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Prevalence of prediabetes and associated factors of prediabetic stages: a cross-sectional study among adults in Nepal

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ABSTRACT

Objectives To estimate the prevalence of prediabetes and to assess the association of prediabetic stages with sociodemographic, lifestyle and clinical factors

Design Cross-sectional study at the screening and inclusion stage of a Diabetes Prevention Education Program (DiPEP) trial

Setting The study was conducted in two urban communities in Nepal (October 2019–March 2020).

Participants A total of 6222 residents of two study sites, aged 18–64 years and without a history of diabetes, were eligible for prediabetes screening. Exclusion criteria were pregnancy, history of diabetes and critical illness. A total of 291 participants with prediabetes were included in this study.

Primary and secondary outcome measures Prevalence of prediabetes based on glycated haemoglobin (HbA1c) criteria (5.7%–6.4%) was the primary outcome of the study. Odds Ratio and 95% CI were estimated to assess the associations between the outcome prediabetic stages (5.7%–5.9% vs 6.0%–6.4%) and sociodemographic, lifestyle and clinical factors in both unadjusted and adjusted models.

Results Out of 6222 screened participants, 308 (5%, 95% CI: 4.4% to 5.5%) individuals were detected with prediabetes based on HbA1c. The mean age of 291 responded participants was 50.3±7.6 years and 67% were females. Among them, 78% aged 45–64 years, 97% had central obesity, 90% had high waist–hip ratio, 63% were hypertensive and 66% had no family history of diabetes. Approximately, 54% and 46% of individuals with prediabetes had HbA1c of 5.7%–5.9% and 6.0%–6.4%, respectively. Female gender was associated with prediabetes with HbA1c 6.0%–6.4% (OR, 1.98, 95% CI: 1.07 to 3.67) in the adjusted model.

Conclusion The estimated prevalence of prediabetes was 5% among screened participants, and female gender was associated with the prediabetic stage. As a large proportion of the population with prediabetes were not aware of their status, this study demonstrates a need for regular community screening programmes to detect individuals with prediabetes and provide them a comprehensive lifestyle intervention for diabetes prevention.

Trial registration number NCT04074148, 2019/783.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ A community-based screening was conducted to detect individuals with prediabetes in the low-income country Nepal.
⇒ The use of three screening tools (Indian Diabetes Risk Score, random blood sugar and glycated haemoglobin (HbA1c) test) ensured the validity of the detection process.
⇒ This study was subjected to selection bias due to voluntary participation at the screening campaigns.
⇒ The predefined criteria used for undergoing the HbA1c test might have misclassified individuals as normoglycemic, leading to underestimated prediabetes prevalence.
⇒ The small sample size gives low precision of the estimated association between prediabetic stages and potential risk factors.

INTRODUCTION

Prediabetes is an intermediate hyperglycaemic state or non-diabetic hyperglycaemic state with no or minimal symptoms.[1] It is a condition with blood glucose levels above normal but below the threshold value of the clinical diagnosis of diabetes.[1] Prediabetes is defined as having fasting blood glucose (FBG) level of 100–125 mg/dL, oral glucose tolerance test (OGTT) for 2 hours, plasma glucose level of 140–199 mg/dL and/or glycated haemoglobin (HbA1c) level of 5.7%–6.4% as per American Diabetes Association (ADA).[1] Impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) are collectively known as pre-diabetes.[2]

The global prevalence of IFG and IGT in 2021 has been estimated to be 6.2% and 10.6%, respectively, and is projected to increase to 6.9% and 11.4% in 2045.[3] Age-adjusted prevalence of IGT has been found to be high in low-income countries such as Nepal, with the age-adjusted prevalence of IFG and IGT of 7.8% and 5.4%, respectively.[3]

A recent meta-analysis from Nepal suggested a high prevalence of prediabetes (9.2%) based on IFG and IGT.[4] The prevalence of prediabetes was especially high in urban settings of Nepal[4] reflecting increased urbanisation and transition to high energy diet and sedentary lifestyle.[5]

Prediabetes is a high-risk state for diabetes development[6 7] with an annual conversion rate of 5%–10%.[7 8] Age, gender and family history of diabetes are non-modifiable risk factors,[6 7] while high energy diet, physical inactivity, obesity, high blood pressure, elevated triglycerides and low socioeconomic conditions are modifiable risk factors of prediabetes.[9 10] Prediabetes reduces the quality of life and increases healthcare expenditure[9] as there has been an association of prediabetes with cardiovascular-related complications, retinopathy, neuropathy and all-cause mortality.[7 11–13] Evidence suggests that high HbA1c level in the prediabetic phase is predictive of increased morbidity[14 15] and mortality,[16 17] and mortality rate has been shown to be higher among individuals with prediabetes with HbA1c 6.0%–6.4% than with HbA1c 5.7%–5.9%.[18] The risk of diabetes is substantially higher among individuals with HbA1c 6.0%–6.4% compared with HbA1c 5.7%–5.9%,[19] and the risk of diabetes increases with elevated HbA1c level in the prediabetic phase.[2 6]

It has been recommended that an effective intervention should be implemented among individuals with HbA1c≥6% to delay their diabetes diagnosis.[6] Although ADA suggested a low risk for developing diabetes among individuals with HbA1c<6%, it recommended considering other factors for diabetes development such as triglycerides, blood pressure, body mass index (BMI) and family history of diabetes to start an intervention with HbA1c<6%.[6] Subcategorisation of prediabetic stages can also be clinically important because the 'International Expert Committee' appointed by ADA has recommended that therapeutic decisions should be taken based on how close the HbA1c level is to the diagnosis of diabetes.[6] Further, it is hypothesised that sociodemographic and clinical characteristics differ between two prediabetic stages determined by HbA1c with a cut-off value of 6%.[20 21] Therefore, subcategorisation at this cut-off value into prediabetic stages might help to better understand the potential risk factors of prediabetic stages.

Underpinning the burden of prediabetes, it is important to detect individuals with prediabetes in its early phase to intervene and prevent diabetes manifestation by recommending comprehensive lifestyle intervention programmes including components of a healthy diet, physical activity and weight management plans.[8] Prediabetes can be reverted to normoglycemia[22] and the risk of diabetes can be lowered by 56%, achieving normal glucose regulation by individuals with prediabetes.[23] It can also be expected that with lifestyle measures there is a higher possibility of reverting the prediabetic stage with HbA1c 5.7%–5.9% to normoglycemia than reverting the prediabetic stage with HbA1c 6.0%–6.4% to normoglycemia.[24] Identification of risk factors for the 'early' prediabetic stage with lower HbA1c may help to plan and execute an effective intervention to prevent diabetes in the population with prediabetes.

