Research Square

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Performance of diabetes screening tests: an evaluation study of Iranian diabetes screening program

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Abstract

Background Diabetes is a common non-communicable disease which is responsible for about 9% of all deaths and 25% reduction in life expectancy and nearly half of the diabetic patients are not aware of their disease. In this regard, diabetes screening to identify un-known diabetic patients is of great importance.The aims of this study were first to evaluate the performance of two commonly used diabetes screening tests, which are currently used by the Iranian national screening program for diabetes (NSPD). Methods Validity of diabetes screening tests among 1057 participants older than 30 years was measured. Screening tests included Capillary fasting blood glucose (CBG) with glucometer and glycated haemoglobin (HbA1c). In addition, the validity of the tests was measured based on venous fasting plasma glucose (VPG) as golden standard test. Results According to the results, the sensitivity of CBG and HbA1c tests were 69.01% and 84.5% and the specificity of the tests were 95.7% and 79.3% respectively. Positive and negative predictive values were 53.84% and 97.72% for CBG and 22.72% and 98.61% for HbA1c respectively. New cut points for CBG (116.5 mg/dl) and HbA1c (7.15%) are obtained. Using these values as new cut points, sensitivity and specificity of CBG raised to 80.30% and decreased 89.10% respectively. Similarly, using 7.15% as cut point of HbA1c test, sensitivity and specificity changed to 77.50% and 94.20% respectively. Conclusions Compared to several other countries, the performance of NSPD is relatively higher. ROC analysis suggested new cut points for significantly better performance of NSPD.

Background

Several factors including socio-economic development and significant progresses in health and medical cares reduced mortality at younger age and raised life expectancy. On the other hand, these changes along with the new sedentary lifestyles caused sharp rises in several chronic diseases[1]. Diabetes mellitus (DM) is a common metabolic disease[2]. which about one half of the patients are unaware of their condition[3]. This is despite the fact that about 9% of total deaths and 25% reduction in life expectancy is associated with diabetes[4, 5]. It is notable that cardiovascular diseases are among the most common diabetes related causes of deaths and about 43% of deaths due to diabetes occurred among individuals under 70 years of age. This means that DM kills patients when they are still socio-economically active[1]. It is also estimated that, about 12% of the global health budget is being spend on diabetes and its related conditions[6]. Figures suggest that DM is alarmingly on the rise and is becoming a serious problem threatening global health and economy[7]. For example, reports suggested that the global prevalence of DM among individuals over 18 years of age was about 9% in 2014[8]. However, the international diabetes federation (IDF) has estimated that the prevalence of diabetes is yet to be raised to 9.9% in 2030[9]. With regard to the geographical distribution of diabetes, it is estimated that 20% of the world's diabetic patients are living in South East Asia and it is predicted that in the near future, the Asian population is more seriously affected by DM compared to the population of the other parts of the world[10, 11].

As the epidemic of DM is expanding, the costs of the disease, including cost of diagnosis and treatment of its complications are also increasing sharply. It is because, on average, the cost of medical complications among DM patients is about 3.2 times higher than the costs of treating non-diabetics patients for the corresponding conditions[12]. addition to the severity and a wide range of health conditions, the economic damages caused by DM in various countries are remarkable. This is why the socio-economic burden of DM in low or middle income countries affects their development[13]. In line with the rest of the world and the Middle East, in Iran over the past three decades the prevalence of diabetes has become doubled. Based on an estimate in 2013, the prevalence of DM in Iran was 13.8% [11]. and the incidence was about 1.6 per 100 person-year among individuals older than 20 years of age[14]. It is also estimated that in 2014, 38079 deaths occurred among Iranian population due cardiovascular complications caused by DM[15]. Reports suggested that in Iran a huge amount of money is being spent on the treatment of diabetes and its related health problems. In this regard, early DM detection is essential in the prevention and management of the sever and irreversible complications[16].

