Community screening for undiagnosed dysglycaemia in a semi-urban locality in Sri Lanka

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ABSTRACT

Introduction: Previous studies on the prevalence of pre-diabetes and diabetes in Sri Lanka have shown conflicting results. We studied the prevalence of pre-diabetes and diabetes using fasting plasma glucose (FPG) and 75g oral glucose tolerance (OGTT) test among a representative sample of adults in a semi-urban locality in Southern Sri Lanka. Sensitivity and specificity of FPG over OGTT in diagnosing pre-diabetes and diabetes were calculated.

Methods: Healthy adults, aged 20-75 years, selected by multi-stage random sampling from one medical officer of health area in Southern Sri Lanka were screened with FPG and 75g OGTT. Subjects known to have diabetes were excluded.

Results: Mean (SD) age of men (n=234) and women (n=593) were 44 (10.1) and 43(10.8) years, respectively. With OGTT, 157 (19.0%) subjects had impaired glucose tolerance while another 60(7.3%) had diabetes. With FPG, 270 (32.6%) had impaired fasting glycaemia while another 51(6.2%) had diabetes. Prevalence of pre-diabetes or diabetes was not different among men and women by OGTT; 55 (23.5%) vs 162 (27.3%), $p=0.293$ while it was significantly different by FPG; 107 (45.7%) vs 214 (36.1%), $p=0.011$. Prevalence of pre-diabetes or diabetes was significantly higher in age group ≥ 45 yrs compared to age <45 yrs by both tests. FPG showed low sensitivity (44.7%) but higher (76.1%) specificity of detecting dysglycaemia. FPG showed sensitivity of 53.3% and specificity of 97.5% in detecting undetected diabetes.

Conclusions: Prevalence of pre-diabetes is higher than in previous studies in Sri Lanka. Significantly higher proportion of males compared to females, had pre-diabetes or diabetes by FPG test. Compared to subjects age <45 years, the prevalence of pre-diabetes or diabetes was significantly higher among those ≥ 45 years. FPG lacks adequate sensitivity and specificity to detect those with diabetes or dysglycaemia.

Keywords: *Fasting plasma glucose, OGTT-Oral glucose tolerance test, pre-diabetes*

Introduction

Abnormalities in glucose tolerance, also known as dysglycaemia, are broadly categorized into two groups; pre-diabetes and diabetes mellitus (1). Pre-diabetes is an intermediate stage which may progress to diabetes, remain same or revert back to normal glucose tolerance (2). Similar to diabetes, pre-diabetes also carries a higher risk of

cardiovascular disease (CVD) compared to those with normal glucose tolerance (3,4).

Oral glucose tolerance test (OGTT) is considered the gold standard in detecting dysglycaemia (5). OGTT is more sensitive than fasting plasma glucose (FPG) to detect dysglycaemia (6). Compared to FPG, OGTT as a screening tool has shown more

accurate estimation of dysglycaemia and risk of cardiovascular disease (5).

Epidemiological surveys in Sri Lanka on the prevalence of dysglycaemia have mostly used FPG as the screening tool (7). We aimed to study the prevalence of dysglycaemia using both FPG and OGTT. We also studied the sensitivity and specificity of FPG over OGTT in diagnosing pre-diabetes and diabetes.

Methods

Participants in the age range of 20 - 75 years were selected from the Southern Province of Sri Lanka using a multi-stage random sampling method. Of the 44 Gramasewaka divisions in one Medical Officer of Health (MOH) area in the Southern Province 22 were selected randomly. Thirty-eight subjects were selected, randomly, from each Gramasewaka division using the latest Voters' register to make a total of 836 individuals in the study sample. Each selected participant was invited to attend a medical consultation during which a detailed medical history was obtained and a clinical examination was performed. Pregnant women and those who already had diabetes were excluded. People on long term medications such as glucocorticoids, statins or other lipid lowering drugs were also excluded from the study. Informed written consent was obtained from each participant after explaining the research protocol. Ethical approval was obtained from Ethics Review Committee, Faculty of Medicine, University of Ruhuna, Sri Lanka (Ref: 26.02.2015: 3.14 and 09.03.2016: 4.1).