There have been attempts to prevent and control non-communicable diseases (NCDs) including diabetes in Nepal through the 'Multisectoral-Action Plan for Prevention and Control of NCDs' (MSPA) (2014–2020)[25] and 'WHO Package of Essential NCD interventions for primary health care in low-resource settings'.[26] MSPA has set a goal to halt the rise in obesity and diabetes by 2025. However, prediabetes and the prevention of diabetes were not prioritised in these actions.[25 26] Furthermore, to the best of researchers' knowledge, so far, no such study investigated prediabetes based on HbA1c in the community setup and assessed factors associated with prediabetic stages in Nepal. In this study, prediabetes was divided into two stages fulfilling ADA recommended HbA1c-based prediabetic range (5.7%–6.4%)[1] and with the cut-off value of ≥6% recommended by International Expert Committee of ADA.[6] Also, previous research have also applied the similar cut-off criteria for HbA1c level.[18 20]

The aim of the present study was to estimate the prevalence of prediabetes using HbA1c and examine the association between sociodemographic, lifestyle and clinical factors, respectively, and prediabetic stages among individuals who were enrolled in the Diabetes Prevention Education Program (DiPEP) trial study[27] conducted recently in Nepal.

METHOD AND MATERIALS

Study setting, study design and study participants

The present study is a community-based cross-sectional study from the DiPEP project which included screening campaigns to detect prediabetes in the community and a cluster randomised controlled trial (RCT).[27] The study was conducted in two urban settings in Nepal, Patan and Dhulikhel, from October 2019 to March 2020. Community screening campaigns were conducted in 10 clusters of Patan and 2 clusters of Dhulikhel. Two originally proposed clusters from Dhulikhel were excluded due to the COVID-19 pandemic.[27] Hence, there were a total of 12 clusters in the study representing urban settlements with similar healthcare services. Permanent residents of the study sites aged 18–64 years with no self-reported history of diabetes were eligible for the screening. Participants who were critically ill or pregnant or had a known case of type 1 or type 2 diabetes were excluded from the screening. It was planned to include 448 individuals with prediabetes in the RCT. That would ascertain 80% power to detect a difference in HbA1c of 0.12% between the intervention and control arm, at a 5% significance level, and assuming an intracluster correlation coefficient of 0.01,[28] SD=0.36[29] and 30% loss to follow-up.[27] Screening was to continue until the necessary number of individuals were included in the RCT, and no specific sample size calculation was made for the screening part. Due to the lockdown during the COVID-19 pandemic, the planned number of trial participants was not reached. The

study protocol approved by the ethical committees was followed. Identical methods and procedures, including staff recruitment and training, were adopted to ensure consistency across the sites. A detail of methods is available in the DiPEP protocol paper.[27]

Screening and recruitment

All eligible participants (age 18–64 years, with no self-reported history of diabetes and permanent residents of the study sites) showing up at the screening campaigns were enrolled in the screening programme to detect prediabetes. They were first screened using the Indian Diabetes Risk Score (IDRS)≥60[30] and random blood sugar (RBS) 140–250 mg/dL to select those at risk of pre-diabetes. Evidence suggests that an IDRS of ≥60 has approximately 72% sensitivity and 60% specificity to predict diabetes,[31] while both sensitivity and specificity to identify prediabetes is 83%.[30]

Prediabetes was ascertained by a point-of-care test (POCT) HbA1c[2] via DCA Vantage 2000 analyser among those whose IDRS was ≥60 and whose RBS was 140–250 mg/dL. The variability for the DCA device was low.[32] DCA had a high specificity at a cut-off of 6.5% HbA1c (48 mmol/mol).[32] HbA1c was measured using a drop of capillary blood via finger prick using all infection prevention measures. Participants were operationalised as normal, having prediabetes or having diabetes if the HbA1c test was less than 5.7%, 5.7%–6.4% and 6.5% or more, respectively, according to the ADA guideline.[1]

Data collection

During the screening campaigns, information on socio-demographic characteristics such as age, gender, residency and ethnicity was collected using the Nepali language via face-to-face interviews. The IDRS takes into account factors such as age, abdominal obesity, self-reported physical activity and family history of diabetes.[30] Hence, participants enrolled in the screening were also asked about family history of diabetes and physical activity (regular vigorous exercise or strenuous activities at home or work/regular moderate exercise or moderate activities at home or work/regular mild exercise or mild activities at home or work/no exercise or sedentary activities at home or work) and were also assessed for abdominal obesity by measuring waist circumference (WC) as part of the IDRS questionnaire. WC (in cm) was measured by placing a plastic tape horizontally, passing the umbilicus (midway between the 12th rib and the iliac crest on the midaxillary line). After calculating the total score of IDRS, participants with a value of IDRS≥60, 30–50 and<30 were defined as having a high, moderate and low risk for diabetes, respectively.[33]

Further, hip circumference, weight and height were also assessed using standardised techniques and calibrated equipment.[34] Hip circumference was measured to all screened participants using a plastic tape around the widest portion of the buttocks, with the tape parallel to the floor, weight (in kg) was registered in light clothing without shoes using 'Omron (HB 2B) digital weighing scale'; and height (in cm) was measured using a steel blade measuring tape.[34] The weighing scale was calibrated before use to ensure reliability. Blood pressure was measured in resting position using the 'Omron (HEM B712) digital blood pressure measurement instrument'. Calibration was done before use. The Omron digital automatic blood pressure monitor was also used in the WHO STEPwise approach to NCD risk factor surveillance (STEP survey).[34] Three blood pressure measurements were taken at least 5 min apart[35] and the average of three measurements was used for the study. Weight, height and blood pressure were measured only among individuals detected with prediabetes.

