DIABETES RESEARCH AND CLINICAL PRACTICE XXX (2015) XXX–XXX

Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

A pragmatic and scalable strategy using mobile technology to promote sustained lifestyle changes to prevent type 2 diabetes in India—Outcome of screening

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ARTICLE INFO

Article history:
Received 3 January 2015
Received in revised form
25 June 2015
Accepted 3 September 2015
Available online xxx

Keywords:
Screening
HbA1c
Primary prevention
Short messaging service

ABSTRACT

Aims: We describe a two-step screening approach using non-invasive risk assessment and glycated hemoglobin (HbA1c) to identify participants for a diabetes prevention trial.
Methods: A total of 6030 non-diabetic persons of 35–55 years were screened using risk assessment for diabetes. Those with three or more risk factors were screened using point of care HbA1c test. For this study, participants in HbA1c categories of 6.0% (42.1 mmol/mol)–6.4% (46.4 mmol/mol) were selected and their characteristics were analyzed.
Results: Among 6030 persons, 2835 (47%) had three or more risk factors for diabetes. Among those screened with HbA1c, 43.2% (1225) had HbA1c values of <6.0% (42.1 mmol/mol), 46.8% (1327) had HbA1c values between 6.0% (42.1 mmol/mol) and ≤6.4% (46.4 mmol/mol) and 10% (283) had undiagnosed diabetes with ≥6.5% (47.5 mmol/mol). Positive family history was present in 53.2%, 81.7% were obese and 14.8% were overweight.
Conclusions: Opportunistic screening using a two-step approach: diabetes risk profile and HbA1c measurement detected a large percentage of individuals with prediabetes. Prediabetic persons recruited to the trial had higher percentage of obesity and presence of positive family history than those who had lower HbA1c values. Outcomes from this trial will enable comparisons with the previous prevention studies that used blood glucose levels as the screening criteria.

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Abbreviations: BMI, body mass index; FBG, fasting blood glucose; GTT, glucose tolerance test; HbA1c, glycated hemoglobin; IDF, International Diabetes Federation; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; LMIC, low and middle income countries; 2hPG, 2-hour post glucose; SMS, short messaging service; T2DM, type 2 diabetes; TTM, transtheoritical model.

http://dx.doi.org/10.1016/j.diabres.2015.09.004
0168-8227/

1. Introduction

The rising prevalence of type 2 diabetes (T2DM) is a major healthcare challenge globally. The burden is the highest in developing countries where more than 80% of the people with diabetes live [1]. According to the recent International Diabetes Federation (IDF) estimates, there were more than 65 million people with diabetes in India in the year 2013. With the current rising trend, the prevalence is bound to increase further to a 100 million in the next 20 years' time [1].

Primary prevention of diabetes is of paramount importance in reducing the burden of the disease. There is unequivocal evidence showing that T2DM is a preventable disorder in populations of varied ethnicity [2,3]. Studies in India have shown the efficacy of lifestyle modification (LSM) in preventing the onset of T2DM in persons with persistent impaired glucose tolerance (IGT) [4–6]. A recent study by our team has shown that text messaging via short messaging service (SMS) using mobile phones can be effectively used for sustained motivation of the participants to follow healthy lifestyle changes to prevent diabetes [6]. This is likely to be a cost-effective method to implement primary prevention strategies in large-scale community projects.

In continuation of our efforts to identify effective methods of reaching the public at large for primary prevention of T2DM, we have taken up another collaborative study with researchers in the UK with the objective of developing 'a pragmatic and scalable strategy using mobile technology to promote sustained lifestyle changes to prevent type 2 diabetes in India and the UK' (Clinical Trials.gov No NCT01570946, Clinical Trials Registry of India No. CTRI/2014/07/004799, ICMR Ref. No. 58/1/6/MRC-ICMR/2009/NCD-II).