A pre-tested, interviewer-administered questionnaire was used to collect data. Data collection was done between January 2016 to January 2017. Height was measured to the nearest cm using a stadiometer and weight was measured to the nearest 100 gm without shoes and heavy cloths. A sample of venous blood (2.5 ml) was obtained after 10 hours of fasting for the FPG. Another 2.5 ml of blood was drawn after 2 hours of ingesting 75 g of glucose in 250 ml of clear water for OGTT. Criteria published by the American Diabetes Association for the diagnosis of diabetes and pre-diabetes were followed (1).

Analysis

Continuous variables of baseline characteristics between the two age groups (Age < 45 years and $\geq$ 45 years) and different glycaemic status were compared by t-test (unpaired) and categorical variables were compared with chi-squared test.

Results

Table 1 shows the baseline characteristics of the study sample. Based on FPG, 506 (61.2%) participants were normoglycaemic, while 270 (32.6%) had impaired fasting glycaemia (IFG) and 51 (6.2%) had diabetes. According to OGTT 2 hr plasma glucose test 610 (73.8%) were normoglycaemic while 157 (19%) had IGT and 60 (7.3%) had diabetes. Among the participants 20.8% had isolated IFG, 8.5% had isolated IGT, and 9.2% had both IGT + IFG.

Table 1: Baseline characteristics of the study sample

Measurement	Mean (SD) (n= 827)
Age (years)	43 (10)
FPG (mg/dL)	98.1 (25.5)
2 hr plasma glucose value of OGTT (mg/dL)	128.7 (59.2)
BMI (kg/m ²)	24.7 (4.3)
Hip circumference (cm)	93.2 (8.5)
Waist circumference (cm)	85.9 (8.9)

FPG - Fasting Plasma Glucose, OGTT- Oral Glucose Tolerance Test, BMI- Body Mass Index.

With FPG, there were more males with IFG alone or combined IFG and DM. With OGTT, however, there was no significant gender difference in either IGT or combined IGT and DM. These results are shown in the Table 2.

As the American Diabetes Association recommends limiting community screening for those >45 years

of age, we estimated the prevalence of dysglycaemia among subjects below and above the age of 45 years in this study sample. Results are shown in the Table 3.

Table 3 shows that age related rising prevalence of dysglycaemia with both methods of testing when the cut off age level is 45 years.

Table 2: Different glycaemic status among male and female participants

Glycaemic status (as %)	Male (n=234)	Female (n=593)	p-value*
FPG test			
Normoglycaemia	127 (54.3)	379 (63.9)	0.03
Impaired fasting glycaemia	89 (38)	181 (30.5)	
Newly diagnosed diabetes mellitus	18 (7.7)	33 (5.6)	
FPG test			
Normoglycaemia	127 (54.3)	379 (63.9)	0.01
Impaired fasting glycaemia + Newly diagnosed diabetes mellitus	107 (45.7)	214 (36.1)	
OGTT test			
Normoglycaemia	180 (76.9)	431 (72.7)	0.3
Impaired glucose tolerance	37 (15.8)	120 (20.2)	
Newly diagnosed diabetes mellitus	18 (7.7)	42 (7.1)	
OGTT test			
Normoglycaemia	179 (76.58)	431 (72.7)	0.3
Impaired glucose tolerance + Newly diagnosed diabetes mellitus	55 (23.5)	162 (27.3)	

*compares the gender difference of dysglycaemia. FPG- Fasting Plasma Glucose, OGTT- Oral Glucose Tolerance Test.