The possibility for prediabetes was determined by obtaining an RBS test via glucometer (B. Braun) using a prick test. High glycaemia (RBS≥200 mg/dL), intermediate glycaemia (RBS: 140–199 mg/dL) and normal glycaemia (RBS<140 mg/dL) were operationalised according to the ADA guideline.[1] A cut-off of 250 mg/dL was set to undergo an HbA1c test since the capillary test usually gives a higher value than a venous test.[36] DCA Vantage 2000 HbA1c POCT analyser was first calibrated and then used to test HbA1c of the participants. DCA Vantage was certified by the National Glycohemoglobin Standardization Program/Diabetes Control and Complications Trial and the International Federation of Clinical Chemistry and Laboratory Medicine.[37]

Individuals with prediabetes detected in this study were further contacted for detailed information on socio-demographic characteristics (education, occupation, marital status, living status and annual household per capita income) and lifestyle characteristics (diet, physical activity, smoking, alcohol intake and sleep history). Information on diet and physical activity was collected using standardised validated questionnaires,[38 39] while questions related to sociodemographics were adapted from a previous Nepali study.[40] A pretest was conducted among 43 adults to determine if participants understood the questions and interpreted the questions correctly. As a result, necessary language editions were implemented in the questionnaire. Face-to-face interview technique was used to collect the detailed information before the COVID-19 pandemic lockdown, and telephone calls were made to collect this information during the lockdown.

All data were collected on tablets using the free version of CommCare software.[41]

Outcomes

The primary outcome was the prevalence of prediabetes (HbA1c 5.7%–6.4%) defined by ADA guidelines.[1] Prediabetes was further categorised into prediabetic stages with HbA1c level 5.7%–5.9% and HbA1c level 6.0%–6.4% to determine their association with potential risk factors. The cut-off value of HbA1c≥6% was suggested to be a clinically meaningful threshold in the literature.[2 6 18–20]

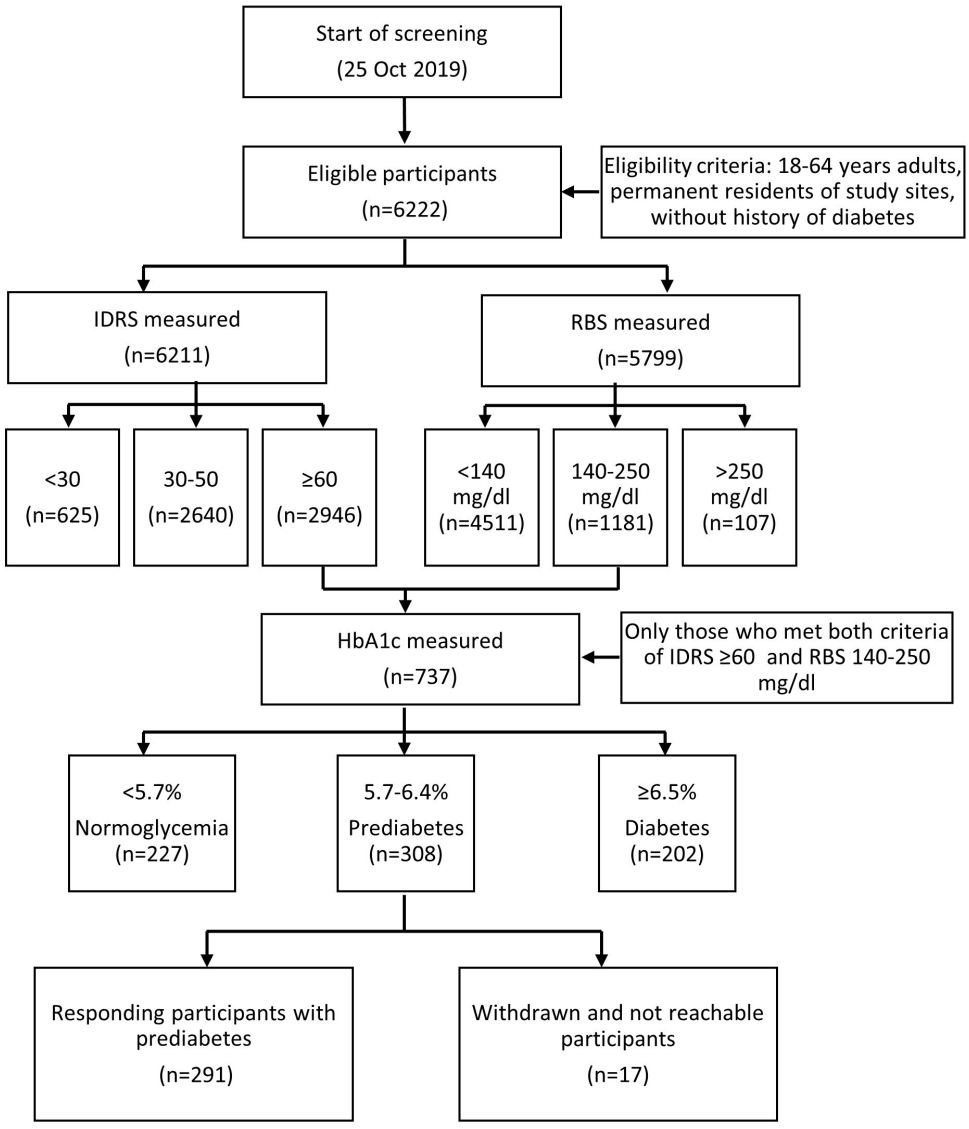

Figure 1 Study flowchart. The screening steps to identify participants with prediabetes. The total number of screened participants was 6222, the total number of participants with prediabetes (HbA1c 5.7%–6.4%) was 308 and the total number of responding participants with prediabetes was 291. HbA1c, glycated haemoglobin ; IDRS, Indian Diabetes Risk Score; RBS, random blood sugar.

Covariates

Sociodemographic variables

Sociodemographic data included age (years), gender (male/female), residency (Patan/Dhulikhel), ethnicity (Newar/Brahmin/Janajati/Chhetri/Madhesi/others), education (no formal education/high school or below/more than high school), occupation (business/housewife/office/others), marital status (currently married/not currently married), living status (living alone/living with family) and annual household per capita income (below international poverty line/above international poverty line). The international poverty line is defined as an annual equivalent of US$1.9 income per day.[42]

Anthropometric measurements and lifestyle characteristics

BMI was calculated using weight (kg)/height (m^2)[43] BMI was categorised as normal (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), obese (≥30 kg/m^2)[43] and central obesity was categorised by WC (female WC>80 cm and male WC>90 cm).[43] Waist–hip ratio (WHR) was also calculated and operationalised as high risk (female≥0.86, male≥1), moderate risk (female: 0.81–0.85, male: 0.96–0.99) and low risk (female≤0.8, male≤0.95).[43]