In this communication we describe the methodology used in India for selection of the study participants in this prospective program and the outcomes of the screening. The benefits of early screening and intervention in diabetes have been demonstrated in earlier studies [2]. However, an effective strategy for opportunistic screening of a large-scale population for dysglycemia remains elusive. Most of the primary prevention programs in diabetes were in persons with IGT and or Impaired Fasting Glucose (IFG), categorized based on the plasma glucose criteria [2,3,7]. The American Diabetes Association (ADA) recommends that HbA1c values between 5.7% (38.8 mmol/mol) and 6.4% (46.4 mmol/mol) indicate the presence of prediabetes [8]. Our earlier primary prevention studies among Asian Indians have indicated that 60% of the incidence of diabetes occurred with HbA1c values of ≥6.0%(42.1 mmol/mol) [9]. So, the selection criterion used in this protocol was an HbA1c value of 6.0% (42.1 mmol/mol) to ≤6.4%(46.4 mmol/mol). This was done to improve the power of the study by faster and higher conversion rate to diabetes. It has also been suggested by the International Expert Committee convened by the World Health Organisation (WHO) and International Diabetes Federation (IDF) that persons with a HbA1c level between 6.0% (42.1 mmol/mol) and 6.5% (47.5 mmol/mol) are at high risk and might be considered for lifestyle intervention programs [10]. In our country this is the first study to report screening using the HbA1c values for prediabetes.

2. Materials and methods

2.1. Objectives

The main objective of this paper is to describe the methods used for selection of participants for the primary prevention study using HbA1c as the diagnostic tool to identify individuals with high risk of conversion to diabetes.

As mentioned earlier, although HbA1c values of 5.7% (38.8 mmol/mol) and 6.4% (46.4 mmol/mol) have been recommended for identifying the state of prediabetes, we have chosen only persons with HbA1c values of (6.0% (42.1 mmol/mol) to ≤6.4% (46.4 mmol/mol)) for this study.

We also describe the methodology using SMS by mobile technology for education and reinforcement of lifestyle advice (diet and physical activity) given to the participants in the intervention arm of the study. This method was found to be an effective strategy in primary prevention of T2DM in Asian Indian men with IGT, in a two-year prospective; randomized controlled study [6].

The transtheoretical model (TTM) of behavioral change was used in tailoring the contents of the SMS sent for this purpose [11].

2.2. Study population

Organizations such as the Indian Railways and other industrial organizations in Chennai city and its peripheral areas were chosen as sites to enroll the study participants. These sites were selected since the working population was mostly non-transferable and therefore were available for a follow-up for two years. Written permissions from the respective administrative authorities were obtained to conduct the study at the work sites. Men and women without known diabetes and aged 35–55 years were invited for screening from 15 sites.

Recruitment was carried out between April 2012 and September 2013. There were a total of 6995 eligible persons aged 35–55 years, without a history of diabetes (Stage 1). Among them, 6030 responded (response rate: 86.2%) to the invitation to undergo screening. Stage 2 of screening was done using non-invasive risk assessment to identify persons at risk of developing diabetes (Fig. 1).

Since the number of women employed in the industrial organizations were less than that of men and many of the women were unwilling or did not satisfy the inclusion criteria there was only a small proportion of women in the study.

Persons with any major illness such as cancer, chronic liver or kidney disease, cognitive impairment, severe depression or mental imbalance and any form of physical disability were excluded. Only those who owned a mobile phone, were able to read English and were familiar in accessing text messages were included because of the nature of the intervention in the trial. Written informed consent was obtained from all participants after explaining the study protocol.

After the initial inclusion criteria (Stage 2) the selected persons were screened with the point-of-care HbA1c testing