The Iranian National Screening Program for Diabetes (NSPD):

Due to the high cost of treatment, life threatening complications and relatively high prevalence of DM, applying effective screening programs to identify people with undiagnosed diabetes is utmost important to the Iranian ministry of health. As a result, the Iranian ministry of health has recently implemented a routine diabetes screening program (DSP) into the primary health care services. The program is to detect un-diagnosed diabetes among rural population older than 30 years of age. From 2016, DPS is being conducted by health centers and health houses to diagnose diabetes among rural residences aged over 30 years with at least one of the following risk factors: BMI ≥30, whist circumference ≥100 for men (or ≥86 cm for women), family history of DM and history of gestational diabetes (among women). In that regard, all rural residences over 30 years of age are to be annually screened by the public health service providers as presented in the flowchart. Accordingly, the individuals are invited to the health houses to be visited by health nurses and voluntary health workers. The eligible individuals are asked to fast for at least 8 hours prior to the morning that they have an appointment to visit the health house that they are registered with. In the health house, the person's capillary fasting blood glucose (CBG) is measured with a glucometer. If the result of the CBG test was positive (FBS≥126mg/dl), the individuals are referred to a health center to take a venus plasma glucose (VPG) test (as diagnostic test). A VPG test result less than 126mg/dl is considered normal.This study is conducted to evaluate the performance of Iranian DSP and its selected cut points for the selected screening tests. In particular, the aims of this study were to evaluate sensitivity, specificity and predictive values of CBG and HbA1c test, using fasting plasma glucose (VPG) as the gold standard[17].

Methods

The settings:

This study was conducted among rural residences of Gerash County, which is located in the southern part of Fars province, Iran. The county consists of 25 villages with about 14456 rural residents. In the study area, 7 health houses and 2 rural health centers deliver primary health services to the defined population.

Figure 1 presents the flowchart of the Iranian diabetes screening program procedures and the additional steps taken by the current study (rectangles).

Data collection:The present study recruited 1057 participants living in rural areas of Gerash County. All participants were over 30 years of age and had at least one of the screening criteria defined by DSP. The participants were invited to the health houses and were interviewed by experienced and trained health nurses. The required data was collected via an interview-administered questionnaire, which was specially designed and evaluated for DSP by the ministry of health. The questionnaire includes demographic data and history of DM in the participants or their relatives. CBG was measured with a glucometer (Easy Gloco). The blood sample was taken from the toe of the middle finger of the left hand. After CBG test was conducted, irrespective of the result, the participant was referred to a public laboratory based in a nearby health center for testing VPG. The test was performed by a classic Alpha auto analyzer. In addition, at the same time, all participants gave a HbA1C test which was conducted by nicocard reader device using glucose oxidase method. Like many other studies, which measured sensitivity and specificity of diabetes screening tests, this study followed WHO's recommendations suggesting VPG as the gold standard for evaluation of capillary blood glucose and HbA1C tests[17].

Inclusion criteria: All participants were included providing they were over 30 years of age, had either of the above mentioned risk factors defined by DSP and reported no history of DM. Women were also to be not pregnant or breast feeding (among female participants). As some of the participants were illiterate, verbal informed consent were obtained from all participants before the interview. The study protocol is approved by Shiraz University of Medical Sciences research committee (approval number=94-01-04-10908).

Sampling and statistical methods:Sample size (n=1010) was calculated based on the global prevalence of diabetes and using the formula provided by Karim Allah Hajian[18]. In practice however, all individuals over 30 years of age with one or more of the previously mentioned risk factors were recruited (n=1057).

The collected data was analyzed in SPSS 19 using frequency, cross-tabs and chi-square test. In addition, ROC curve analysis was applied to define best cut points for CBS and HbA1c in screening DM among the study population.

Results

Totally, 1057 individuals, who were over 30 and were living in rural areas of Gerash county participated in this study. The sex ratio (female/male) of the sample was 2 ($P<0.05$) and almost similar age distributions in the two genders were observed ($P>0.05$). The frequency distribution of the participants based on their tests results is presented in Table1 (in the Supplementary Files).

Accordingly, the rate of positive results of FBS test (setting ≥126mg/dl as cut point) based on CBG and VPG were 8.60% and 6.70% respectively, which were significantly different ($P<0.001$). However, according to the results of HbA1c, the prevalence of DM was 25% if the cut point was set at 6.50% (as recommended by DSP).

The validity of CBG and HbA1c tests:

Using VPG (≥126mg/dl) test results as the gold standard for diagnosis of DM, sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPV) for CBG and HbA1c were calculated and presented in table 2 (in the Supplementary Files).

As presented in Figure 2, receiver operating characteristic analysis revealed new cut-points for screening of diabetes based on CBG and HbA1c. Accordingly, at the cut-point recommended by DSP, the area under curve (AUC) were 0.886% and 0.928% for CBG and HbA1c respectively. However, the suggested two new cut points obtained by ROC

Analysis for the screening tests seems to cause better performance among the study population (Table 3 in the Supplementary Files).