Lifestyle characteristics such as diet, physical activity, smoking, alcohol intake and sleep history were also collected. Information on the diet using two 24-hour dietary recalls[38] was also obtained and grams per day intake (total grain, total protein, total vegetables, total fruits, total fat, total drinks, total salt and total mixed food) were computed. The information on a self-reported balanced diet (yes/no/no information), small frequency meals (yes/no/no information), sugary food consumption (always/sometimes/occasionally/never), smoking status (non-smoker/former smoker/current smoker) and alcohol (never consumed/former drinker/

Table 1 Characteristics of screened participants (n=6222)

Variables	Total (n=6222) Freq. (%)
Age (years),* mean±SD	42.6±10.9
Gender	
Female	3428 (55.1)
Male	2794 (44.9)
Residency	
Dhulikhel	521 (8.4)
Patan	5701 (91.6)
Ethnicity	
Newar	4314 (69.3)
Brahmin	581 (9.4)
Janjati/Magar/Tamang/Rai/Limbu	562 (9.0)
Chhetri/Thakuri/Sanyasi	416 (6.7)
Madhesi/Shah/Tharu/Jha	153 (2.5)
Dalit	101 (1.6)
Others	95 (1.5)
Family history of diabetes†	
Both parent	174 (2.8)
Either parent	1239 (20.1)
No family history	4765 (77.1)
Physical activity†, ‡	
Regular vigorous exercise or strenuous (manual) activities at home/work	82 (1.3)
Regular moderate exercise or moderate physical activities at home/work	662 (10.7)
Regular mild exercise or mild physical activities at home/work	5348 (86.6)
No exercise and/or sedentary activities at home/work	86 (1.4)
Central obesity§, ¶	
Yes	4504 (72.7)
No	1693 (27.3)
WHR category§, **	
High WHR	3372 (54.4)
Moderate WHR	1270 (20.5)
Low WHR	1555 (25.1)
IDRS category††, ‡‡	
IDRS≥60	2946 (47.4)
IDRS: 30–50	2640 (42.5)
IDRS<30	625 (10.1)
HbA1c§§, mean±SD	6.3±1.3
HbA1c category§§, ¶¶	
HbA1c≥6.5%	202 (27.4)
HbA1c: 5.7%–6.4%	308 (41.8)***
HbA1c≤5.6%	227 (30.8)
RBS†††, mean±SD	123.9±41.8
RBS category†††, ‡‡‡	
High RBS≥200 mg/dL	253 (4.4)
Intermediate hyperglycaemia (RBS: 140–199 mg/dL)	1035 (17.8)
Normal RBS<140 mg/dL	4511 (77.8)

*n=6214
†n=6178
‡As per IDRS Physical activity category.
§n=6197.
¶as per WHO guideline for Central Obesity for Asian population based on waist circumference (Female>80 cm, Male>90 cm).
**As per WHO guidelines for WHR Category [High WHR (Female≥0.86, Male≥1), Moderate WHR (Female: 0.81–0.85, Male: 0.96–0.99), Low WHR (Female≤0.8, Male≤0.95)].
††n=6211.
‡‡IDRS≥60: High risk, IDRS 30–50: Moderate risk, IDRS<30: No risk.
§§n=737.
¶¶ as per the American Diabetes Association standard of care, Diabetes: HbA1c≥6.5%, Prediabetes: HbA1c: 5.7–6.4%, Normal HbA1c≤5.6%.
***Total number of participants detected with prediabetes in the screening program.
†††n=5799.
‡‡‡As per American Diabetes Association standard of care, High RBS≥200 mg/dl, Intermediate Hyperglycaemia (RBS: 140-199 mg/dl), Normal RBS<140 mg/dl.
HbA1c, glycated haemoglobin; IDRS, Indian Diabetes Risk Score; RBS, random blood sugar; WHR, waist–hip ratio.

current drinker) were obtained. Physical activity (metabolic equivalents (METs) min per week) was assessed using a Global Physical Activity Questionnaire and was categorised into two groups as per WHO recommendation (<600 min per week (not recommended)/≥600 min per week (recommended)).[39] In addition, self-reported duration of sleep was collected and was categorised as recommended (7–9 hours)/may be appropriate (6–6.99 or 9.1–11 hours)/not recommended (<6 or >11 hours) as per National Sleep Foundation.[44]

Clinical characteristics

Clinical history included self-reported history of hypertension awareness (yes/no/do not know); hypertension status based on systolic blood pressure (SBP)≥140[45] or diastolic blood pressure (DBP)≥90[45] or self-reported antihypertensive medication history (yes/no); RBS (mg/dL); and family history of diabetes (both/either/no family history).

Statistical analysis

Continuous variables were presented as mean and SD (if the distribution was approximately normal) and median and interquartile ranges (if distributions were skewed). Categorical variables were presented as

Table 2 Sociodemographic characteristics of participants with prediabetes (n=291)‡‡

Variables	Prediabetes HbA1c (5.7%–5.9%) (n=156) Freq. (%)	Prediabetes HbA1c (6.0%–6.4%) (n=135) Freq. (%)	Total (n=291) Freq. (%)	P value
Age (years), mean±SD	50.2±7.5	50.5±7.8	50.3±7.6	0.79
Age (categorical), years				
18–44	36 (23.1)	28 (20.7)	64 (22)	0.63
45–64	120 (76.9)	107 (79.3)	227 (78)	
Gender				
Female	97 (62.2)	99 (73.3)	196 (67.3)	0.04
Male	59 (37.8)	36 (26.7)	95 (32.7)	
Ethnicity				
Newar	129 (82.7)	117 (86.7)	246 (84.5)	0.35
Other*	27 (17.3)	18 (13.3)	45 (15.5)	
Education				
No formal education	48 (30.8)	43 (31.9)	91 (31.3)	0.73
High school or below	87 (55.8)	70 (51.8)	157 (53.9)	
More than high school	21 (13.4)	22 (16.3)	43 (14.8)	
Occupation				
Business	54 (34.6)	46 (34.1)	100 (34.4)	0.12
Housewife	49 (31.4)	50 (37.0)	99 (34.0)	
Office	22 (14.1)	25 (18.5)	47 (16.1)	
Other†	31 (19.9)	14 (10.4)	45 (15.5)	
Marital status				
Currently married	146 (93.6)	129 (95.6)	275 (94.5)	0.46
Not currently married‡	10 (6.4)	6 (4.4)	16 (5.5)	
Living status				
Living alone	5 (3.21)	3 (2.22)	8 (2.75)	0.73**
Living with family	151 (96.79)	132 (97.78)	283 (97.25)	
Annual household per capita income in US$§	(n=155)	(n=135)	(n=290)	
Median (IQR)	827.8 (517.4–1241.7)	862.3 (620.9–1293.4)	862.3 (517.4–1293.4)	0.17††
Below poverty line¶	67 (43.2)	45 (33.3)	112 (38.6)	0.08
Above poverty line	88 (56.8)	90 (66.7)	178 (61.4)	