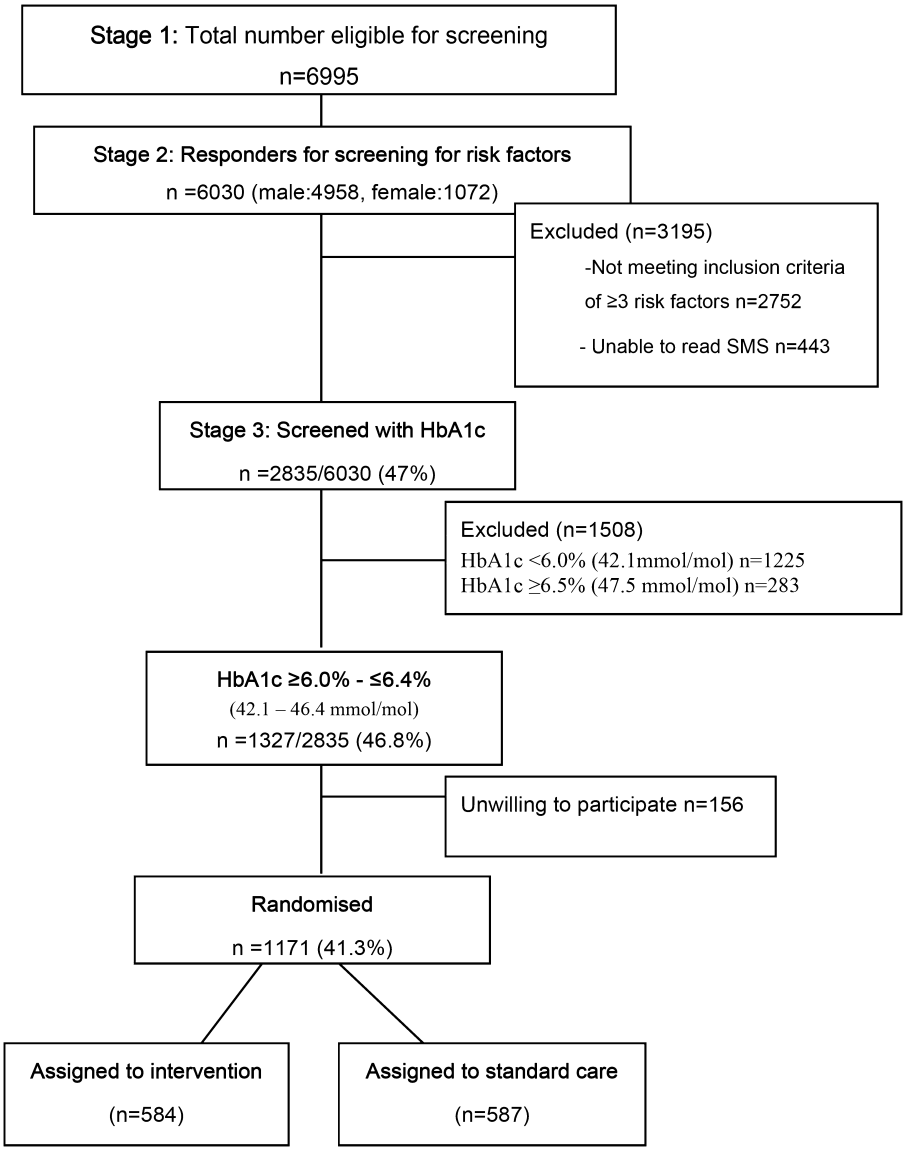

Fig. 1 – Flow diagram showing the steps in selection of study participants.

(Stage 3). Persons having HbA1c values between 6.0% (42.1 mmol/mol) and ≤6.4% (46.4 mmol/mol) were invited to participate in the study followed by randomization in the standard care or the intervention arms.

2.3. *Study assessment*

A structured questionnaire was used to capture participants' details on demography, age, gender, educational level, occupation, smoking and drinking habits, presence of co-morbid conditions, family history of diabetes, heart disease and stroke.

Anthropometric measurements were made with the participant wearing light clothes without footwear. Body mass index (BMI) was calculated (kg/m^2). Waist circumference (WC) was measured midway between the lower rib margin and iliac crest. Supine blood pressure was measured using a standard mercury sphygmomanometer after a 5-min rest. An average of two readings were recorded. The high-risk group was defined as those having any three or more of the following risk variables; positive first degree family history of diabetes, increased waist circumference (men ≥ 90 cm, women ≥ 80 cm), increased body mass index (≥23 kg/m^2), history of hypertension, habitual sedentary habits and history of prediabetes. Persons with three or more risk factors inclusive of age ≥35 - ≤55 years were selected for the second stage of screening using measurement of HbA1c.

The HbA1c test was performed using a point-of-care method (Bio-Rad in2it system). Comparison of HbA1c values by the point-of-care method and immunoturbidimetric assay used in the laboratory (Tina Quant II assay, Roche Diagnostics, Germany) in randomly selected participants yielded a correlation coefficient of 0.887 (p value <0.0001, n = 111). The two-stage screening was performed on the same day.