Table 3: Glycaemic status in different age groups

Glycaemic status	Age < 45 years (%)	Age ≥ 45 years (%)
FPG test		
Normoglycaemia	300 (66.1)	206 (55.2)
Impaired fasting glycaemia	134 (29.5)	136 (36.5)
Newly diagnosed diabetes mellitus	20 (4.4)	31 (8.3)
OGTT test		
Normoglycaemia	359 (79.1)	251 (67.3)
Impaired glucose tolerance	72 (15.9)	85 (22.8)
Newly diagnosed diabetes mellitus	23 (5.1)	37 (9.9)

FPG - Fasting Plasma Glucose, OGTT - Oral Glucose Tolerance Test

Table 4: BMI, waist to hip ratio and blood pressures (mean and SD) among individuals with dysglycaemia in two different age groups

	Age < 45 years	Age = 45 years	p-value
BMI (kg/m ²)	26.1 (3.8)	25.1 (4.3)	0.12
Waist to hip ratio for females	0.92 (0.05)	0.93 (0.05)	0.69
Systolic blood pressure (mmHg)	122 (13)	128 (14)	0.001
Diastolic blood pressure (mmHg)	77 (8)	80 (8)	0.01
Fasting blood sugar (mg/dL)	112 (34)	118 (39)	0.26

BMI - Body Mass Index

Subjects aged 45 years or above with dysglycaemia had higher systolic and diastolic blood pressures when compared with subjects below 45 years with similar condition (Table 4). Waist to hip ratio and BMI, however, were not significantly different between the two groups.

When OGTT was considered the gold standard to detect dysglycaemia, FPG had low sensitivity (44.7%) but higher specificity (76.1%) of detecting dysglycaemia. Furthermore, FPG showed a sensitivity of 53.3% and specificity of 97.5% in detecting undetected diabetes.

Discussion

This cross-sectional, community-based study conducted in a semi-urban area in Southern Sri Lanka reveals several important findings. We found 7.3% people to have undetected diabetes based on the OGTT. Prevalence of IFG was about 1.7 times higher than the prevalence of IGT. Further, males have a higher prevalence of dysglycaemia compared to females. Among our subjects, isolated IFG prevalence is 2.4 times higher than isolated IGT. Compared to subjects below 45 years, those aged 45 years or above had higher systolic and diastolic blood pressures and a higher prevalence of dysglycaemia.

Several community based studies have reported different prevalence rates of diabetes and pre-diabetes in Sri Lanka (8,9). Most of them have reported the overall prevalence (both previously known and newly diagnosed) of diabetes. Except one study which used both FPG and OGTT, all other studies have used only FPG as the screening test.

The largest study conducted in Sri Lanka which included 6047 subjects from four provinces revealed diabetes prevalence of 14.2% in men and 13.5% in women (10). In the same study, IFG, was detected in 14.2% and 14.1% in men and women respectively. A national survey carried out in 2005 and 2006 representing all districts in the country including a sample of five thousand participants over the age of 18 years revealed 10.3% prevalence of diabetes with nearly one third (3.8%) of newly diagnosed patients (11). The prevalence of pre-diabetes (IGT) was 11.5% in this study. However, in this survey, OGTT was carried out only in participants who were not found to have diabetes with FPG test and this may have led to underestimation of prevalence of dysglycaemia. Pinidiyapathirage, *et al.*, in 2007 reported a prevalence of newly diagnosed diabetes as 9.4%. Prevalence of undiagnosed diabetes mellitus was high with increasing age and in female gender compared to males (7). In this study too, slightly more than one third (35%) of all patients with diabetes were newly detected subjects with diabetes. The prevalence of IFG in this study was 50.3%. The higher prevalence of dysglycaemia in this study could partly be due to the selection of study sample from an urban community. According to a recent study conducted in urban, rural and plantation sectors of Kalutara district, age and sex adjusted prevalence of IFG was 14.3% (8).

A national survey carried out in 2005 and 2006 showed non-significant difference of prevalence of pre-diabetes between males and females, even though the females found to have significantly higher prevalence of isolated IGT

and IGT+IFG (11). Pubudu De Silva, *et al.*, showed that females have significantly higher prevalence of IFG when compared to males (8). An Indian study done in 2011 showed almost similar results and prevalence of IFG was 2 to 2.4 times higher than IGT (12). A New Zealand study done in 2017 also showed 2.7 times higher prevalence of IFG than IGT (13).