*Brahmin, Chhetri, Magar, Tamang, Sherpa, Rai, Limbu, Madhesi, Shah and Dalit.
†Agriculture, driver, teacher, student, retired, unemployed and other.
‡Never married, separated and widowed.
§US$1 = NRs115.97, dated 8 February 2021.
¶International poverty line is defined as annual equivalent of US$1.9 income per day = NRs80 425 per year.
**Fisher's exact test.
††Wilcoxon-Mann-Whitney test.
‡‡This table includes responding participants with pre-diabetes.
HbA1c, glycated haemoglobin.

frequencies and percentages. All data were presented without missing data, which led to varied sample sizes for each variable.

The prediabetic stage was used as the binary outcome variable. The χ^2 test was used to identify the association between prediabetic stages (outcome) and categorical variables (exposure) when ≤20% of expected cell counts are less than 5, while Fisher's exact test was applied when >20% of expected cell counts were less than 5.[46] Continuous variables were compared by T-test if approximately normally distributed and by Wilcoxon-Mann-Whitney test if distributions were skewed.[47 48]

The definition of categorised variables was as follows: annual household per capita income (below international

Table 3 Anthropometric measurements and lifestyle characteristics of participants with prediabetes (n=291)*

	Prediabetes		Total	
	HbA1c (5.7%–5.9%) (n=156)	HbA1c (6.0%–6.4%) (n=135)	(n=291)	
Variables	**Freq. (%)**	**Freq. (%)**	**Freq. (%)**	**P value**
BMI (kg/m^2), mean±SD	(n=102)	(n=86)	(n=188)	
	28.9±3.4	28.7±4.7	28.8±4.0	0.72
BMI categories (kg/m^2)†	(n=102)	(n=86)	(n=188)	
Normal (18.5–24.9)	13 (12.8)	14 (16.3)	27 (14.4)	0.65
Overweight (25–29.9)	50 (49.0)	44 (51.2)	94 (50.0)	
Obese (≥30)	39 (38.2)	28 (32.5)	67 (35.6)	
Central obesity‡				
Yes	152 (97.4)	131 (97)	283 (97.2)	0.99§
No	4 (2.6)	4 (3)	8 (2.8)	
WHR categories¶				
High WHR	134 (85.9)	129 (95.6)	263 (90.4)	0.02
Moderate WHR	11 (7.0)	3 (2.2)	14 (4.8)	
Low WHR	11 (7.1)	3 (2.2)	14 (4.8)	
Smoking status	(n=155)	(n=135)	(n=290)	
Non-smoker	132 (85.2)	117 (86.7)	249 (85.9)	0.48§
Former smoker	3 (1.9)	5 (3.7)	8 (2.7)	
Current smoker	20 (12.9)	13 (9.6)	33 (11.4)	
Alcohol status	(n=155)	(n=134)	(n=289)	
Never consumed alcohol	87 (56.1)	82 (61.2)	169 (58.5)	0.30§
Former drinker	7 (4.5)	2 (1.5)	9 (3.1)	
Current drinkers	61 (39.4)	50 (37.3)	111 (38.4)	
METs, min per week	(n=155)	(n=135)	(n=290)	
Median (IQR)	840 (180–2160)	600 (0–1440)	820 (0–1680)	0.01**
METs category††	(n=155)	(n=135)	(n=290)	
<600 min per week	58 (37.4)	66 (48.9)	124 (42.8)	0.05
≥600 min per week	97 (62.6)	69 (51.1)	166 (57.2)	
Sleep duration category‡‡	(n=152)	(n=132)	(n=284)	
Recommended (7–9 hours)	115 (75.7)	94 (71.2)	209 (73.6)	0.70
Maybe appropriate (6–6.99 or 9.1–11 hours)	30 (19.7)	31 (23.5)	61 (21.5)	
Not recommended (<6 or >11 hours)	7 (4.6)	7 (5.3)	14 (4.9)	
Balanced diet	(n=155)	(n=135)	(n=290)	
Yes	25 (16.1)	24 (17.8)	49 (16.9)	0.84
No	106 (68.4)	93 (68.9)	199 (68.6)	
No information	24 (15.5)	18 (13.3)	42 (14.5)	
Small frequent meals	(n=155)	(n=135)	(n=290)	
Yes	14.00 (9.0)	12.00 (8.9)	26 (9.0)	0.70
No	132.00 (85.2)	118.00 (87.4)	250 (86.2)	
No information	9.00 (5.8)	5.00 (3.70)	14 (4.8)	
Sugary food consumption	(n=155)	(n=134)	(n=289)	
Always	31 (20.0)	29 (21.7)	60 (20.8)	0.96
Sometimes	75 (48.4)	65 (48.5)	140 (48.4)	
Occasionally	5 (3.2)	5 (3.7)	10 (3.5)	

Continued

Table 3 Continued

Variables	Prediabetes HbA1c (5.7%–5.9%) (n=156) Freq. (%)	HbA1c (6.0%–6.4%) (n=135) Freq. (%)	Total (n=291) Freq. (%)	P value
Never	44 (28.4)	35 (26.1)	79 (27.3)	
Food group categories (g per day)				
Total grains	(n=153)	(n=135)	(n=288)	
Median (IQR)	538.5 (425.5–661.5)	596 (445.5–698.5)	556.9 (437.8–684)	0.07**
Total protein	(n=146)	(n=129)	(n=275)	
Median (IQR)	282 (191–402.5)	300 (225–402.5)	300 (200–402.5)	0.29**
Total vegetables	(n=152)	(n=134)	(n=286)	
Median (IQR)	176.4 (110.3–238.3)	199.9 (125.5–262.3)	190.1 (117.3–249.2)	0.11**
Total fruits	(n=28)	(n=25)	(n=53)	
Median (IQR)	57.5 (42.3–84.8)	49.5 (37.5–87)	57.5 (40–87)	0.48**
Total fats oil	(n=151)	(n=130)	(n=281)	
Median (IQR)	3.5 (2.9–5)	4.8 (3–6.5)	4.2 (3–5.5)	0.01**
Total salt	(n=153)	(n=133)	(n=286)	
Median (IQR)	2.8 (2–4)	3.2 (2.5–4.6)	3.0 (2.1–4.3)	0.01**