Objective measurement of physical activity and sedentary behavior was undertaken using an accelerometer (Actigraph®).

Participants were asked to wear the activity monitor for seven consecutive days for a minimum wear time of 960 min per day. This is being done to assess physical activity, defined as minutes per day of moderate-to-vigorous physical activity (MVPA), sedentary time and sleep duration. Changes in activity from the baseline through the follow-up visits would repeatedly be recorded.

At each visit the participant was assessed on the quality of health outcomes using the EuroQol (EQ-5D-3L) [12]. A validated physical activity questionnaire; recent physical activity questionnaire (RPAQ) was used to assess physical activity energy expenditure [14].

The 24-h diet recall method was used for obtaining and analyzing the participant's dietary information. This method has been validated and used in our previous studies [4–6]. This enumerates the participant's eating pattern during the past 24 h. The routine dietary pattern is recorded and information on eating habits, food choices, food frequency and general dietary quality are assessed. Energy and nutrient intake are calculated based on this information.

At the start of the study, participants in both arms received standard lifestyle advice on diet and physical activity. The prescribed lifestyle changes were similar to those used in a previous trial in India [6]. Participants in the intervention arm, in addition, receive customised text messages based on the TTM stages. The process of behavioral change in the TTM is categorized in five stages: precontemplation (not ready), contemplation (getting ready), preparation (ready) action and maintenance. The individuals traverse between the qualitatively different stages when modifying behavior. Each TTM stage had 50 messages both on diet and physical activity. Each text message was not more than 160 characters in length. The messages were sent to individual participants based on their TTM stage.

An automated mobile phone messaging delivery manager was built in an online portal system and hosted in the server. The online portal had the SMS database and the participants' information stored in it. The messages were delivered by a commercial service provider (mVayoo). Each participant received three messages per week at their preferred time. Our previous study had shown that a frequency of three messages per week was preferred by the participants [6].

The messages are based on healthy lifestyle principles that provide positive reinforcement, encouragement for improved behaviors, personal strategies for lifestyle change and for overcoming barriers.

The study protocol is approved by the Ethics Committee of India Diabetes Research Foundation. An independent data and safety monitoring committee was formed for interim assessment of the progress of the study.

2.4. *Randomization and masking*

At a particular site, randomization was done on the week after completing the screening phase. A computer-generated randomization sequence, Matlab randpern version 6 based on Marsaglia's algorithm [13] was used to randomly assign the participants (1:1) in the intervention arm or to the standard care arm.

2.5. *Statistical analysis*

Mean values and standard deviations for age, BMI, WC, HbA1c, systolic and diastolic blood pressure were calculated. Group means were compared using Students' unpaired 't'-test, categorical variables were compared by chi-square test.

3. Results

Overall, from the 15 study sites there were 6995 eligible persons aged 35–55 years, without a history of diabetes (Stage 1). Among them, 6030 responded (response rate: 86.2%) to the invitation to undergo screening procedures (Stage 2); there were 4958 men (82.2%) and 1072 women (17.8%). At this stage 3195 persons were excluded; 2752 individuals had <3 of the defined risk factors and 443 were unable to read SMS. Among the total persons screened ($n = 6030$), 2835 (47%) were eligible for Stage 3 of screening with HbA1c.

As per the ADA criteria for prediabetes, there were 1501 (52.9%) persons with an HbA1c value of 5.7% (38.8 mmol/mol) to 6.4% (46.4 mmol/mol).

Based on the HbA1c values, 2835 participants were categorised in three groups as having HbA1c values of <6.0% (42.1 mmol/mol) (group1), values 6.0% (42.1 mmol/mol) to ≤6.4% (46.4 mmol/mol) (group 2) and values ≥6.5% (47.5 mmol/mol) (group3). Among the 2835, 1225(43.2%), 1327(46.8%) and 283 (10.0%) were in groups 1, 2 and 3, respectively.

From group 2 ($n = 1327$), which was the target group for the study, 156 were unwilling to participate and were excluded. A total of 1171 were enrolled and randomized in the two study groups. The intervention arm had 584 participants and the standard care arm had 587 (Fig. 1).