Accordingly, the optimum cut points for CBG (116.50 mg/dl) and HbA1c (7.15%) are considerably lower than what were recommended by NSPD. Using these values as new cut points, sensitivity and specificity of CBG raised from 69.01% to 80.30% and decreased from 95.74% to 89.10% respectively. Similarly, using 7.15% as cut point for HbA1c test, sensitivity and specificity changed form 84.50% to 77.50% and from 79.31% to 94.20% respectively (Table 4 in the Supplementary Files).

Discussion

Early detection of DM is essential in the prevention and management of the related life threatening complications. An efficient screening program for early diagnosis of DM is essential to prevent the DM complications. Although, several tests are introduced to identify diabetic patients, serious debates are still going over the validity and reliability of the results[19–21]. The inconsistency in the validity of test results is due to several reasons. For example, in a study conducted in India, a bimodal distribution of fasting blood glucose was observed. Obviously, this phenomenon could not be detected by FBS with a cut-point between 140-120 mg/dl[22]. In addition, the American Diabetes Association (ADA) has suggested that glucose level of blood changes over time depending on several factors including the disease progress[20]. In fact, despite the presence of DM, the metabolic changes may be not big enough to detectably raise blood sugar[23]. CBG is a test which is more frequently used due to its low cost and ease of use in DM screening programs. However, in several studies the validity of the results of CBG test has been questioned[21, 24]. Technical issues as well as environmental, psychological and medical conditions are listed as factors which affect the validity of the results of a test run by a glucometer[21]. In this study, sensitivity, specificity and positive and negative predictive values of the two tests suggested that the results (selecting VBG as gold standard test) are almost similar for CBG (69.01%, 95.74%, 53.84% and 97.72% reported by the current study respectively) but significantly lower for HbA1c (84.50%, 79.31%, 22.72% and 98.61% reported by the current study respectively) when compared to what obtained by Benja Muktabhant et al[25] who reported sensitivity, specificity and positive and negative predictive values for CBG (81.4%, 97.8%, 71.4% and 98.7% respectively) and HbA1c (39.70%, 96.70%, 56.80% and 93.70% respectively). Another study by Balaji Bhavadharini et al. on pregnant women provided different conclusions[25]. In that study, the sensitivity, specificity, positive and negative predictive values for CBG test were 70.80%, 63.00%, 18.00% and 95.00% respectively, which are in accordance with sensitivity and negative predictive value of the current study. It is to be noted that sensitivity and

specificity are independent from the prevalence of disease in the community, but positive predictive value increases when prevalence increases and negative predictive value increases when the prevalence of the disease decreases. As a result, the predictive values of a test in a community are not comparable to those form communities with different prevalence rates.

As it was recommended by American and European Diabetes Associations, HbA1c is commonly used as a test for screening or clinical diagnosis of diabetes[7, 26]. In Iran, in line with WHO, HbA1c test is used for diagnosis of diabetes with a cut-point as >6.50% . However, some studies indicated significant contradictions in the results of the test. For example, according to a report from the International Expert Committee for Diagnosis and Classification of Diabetes, HbA1c test results may be affected by conditions such as hemoglobinopathies, pregnancy, uremia, blood transfusion, and hemolytic anemia and also by the laboratory methods used. However, based on the results of a study by D. M. Nathan et al., due to the strong correlation between HbA1c test result and diabetic complications, the test is highly recommended as a DM care assessment measure[27]. However, use of HbA1c is more costly and requires sophisticated laboratory facilities which is hardly affordable by many developing countries. In addition, in a study, results of HbA1c compared to two-hour blood glucose levels and fasting blood glucose was less accurate in identifying people who were at risk of diabetes[28]. The researchers used HbA1c as a screening test and they announced sensitivity, specificity, and positive and negative predictive values for HbA1c as 84.50%, 79.31%, 22.72% and 98.61% respectively. However, Farahani et al compared HbA1c results with VPG as the gold standard test (with a cut-point at 110 dl/ mg) and obtained 100% sensitivity, 12.50% specificity, 82.10% positive and 66.70% negative predictive values[29].