*This table includes responding participants with pre-diabetes.
†As per WHO guidelines for Standard BMI Category.
‡As per WHO guidelines for Central Obesity for Asian population based on waist circumference (female>80 cm, male>90 cm).
§Fisher's exact test.
¶As per WHO guidelines for WHR Category (high WHR (female≥0.86, male≥1), moderate WHR (female: 0.81–0.85, male: 0.96–0.99), low WHR (female≤0.8, male≤0.95)).
**Wilcoxon-Mann-Whitney test.
††As per the Global Physical Activity Questionnaire.
‡‡As per National Sleep Foundation (recommended (7–9 hours), maybe appropriate (6–6.99 or 9.1–11 hours), not recommended (<6 or >11 hours)).
BMI, body mass index; HbA1c, glycated haemoglobin; METs, metabolic equivalents; WHR, waist–hip ratio.

poverty line (US$≤1.9 income per day)/above international poverty line (US$>1.9 per day)),[42] central obesity as 'yes' or 'no' (female WC>80 cm and male WC>90 cm),[43] BMI categories (normal (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), obese (≥30 kg/m^2)),[43] METs defining physical activity (<600 min per week (not recommended)/≥600 min per week (recommended))[39] and hypertension as 'yes or no' (based on SBP≥140[45] or DBP≥90[45] or self-reported antihypertensive medication history (yes/no)).

Multiple logistic regression analyses were performed to assess the association between the prediabetic stages (HbA1c 5.7%–5.9%=0, HbA1c 6.0%–6.4%=1) and socio-demographic and lifestyle characteristics. As a first step, separate models for each independent variable of interest were analysed. Thereafter, variables to be included in an adjusted model were identified partly based on the prior literature on risk factors for prediabetes[9 10] with a hypothesis that the same factors might also be associated with prediabetic stages. Some variables were excluded because they were identified as mediator (eg, central obesity) or collider (eg, hypertension) or the validity of self-reported measures was considered uncertain or low (eg, annual household per capita income and total fat). The association between the outcome and every single predictor was estimated assuming each variable in the model to be a potential confounder for each other and thus adjusted for all other variables in the model. The final adjusted model included the following variables: age (continuous), gender(male=0/female=1), education (no formal education=0/high education or below=1/more than high education=2), physical activity (METs<600 min per week=0/METs≥600 min per week=1), total grain (continuous), total vegetables/fruits (continuous), alcohol consumption (no=0/yes (former or current drinker)=1) and smoking (no=0/yes (former or current smoker)=1). Adjusted OR and corresponding 95% CI were estimated to assess these associations. A p value of <0.05 was regarded as statistically significant. All statistical analyses were performed using STATA V.17 (IBM, USA).

The Strengthening the Reporting of Observational Studies in Epidemiology checklist[49] has been followed to report this cross-sectional study.

Table 4 Clinical characteristics of participants with pre-diabetes (n=291)*

	Prediabetes		Total	P value
	HbA1c (5.7%–5.9%) (n=156)	HbA1c (6.0%–6.4%) (n=135)	(n=291)	
Variables	Freq. (%)	Freq. (%)	Freq. (%)	
Hypertension awareness (self-report)	(n=156)	(n=135)	(n=291)	
Yes	52 (33.3)	47 (34.8)	99 (34.0)	0.83
No	96 (61.6)	83 (61.5)	179 (61.5)	
Do not know	8 (5.1)	5 (3.7)	13 (4.5)	
Hypertension status (SBP≥140 or DBP≥90 or anti-hypertensive medication)	(n=147)	(n=127)	(n=274)	
Yes	90 (61.2)	82 (64.6)	172 (62.8)	0.57
No	57 (38.8)	45 (35.4)	102 (37.2)	
RBS (mg/dL), mean±SD	161.1±20.2	168.2±24.6	164.4±22.6	0.01
Family history of diabetes	(n=155)	(n=134)	(n=289)	0.86
Both parent	7 (4.5)	5 (3.7)	12 (4.2)	
Either parent	48 (31.0)	39 (29.1)	87 (30.1)	
No family history	100 (64.5)	90 (67.2)	190 (65.7)	

*This table includes responding participants with pre-diabetes.
DBP, diastolic blood pressure; HbA1c, Glycated haemoglobin; RBS, random blood sugar; SBP, systolic blood pressure.

Patient and public involvement

The general public or patients were not involved in forming research questions and developing a research design. However, both representatives from the public and community healthcare workers were involved in selecting the local areas to conduct screening campaigns at the study sites. They will also be involved in the dissemination of the results.

RESULTS

A total of 6222 individuals who were permanent residents of study sites, aged 18–64 years with no self-reported history of diabetes, were screened for prediabetes using IDRS and RBS. Out of these, 737 participants who met both the criteria of IDRS≥60 and RBS 140–250 mg/dL were tested for HbA1c biomarkers. We used this approach to make the study cost-effective and sustainable. Out of 6222 screened individuals, 308 (5%, 95% CI: 4.4% to 5.5%) had prediabetes and 202 (3.2%, 95% CI: 2.8% to 3.7%) had diabetes based on the HbA1c cut-off values. The response rate of participants detected with prediabetes was 94.5% (291 out of 308 participants with pre-diabetes), for whom we had complete data on sociodemographic, lifestyle and clinical characteristics. The reasons for the non-participation of 17 individuals were leaving study before data collection (n=8) and not being reachable due to no contact number (n=9). The number of participants in each of these steps is illustrated in figure 1.

Table 1 shows the characteristics of all screened participants. Of 6222 screened participants, 55% were female, 69% were of Newar ethnicity and 73% had central obesity. The mean age was 42.6±10.9 years (n=6214). The mean RBS was 123.9±41.8 mg/dL. Out of 5799 participants whose RBS was measured, 78% had normal glycaemia, 18% had intermediate hyperglycaemia and 4% had hyperglycaemia. Among 737 participants whose HbA1c was measured, the mean HbA1c was 6.3%±1.3% and the test detected prediabetes (HbA1c: 5.7%–6.4%) in 42% and diabetes in 28% (HbA1c: ≥6.5%).