The mean age and BMI of the persons screened with HbA1c ($n = 2835$) was 45.9 ± 5.6 years and 27.7 ± 3.4 kg/m^2, respectively. Due to the selection criteria, 81.7% were obese (BMI≥25.0 kg/m^2) and 14.8% were overweight (BMI ≥23.0 - <25.0 kg/m^2).

Table 1 shows the comparison of the characteristics of the three HbA1c subgroups. Mean age of the persons in group 3 was significantly higher than that of other two groups ($p < 0.001$ vs group 2, $p < 0.005$ vs group 1). WC ($p < 0.005$ vs group 1), systolic and diastolic blood pressure were also significantly higher in group 3 ($p < 0.001$ vs group 2, $p < 0.005$ vs group1).

The highest percentage with a positive family history was seen in group 2, ($p = 0.027$ vs group 1). Percentage of obesity was significantly higher in group 2 ($p = 0.017$) when compared with group 1. Among women, abdominal obesity was significantly higher in group 2 ($p < 0.0001$) in comparison with group 1. Group 3 also had the highest percentage of newly diagnosed hypertension ($p < 0.02$ vs group 2, $p < 0.0001$ vs group1).

4. Discussion

The two-stage screening strategy using risk assessment and HbA1c testing found that among those with three or more risk

Table 1 – Characteristics of participants in different ranges of HbA1c values.

	HbA1c <6.0% (42.1 mmol/mol) Group 1 1225 (43.2)	HbA1c 6.0% - ≤ 6.4% (42.1–46.4 mmol/mol) Group 2 1327 (46.8)	HbA1c ≥ 6.5% (47.5 mmol/mol) Group 3 283 (10.0)
Characteristics (values are mean ± SD)			
Age in years	45.4 ± 5.6	45.9 ± 5.5*	47.4 ± 5.5**,#
Body mass index (BMI) (kg/m^2)	27.4 ± 3.2	28.1 ± 3.5*	27.7 ± 3.3
Waist circumference (cm)	94.5 ± 7.5	95.7 ± 8.0*	95.9 ± 8.4#
Blood pressure (mmHg)			
Systolic	128.2 ± 16.6	129.4 ± 17.4	133.4 ± 18.4**,#
Diastolic	81.7 ± 10.4	82.4 ± 10.4	85.2 ± 11.9**,#
HbA1c % (mmol/mol)	5.3 ± 0.4 (34.4 mmol/mol)	6.1 ± 0.1* (43.2 mmol/mol)	7.7 ± 1.4**,# (60.7 mmol/mol)
Presence of risk factors n (%)			
Positive family history	622 (50.8)	733 (55.2)•	153 (54.1)
Overweight BMI 23.0–24.5 kg/m^2	193 (15.8)	179 (13.5)	47 (16.6)
Obese BMI ≥25.0 kg/m^2	980 (80.0)	1111 (83.7)••	226 (79.9)
Abdominal obesity in men (WC ≥90 cm)	737 (60.2)	797 (60.1)	184 (65.0)
Abdominal obesity in women (WC ≥80 cm)	217 (17.7)	314 (23.7)†	46 (16.3)‡
History of prediabetes	39 (3.2)	118 (8.9)†	39 (13.8)‡, ô
Hypertension—newly diagnosed (≥140/90 mmHg)	265 (21.6)	309 (23.3)	89 (31.4)‡, ô
Hypertension—known	259 (21.1)	294 (22.2)	68 (24.0)
Sedentary lifestyle	647 (52.8)	982 (74.0)	164 (58.0)

* $p < 0.02$—Gp1 vs Gp2.
** $p < 0.001$—Gp2VsGp3.
\# $p < 0.005$—Gp1VsGp3.
• $p = 0.027$.
•• $p = 0.017$.
† $p < 0.0001$ vs group1.
‡ $p < 0.02$ vs group 2.
ô $p < 0.0001$ vs group1.

factors, 10.0% had undiagnosed diabetes as indicated by an HbA1c of ≥6.5% (47.5 mmol/mol). A larger percentage (52.9%) had HbA1c values in the prediabetic range; 5.7 (38.8 mmol/mol)–6.4% (46.4 mmol/mol) as suggested by the ADA [8]. Among the prediabetic group, those with HbA1c values of 6.0% (42.1 mmol/mol) - ≤6.4% (46.4 mmol/mol) (88.3%) were included in this study.

