years, mean age (53.80$\pm$12.11) years, who had orally consent of detecting diabetes in health check up were recruited from May 2010 to August 2011 in Health Check-up Center of our hospital in Hainan Island.

2.2. Physical examination

All participants followed the instruction of physical examination. Data of medical history, age, height, weight, blood pressure [systolic blood pressure (SBP) and diastolic blood pressure (DBP)] were recorded. The body mass index (BMI) was calculated as weight (kg) divided by squared height (m^2).

2.3. Exclusion criteria

A total of 32 participants with medical history of diabetes or antihyperglycemia agents, 8 with hepatic or kidney disease, 7 with anemia, 5 with kidney malfunction or suspicious infection were excluded.

2.4. Biochemical index determination

Venous blood samples of all participants were drawn from antecubital vein in the same morning after overnight 10 hours fasting. FPG (glucose oxidase method) and HbA_{1c}, hemoglobin, triglycerides (TG), total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), and low density lipoprotein cholesterol (LDL-C), uric acid (UA) , alanine aminotransaminase (ALT), aspartate aminotransferase (AST), glutamyltranspeptidase (GGT) were measured by an automatic biochemistry analyzer (Siemens Dimension Rxl MAX). Both intra- and inter-assay coefficients of variation (CVs) were in 3%. HbA_{1c} was measured by high-performance liquid chromatography D10 (Bio-Rad, USA) with a normal range of 4.0%-6.0%. The intra- and inter-assay CVs were $\leqslant$2.3% and $\leqslant$3% for HbA_{1c} at values $\leqslant$8.5%, respectively.

2.5. Oral glucose tolerance test (OGTT)

Subjects with HbA_{1c}>5.9% or FPG$\geqslant$6.1 mmol/L underwent a 82.5 g-glucose (containing a molecule of water) OGTT in one week.

2.6. Diagnostic criteria

Diabetes was defined according to the World Health Organization diagnostic Criteria in 1999, FPG$\geqslant$7.0 mmol/L, OGTT 2 h-PG$\geqslant$11.1 mmol/L, or both[10].

2.7. Statistical analysis

All data were analyzed using SPSS, Windows version 16.0. The continuous variables were presented as means$\pm$SD, the skewed variables presented as medians (interquartile range).The categorical variables were presented as number (percentages, %). Clinical characteristics of the values were analyzed by *t* test, or *Chi*-square test, the skewed variables were analyzed by Wilcoxon test. The sensitivity and specificity values of FPG and HbA_{1c} were determined by the receiver operating characteristic curve. *P* values less than 0.05 was considered as statistically significant for a two sided test.

3. Results

The clinical characteristics of the participants were shown in Table 1.

We found participants with HbA_{1c} <6.0% had significant lower SBP, DBP, BMI, FPG, TG, LDL, UA, GGT and age (*P*<0.001), and higher HDL (*P*<0.001), lower TC, ALT (*P*<0.01) than those with $HbA_{1c} \geqslant 6.0\%$. The percentage of male subjects with $HbA_{1c} \geqslant 6.0\%$ was significantly higher than that of female (*P*<0.001) in our study. A total of 842 subjects had HbA_{1c}<6.0%, in which 32 had isolated FPG$\geqslant$6.1 mmol/L, and 495 had $HbA_{1c} \geqslant 6.0\%$. A total of 527 subjects who had $HbA_{1c} \geqslant 6.0\%$ or FPG$\geqslant$6.1 mmol/L underwent a 82.5 g-OGTT test, and 234 subjects were newly diagnosed as diabetes, with the incidence rate as 44.4% (234/527). Among those 234 subjects, 123 (123/234, 52.6%) had FPG$\geqslant$7.0 mmol/L, and 111 (111/234, 47.4%) had isolated 2 h-PG $\geqslant$11.1 mmol/L. A total of 181 subjects had $HbA_{1c} \geqslant 6.5\%$ alone (181/234, 77.35%), and 215 had $HbA_{1c} \geqslant 6.3\%$ alone (215/234, 91.88%) in newly diagnosed diabetes by criterion of WHO 1999. The different influence of criteria for diabetes diagnosis in this cohort was showed in Table 2.

Table 1
Clinical characteristics of participants.