Table 2 shows the sociodemographic characteristics of 291 responded participants with prediabetes. The mean age was 50.3±7.6 years, 67% were female and 85% were of Newar ethnicity. In this sample, 54% had attained education in high school or below, 34% were engaged in business, 95% were currently married and 97% lived with family members. The proportion of responded participants with prediabetes was 5.7% (196 out of 3428) in females and 3.4% (95 out of 2794) in males.

Table 3 shows anthropometric measurements and lifestyle characteristics of responded participants with prediabetes. The mean BMI was 28.8±4.0 kg/m^2 (n=188), 50% were overweight (BMI, 25–29.9 kg/m^2) and 97% had central obesity measured by WC. Majority of the participants were non-smokers (86%). The proportion reporting alcohol intake was 42%. More than half of the participants (57%) reported performing the physical activity as recommended by WHO. Around 74% of participants had a recommended sleep duration (7–9 hours) as

Table 5 Multiple logistic regression to assess the association between prediabetic stages and sociodemographic, lifestyle and clinical factors§

	Univariate			Adjusted model (n=285)		
Variables	**OR**	**95% CI**	**P value**	**OR**	**95% CI**	**P value**
Age (n=291)	1.00	0.97 to 1.04	0.80	1.00	0.97 to 1.04	0.73
Gender (n=291)						
Male	Ref			Ref		
Female	1.67	1.01 to 2.76	0.04	1.98	1.07 to 3.67	0.03
Education (n=291)						
Illiterate or no formal education	Ref			Ref		
High school and less	0.90	0.53 to 1.51	0.69	1.16	0.66 to 2.04	0.62
More than high school	1.17	0.57 to 2.42	0.67	1.67	0.74 to 3.73	0.21
Physical activity category (n=290)						
<600 METs	Ref			Ref		
≥600 METs	0.63	0.39 to 1.00	0.05	0.65	0.39 to 1.06	0.09
Total grains, per 50 g per day (n=288)	1.04	0.98 to 1.10	0.18	1.05	0.99 to 1.12	0.13
Total fruits/vegetables, per 50 g per day (n=286)	1.06	0.96 to 1.18	0.27	1.04	0.93 to 1.17	0.50
Alcohol consumption (n=289)						
Never drinker	Ref			Ref		
Ever drinker	0.81	0.51 to 1.30	0.39	1.00	0.58 to 1.73	0.99
Smoking status (n=290)						
Never smoker	Ref			Ref		
Ever smoker	0.88	0.45 to 1.72	0.71	1.19	0.56 to 2.54	0.65
Central obesity (n=291)*†						
No	Ref					
Yes	0.86	0.21 to 3.52	0.84			
BMI (n=188)†‡						
Normal	Ref					
Overweight	0.82	0.35 to 1. 93	0.65			
Obese	0.67	0.27 to 1.64	0.38			
Hypertension status (SBP≥140 or DBP≥90 or anti-hypertensive medication) (n=274)†						
No	Ref					
Yes	1.15	0.70 to 1.89	0.57			
Family history of diabetes (n=289)†						
No family history	Ref					
Family history	0.89	0.55 to 1.45	0.64			

*As per WHO guidelines for Central Obesity for Asian population based on waist circumference (female>80 cm, male>90 cm).
†Central obesity, BMI, hypertension status and family history of diabetes were included only in unadjusted analyses.
‡As per WHO guidelines for Standard BMI Category.
§Dependent variable: Pre-diabetes subgroup (Group 1: HbA1c 5.7%–5.9% and Group 2: HbA1c 6.0%–6.4%).
BMI, body mass index; DBP, diastolic blood pressure; HbA1c, glycated haemoglobin; METs, metabolic equivalents; SBP, systolic blood pressure.

per National Sleep Foundation. Most of the participants did not have a balanced diet (69%) and did not take small frequent meals (86%).

Table 4 shows the clinical characteristics of responded participants with prediabetes. Around 66% had no family history of diabetes, 62% did not report a self-history of hypertension but 63% were detected with hypertension. Among responded participants with prediabetes (n=291), the mean HbA1c was 5.8%±0.1%, 6.2%±0.1% and 6.0%±0.2% among prediabetic stages with HbA1c 5.7%–5.9%, HbA1c 6.0%–6.4% and total population (HbA1c 5.7%–6.4%), respectively.

Table 5 shows both unadjusted and adjusted estimates of the association between prediabetic stages

and sociodemographic, lifestyle and clinical characteristics. Multiple logistic regression analyses showed that after adjustments for age, education, physical activity, total grains, total vegetables/fruits, alcohol intake and smoking, the OR for having a prediabetic stage with HbA1c 6.0%–6.4% was higher in females than in males (OR=1.98, 95% CI: 1.07 to 3.67). Further, there was no association between lifestyle variables and the prediabetic stage. An expected lower OR for physical activity (OR=0.65) was observed.

DISCUSSION

In this community-based cross-sectional study including 6222 Nepalese adult participants, the HbA1c-based prediabetes (HbA1c, 5.7%–6.4%) and diabetes (HbA1c≥6.5%) were found in 5%, and 3.2%, respectively. Among 291 responded participants with prediabetes, 156 (54%) and 135 (46%) had HbA1c levels between 5.7%-5.9% and HbA1c between 6.0%-6.4%, respectively. A large proportion with prediabetes were females, aged 45–64 years, had no family history of diabetes, were mostly non-smokers, were overweight, had central obesity and high WHR, followed an unbalanced diet and did not take small frequent meals. There was an association of prediabetic stages with female gender in the adjusted analyses and non-significant reduced OR in relation to physical activity (METs) cannot be ignored.

The HbA1c test was performed only among those participants who met the criteria of IDRS≥60[30] and RBS value 140–250 mg/dL. This step was taken to avoid the high expenses of HbA1c in the screening campaigns. A high standard point-of-care testing for the HbA1c test using a drop of blood was used for the study. This was a convenient approach for the participants as it did not need a fasting phase and thus avoided a long waiting time for the results.[1] This strategy proved to be an efficient way of including participants in community-based screening programmes.[1]

HbA1c is one of the standard tests recommended by the ADA to diagnose prediabetes and diabetes.[1] However, since HbA1c test is expensive, IFG and IGT tests are often used in both clinical and community settings.[1] Evidence suggests an imperfect concordance between HbA1c and glucose-based tests, which might affect the comparability of estimated prediabetes prevalence.[1] For instance, prior studies from Nepal used IFG or IGT to detect prediabetes, resulting in an estimated wide range in prevalence from 1.3% to 19.4%.[4 50–54] Likewise, studies from India where individuals generally follow a similar lifestyle and have a dietary pattern like in Nepal have reported an estimated prevalence of prediabetes in the range 5.6%–14.7% using FBS and RBS test,[55–57] somewhat higher than in the present study. The observed differences may be due to differences in study populations, inclusion criteria of age, study design, use of different prediabetes criteria (WHO or ADA), use of different test methods (HbA1c or FBG or OGTT or RBS), study setup (healthcare centres or community setup) as well as true differences in the prevalence of prediabetes between two countries.