More than 80% of the 382 million people with diabetes live in low and middle income countries (LMICs)[1]. In addition to having a high prevalence of T2DM, people in LMICs develop diabetes at a much younger age than in the developed countries [1,15]. Prediabetic stages are seldom recognized or looked for. In fact, the benefit of screening would be much higher in the LMICs since the sensitivity of screening for dysglycemia is higher in populations with higher prevalence of diabetes[16]. Early diagnosis of diabetes and early intervention help to prevent occurrence of vascular complications[17]. Identification of prediabetic stage offers a chance to prevent the development of clinical diabetes. Therefore screening strategies using simple diagnostic tools are of great importance. However, an ideal strategy for opportunistic screening of at-risk individuals or undiagnosed diabetes remains a major concern especially in developing countries.

We had earlier noted that HbA1c was a strong predictor of incident diabetes and 60% of the incident cases in the Indian Diabetes Prevention Programmes had baseline values of ≥6.0% (42.1 mmol/mol) [9]. This is the first primary prevention trial in diabetes in India in which the selection of prediabetic participants has been made using the HbA1c criterion.

As HbA1c reflects long-term status of glycemia, it may provide a better screening criterion than 2-h post glucose (2hPG) values for identifying individuals who may benefit from interventions designed to limit deterioration in glycemia. This trial will enable comparison with outcomes from our previous prevention studies in which at-risk individuals have been identified on the basis of 2hPG levels. However, this analysis can only be done after the prospective data has been completed and compared with the previous prevention trials.

In comparison with the selection of study participants using the 2-h oral glucose tolerance, the recruitment based on the HbA1c test was less time consuming, simple and less labour intensive. The procedure was also convenient and acceptable to the participants.

Using the two-stage screening involving selection of persons with high risk of developing diabetes followed by testing with HbA1c, 16.7% of the eligible persons could be recruited for the study. In our previous prevention studies which used selection of participants positive for IGT on two Glucose Tolerance Tests (GTT), only 5–6% of the selected persons could be recruited [4,6,18]. However, the two procedures were not strictly comparable since the selection criteria were different. In the present study we had selected persons who had HbA1c values in the upper tertile denoting prediabetes. To facilitate on-site screening and reporting of HbA1c values on the same day, a point-of-care device was used. This provided results in 15 min using capillary blood samples.

Although expensive, there are several advantages of using HbA1c as a screening test vs fasting blood glucose (FBG) or the

oral glucose tolerance test [19,20]. Flexibility of random sampling, low biological variability and high reproducibility makes HbA1c an ideal tool for diagnosis of diabetes and prediabetic stages.

It is proved that sustained intervention on healthy lifestyle habits using tailored text messages helps to improve the behavior of the participants and thereby reduces the incidence of T2DM when compared with the participants in the control arm of the study [6].

It is a limitation of the study that the number of women included has been small; as the proportion employed in the selected organizations has been low in comparison with that of men. However, it is unlikely that the behavior and impact of mobile technology to be varied among adult men and women.

Although testing of HbA1c definitely has several advantages over that of blood glucose, the higher cost of the test may be a limitation.

Funding

This trial (Ref. No. 58/1/6/ICMR-MRC/2009-NCD-II) was funded by the Indian Council of Medical Research–Medical Research Council Joint Initiative Chronic Non-Communicable Diseases Research Funding. The trial is also supported by the Medical Research Council through funding to NW (MC_UU_12015/1 and MC_UU_12015/3).

Conflict of Interest

We declare that we have no conflicts of interest.

Acknowledgments

We thank Tamilselvan K, Vedasree P and Karthikeyan M of the epidemiology team of the India Diabetes Research Foundation in coordinating for data collection and Vijaya Balaji for the statistical support rendered in this study. We acknowledge the support of the physical activity team of the MRC Epidemiology Unit and in particular, Dr Soren Brage, Kate Westgate, Stefanie Mayle and Lewis Griffiths.

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