Characteristics	Total(n=1 337)	HbA_{1c}<6.0%(n=842)	HbA_{1c}≥6.0%(n=495)
SBP	124.89±18.47	121.12±17.64	131.28±18.09**
DBP	77.38±11.54	75.85±11.20	79.96±11.65 **
BMI	24.76±3.24	24.19±3.15	25.69±3.16 **
FPG	5.63±1.58	5.09±0.58	6.53±2.20 **
TC	5.38±0.97	5.32±0.89	5.48±1.07 *
TG	1.66±1.34	1.49±1.04	1.94±1.71**
HDL	1.30±0.42	1.33±0.43	1.24±0.39 **
LDL	3.30±0.81	3.23±0.75	3.40±0.89 **
UA	334.05±87.16	306.83±88.56	342.69±83.25**
AST	27.00±10.38	26.91±9.95	27.15±11.07
ALT	33.13±15.76	32.07±14.73	34.93±17.22*
GGT	38.04±37.00	33.43±32.98	45.90±41.88 **
Age	53.80±12.11	49.14±10.41	57.67±12.75 **
Gender (m/f)	850/487	472(55.6%)/370(76.0%)	378(44.4%)/117(24.0%)**

Data are expressed as mean±SD or number (%).**P<0.001, *P<0.01 HbA1c <6.0% vs. HbA1c≥6.0%.

Table 2
Positive and negative rate of different criteria for diabetes diagnosis based on the criterion of WHO 1999.

Different criteria for diagnosis diagnosis	Positive rate	Negative rate
HbA_{1C}≥6.5	77.35% (181/234)	22.65%(53/234)
HbA_{1C}≥6.3*	91.88%(215/234)	8.12%(19/234)
HbA_{1C}≥6.3 or FPG≥7.0	96.58%(226/234)	3.42%(8/234)
HbA_{1C}≥6.5 or FPG≥7.0	85.90%(201/234)	14.10%(33/234)

* Threshold recommended by Bao *et al*. Glycated haemoglobin A_{1C} for diagnosing diabetes in Chinese population: Cross sectional epidemioloy survey.

4. Discussion

This study was based on routine health check up. We used HbA_{1c} test as a screening tool of diabetes in routine heath check up and grouped participates into one with HbA_{1c}<6.0% and other with HbA_{1c} ≥6.0% at high risk of diabetes[8]. The analysis of their clinical features showed that subjects with HbA_{1c}<6.0% had significant decreased blood pressure, BMI, TC, TG, LDH, UA, age, ALT, GGT, and higher HDL. Elevated blood pressure, BMI, TC, TG, LDH, age, and lower HDL were risk factors of diabetes[8,9]. While higher UA, ALT, GGT in subjects with HbA_{1c}≥6.0% are possibly related to increased HbA_{1c}, but the reason is unknown. Previous studies[11,12] reported HbA_{1c} was a significant risk factor for T2DM in people with FPG≥110 mg/dL or FPG≤100 mg/dL. Participants with HbA_{1c}≥6.0% had more diabetes-related metabolic disorders[8]. In our investigation, the incidence of undiagnosed diabetes was 52.6% in routine heath check-up by use of FPG only. We detected undiagnosed diabetes in subjects with HbA_{1}≥6.0% or FPG≥6.1 mmol/L by OGTT test, and 47.4% diabetes patients were diagnosed with isolated 2 h-PG≥11.1 mmol/L in OGTT test. This indicated that nearly 50% of undiagnosed diabetes will be missed if only FPG test is used in routine heath check up. Several studies have shown that HbA_{1c} is similar or superior to FPG in screening or diagnosis of diabetes compared with the oral glucose tolerance test[9,13,14]. Bao *et al*[9] reported that an HbA_{1c} threshold of 6.3% was highly specific for detecting undiagnosed diabetes in Chinese adults. Our study showed HbA_{1c}≥6.3%[9] alone was efficient than FPG≥7.0 mmol/L and HbA_{1c}≥6.5% in detecting undiagnosed diabetes, and HbA_{1c} was a practical and convenient test for screening diabetes than FPG did in routine heath check up. HbA_{1c}≥6.3% combined FPG≥7.0 mmol/L is optimal for detecting early diabetes without clinical symptoms or newly onset diabetes with a normal HbA_{1c} in routine heath check up. Our result is consistent with previous reports[9, 15-17]. HbA_{1c}≥6.3% combined FPG≥7.0 mmol/L is effective on screening of early diabetes in routine health check-up, and can benefit future cost-effectiveness of diabetic treatment.

Conflict of interest statement

We declare that we have no conflict of interest.

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