WC is considered to be one of the strongest risk factors for prediabetes.[58] It is also considered to be better than BMI for determining the risk of diabetes[43] although ADA guidelines suggest using BMI≥25 kg/m^2 criteria for screening diabetes for asymptomatic undiagnosed adults.[1] In the present study, WC was measured for all screened participants as it was one of the parameters of IDRS,[30] and weight and height were measured only for participants with prediabetes during their detailed data collection. The study was partly obstructed by the government-mandated COVID-19 lockdown and thus, the weight and height of 111 participants could not be measured. Due to the high proportion of missing data, the association between BMI and prediabetes could not be reliably estimated in the present study. However, it was found to have around 97% of responded participants with high central obesity assessed by WC which was relatively high compared with studies from India.[59 60] The higher proportion may be due to the selection of participants with IDRS≥60. It is also worth noting that the rate of central obesity was high in the present study despite a higher rate of physically active participants. This can be interpreted in several ways. Either self-reporting of physical activity was insufficient to determine the actual physical activity of the participants[61] or their physical activities were not up to the recommended level to reduce central obesity.[62]

Majority of the previous studies have focused on the association of potential predictors with the risk for prediabetes rather than prediabetic stages,[8,56,63,64,65] and few studies on risk factors for prediabetes stages exist.[18 20] One study showed that individuals were older, had lower education, high BMI and a higher rate of hypertension with increasing HbA1c from 5.7%–5.9% to HbA1c 6.0%–6.4%.[18] The present study did not demonstrate all these as significant risk factors, which might be due to the small sample size. Another study showed that the proportion with obesity and a positive family history of diabetes was higher among individuals with HbA1c 6.0%–6.4%,[20] which were not in line with this present study.

It can be argued that risk factors for prediabetic stages are important for further clinical assessment and intervention as HbA1c values in prediabetic ranges convey unequal risk for the development of diabetes.[66] Individuals with HbA1c≥6% have a higher and quicker possibility to land up with diabetes and therefore require more robust lifestyle intervention to delay diabetes than individuals with HbA1c<6%.[6] On the other hand, individuals with HbA1c<6% with other potential factors and comorbidities should also be considered for intervention.[6] Though risk factors for prediabetes may not necessarily be associated with prediabetic stages, these factors were obvious candidates to study. There was no significant association of prediabetic stages with the potential risk factors except gender in the present study. However, the findings should not be seen as contrasting to previous findings since risk

of prediabetic stages and risk of prediabetes are different outcomes. Furthermore, the number of participants with prediabetes in the present study might have been too low to detect moderate or weak associations between prediabetic stages and potential risk factors.

The main strength of the present study was that it identified individuals with prediabetes and diabetes who were unaware of their status using standard tests and techniques. Also, this study contributes to the literature on the prevalence of prediabetes using HbA1c and the association of prediabetic stages with potential risk factors in low-income and middle-income countries like Nepal. The present study is not without limitations. The convenience sampling technique in the screening campaigns might have led to selection bias, which needs to be considered while interpreting the results of the study. Voluntary participation at the screening campaigns might have led to either over or underestimation of the prevalence of prediabetes in the population. Furthermore, due to costs, only individuals who met the criteria of predefined IDRS and RBS cut-off value were selected to undergo the HbA1c test, and thus some individuals may have been misclassified as normoglycemic, leading to a potentially underestimated prevalence of prediabetes. The results come from two urban setups which preclude generalisation to the rural communities. Furthermore, the small sample size leads to low precision of the estimated association between prediabetic stages and potential risk factors, and the power to detect weak or moderate associations was low. In addition, self-reported diet-related and physical activity questionnaires might be tied to information and recall bias. Lastly, some potential variables of interest like cholesterol and other lipid-related parameters have not been measured.

Conclusions and implications

In conclusion, the prevalence of prediabetes was 5% in this community-based study from two urban areas of Nepal. Female gender was associated with prediabetic stages. A large proportion of individuals with HbA1c-based prediabetes aged 45–64 years, had high central obesity or WHR, followed an unbalanced diet, were never smokers, were non-alcohol drinkers, were hypertensive and had no family history of diabetes.

This community-based survey for the detection of prediabetes has a potential impact on the country's policy related to NCDs. It has served as an opportunity for the local governments to initiate activities in their constituencies to detect conditions like prediabetes and diabetes. The study results indicate that comprehensive lifestyle interventions for diabetes prevention may be important in the Nepalese population and points to regular mass screening programmes and early lifestyle interventions in collaboration with local governments as a tool to prevent diabetes at the community level.

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Contributors All authors conceived the study idea, designed the study and finally approved the version for submission. PS and ArS did sample size calculations for the randomised controlled trial. PS analysed the data and drafted the manuscript. ES, ArS and AbSe critically reviewed the analysis and revised the manuscript for important intellectual content. BK, BMK and AbSh reviewed the manuscript. PS took full responsibilty for the study as a guarantor.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design of this research. However, they were involved for selection of sites for screening campagins and they will be involved in dissemination of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval All ethical aspects were considered for the study. The study was approved by the Regional Committee for Medical and Health Research Ethics (REK), Norway [Reg. no. 2019/783]; Nepal Health Research Council (NHRC), Nepal [Reg. no. 324/2019] and Institutional Review Committee, Kathmandu University School of Medical Sciences (IRC-KUSMS), Nepal [Reg. no. 196/19]. In addition, written permission from Dhulikhel Municipality and Lalitpur Metropolitan City (LMC) for Patan was obtained to conduct the study. Written informed consent was taken from all the participants. Patient integrity was maintained using research code. All methods were performed following the relevant guidelines and regulations. The results will be disseminated in the allocated local committees, administrative units, municipalities, universities and diabetes-related organisations and associations.

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