The current evaluation study on 1057 participants, who had no history of diabetes, measured the validity indexes of DSP for Iranian population. Based on the results, when CBG (with a cut point at 126 mg/dl) as screening test and VPG (with a cut point at 126 mg/dl) as a gold standard test were applied, sensitivity, specificity and positive predictive value of the tests appeared to be convincing when compared to the results from other countries. Based on the results form ROC curve analysis, the optimal cut-point was 116.50 mg/dl with sensitivity and specificity of 80.30% and 89.10%. When the performance of the NSPD is compared with the results of studies from European (AUC=0.844) and Arab (AUC=0.847) countries, the performance of HbA1c and CBG for the Iranian DSP is significantly better (AUC=0.925 for HbA1c and AUC=0.902 for CBG)[17]. However, using CBG test, 30.99% of people with DM were not detected while 4.26% of the healthy subjects undergone unnecessary clinical and laboratory procedures (false positive). When HbA1c was used as screening test, 15.50% of diabetes patients were not detected while 20.69% of the healthy subjects undergone unnecessary clinical and laboratory procedures (false positive). In that regard, best cut point for HbA1c was at 7.15%, with sensitivity and specificity of 77.50% and 94.20% respectively.

Compared to several other countries, the performance of the Iranian SDP is reasonably higher. This may be due to the differences in the defined criteria for selecting populations for screening (high risk groups) in different countries. In this study, ROC analysis suggested new cut points for even better performance of DSP in Iran. Further studies are needed to understand different aspects of the suggested cut points and the risk factors selected by DSP to define the high risk population to achieve a better performance of the program.

Implications for Policy & Practice

This study evaluated the performance of diabetes screening of Iran using a population based sampling method

All procedures, instruments and personnel used in this study were similar to what is used by the national screening program making the results more representative and applicable

New cut points are provided to increase the performance of the screening tests

Limitations:

The participants in this study were all rural residences with different lifestyles of urban population. As a result, our findings should be validated in urban populations.

Declarations

Competing interest

No conflict of interest is declared.

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Tables

Due to technical limitations, tables are only available as a download in the supplemental files section.

Figures

Figure 1: Flowchart of the Iranian diabetes screening program and the current study (rectangles represent additional steps taken by current study)

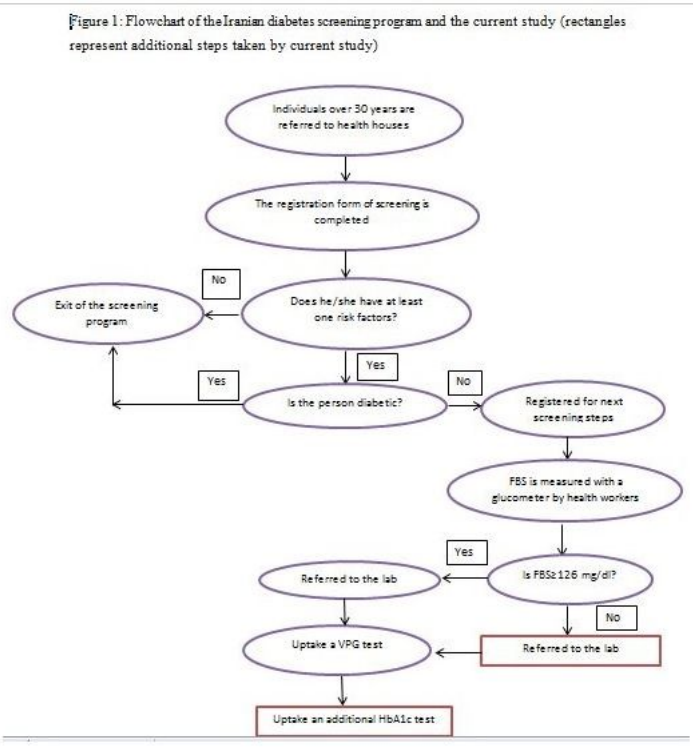

Figure 1

Flowchart of the Iranian diabetes screening program and the current study (rectangles represent additional steps taken by current study)

Figure 2: ROC curve with screening variables and VPG as

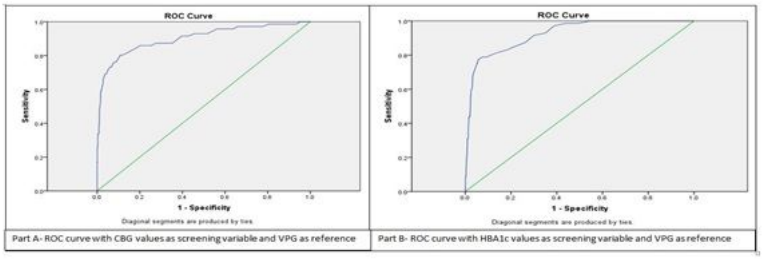

Figure 2

ROC curve with screening variables and VPG as

Supplementary Files

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- Table3.jpg
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- Table1.jpg
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