According to the American Diabetes Association, screening for diabetes or pre-diabetes should be started at all asymptomatic adults at the age of 45 years (14). Sri Lankan studies conducted in 2005 - 2007 showed the rising prevalence of newly diagnosed diabetes with aging (11,15). Several studies in Asian countries and western countries also showed significant increase in prevalence of pre-diabetes or dysglycaemia with aging (16). A study conducted in Malaysia in 2011 showed almost half of the adults with pre-diabetes in aged group between 30 - 49 years and age as a risk factor for the development of pre-diabetes (17).

Current study, conducted in a semi-urban community in Southern Sri Lanka in 2017 revealed that the prevalence of newly diagnosed diabetes has doubled (from 3.8% in 2006 to 7.3% in 2017 with OGTT) in semi-urban setting. The prevalence of IGT has shown an upward trend from 11.5% in the nationwide study in 2006 to 19% in the current study. Exponential rise in the incidence of both forms of dysglycaemia; newly diagnosed diabetes and pre-diabetes, compared to last decade in the Sri Lankan community is the most striking finding of the current study.

With rising incidence of both forms of dysglycaemia in the Sri Lankan community, it would be useful to explore the sensitivity and specificity of the most commonly used screening tools, FPG estimation and OGTT in the diagnosis of diabetes mellitus and pre-diabetes. This would be relevant in the background of increasing evidence in the literature on the association of pre-diabetes with increased risk of CVD. Further, adherence to special lifestyle modifications and use of specific pharmacotherapy to delay the progression pre-diabetes to diabetes with favourable clinical outcomes is recommended by professional organizations (18). One study was conducted in 2019 to compare the sensitivity and specificity of FPG with OGTT in the diagnosis of

pre-diabetes in the local setting and it showed low sensitivity to detect pre-diabetes similar to our finding. Even the nationwide survey conducted in 2006-2007, has not screened every participant with both FPG and OGTT (7). According to our findings in Sri Lankan setting, classification of IFG as pre-diabetes is not diagnostically accurate, when compared with the diagnosis of IGT with the gold standard OGTT. Studies conducted in Asian and Caucasian populations have revealed similar findings (6,19). One recent study was conducted to compare the sensitivity and specificity of FPG with OGTT in the diagnosis of pre-diabetes in the local setting and it showed FPG has low sensitivity to detect pre-diabetes similar to our findings (20). Use of OGTT or alternative screening tools such as glycosylated hemoglobin in addition to FPG to diagnose individuals with the pre-diabetes have been recommended to improve the diagnostic yield of pre-diabetes (5).

Although this study revealed the value of screening tests in the diagnosis of dysglycaemia in the community setting in Sri Lanka, it has few limitations. At the outset, this study sample excluded individuals with previous diagnosis of diabetes and it prevented us from the estimation of overall prevalence of diabetes in this community. As the study was conducted in a one semi-urban geographical area, findings on the prevalence rates of dysglycaemia may not extrapolated to the whole country. Comparison of prevalence of newly diagnosed diabetes and pre-diabetes in the rural and urban settings was also not possible with the finding of this study. The most significant strength of this study is that, it was done on a randomly selected large sample and all participants were tested with both FPG and OGTT. This enabled us to discover that FPG is not as good as OGTT to detect newly diagnosed diabetes in the community and its performance in the detection of dysglycaemia is also not satisfactory as a screening test. Diabetes needs to be excluded when patients present with vascular diseases like peripheral arterial disease, cerebrovascular disease and cardiovascular disease. As FPG has a limitation to diagnose dysglycaemia, we consider to use more specific investigations like HbA1c to screen individuals for dysglycaemia since OGTT is cumbersome. We hope these findings would be useful in planning out large-scale studies

in future and selecting appropriate screening tools to detect different categories of dysglycaemia.

In conclusion, we report that the prevalence rates of newly diagnosed diabetes and pre-diabetes have doubled during the last decade in Sri Lanka. As a screening tool in the community setting, FPG lacks adequate sensitivity and specificity to detect those with diabetes or dysglycaemia.

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Conflicts of interests

There is no conflict of interest.

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