Type 2 diabetes mellitus has become a global epidemic, affecting approximately 8.5% of all individuals and leading to 3 million deaths globally, as a result of its complications every year. By 2025, of those diagnosed with diabetes, it is predicted that almost three quarters will live in developing countries.

In South Africa, the prevalence of diabetes is estimated at 6%, affecting approximately 1.9 million of 30 million adults. During 2004-2005, diabetes was responsible for the second highest increase in cause of death after HIV, placing a substantial burden on the already resource-constrained South African health care system. The prevalence varies among ethnic groups, with a marked increase in people of Indian ethnicity, who are vulnerable to developing premature CV disease as a consequence of diabetes. There is currently little data available on the number of individuals who have undiagnosed diabetes in this population, nor have optimal screening tools been identified in this group.

Currently, the American Diabetes Association (ADA) recommends the use of the fasting plasma glucose (FPG) and the two-hour postprandial oral glucose tolerance test (OGTT) for the detection of diabetes. Although more convenient, FPG has lower sensitivity in identifying diabetes than the OGTT.

In 2009 the ADA and the WHO recommended HbA1c as a diagnostic tool for the detection of diabetes using a cutoff >6.5%, but this test is limited due to the lack of standardization of reference ranges across ethnic groups and age. A meta-analysis showed a 0.65% higher HbA1c level underscores the need for ongoing national surveillance data.

#### Objectives

There is no definitive consensus on the screening algorithm in high-risk communities for diabetes. The aims of our study were to determine the prevalence of undiagnosed diabetes in a high-risk community using the oral glucose tolerance test (OGTT), as well as determine the value of anthropometric measurements and other measures of glycemia in the detection of diabetes.

#### Method

All participants from the Phoenix Lifestyle project without known diabetes, and who had undergone an OGTT were selected for study. Anthropometric measurements were collected according to accepted guidelines. Diabetes was diagnosed if fasting plasma glucose (FPG) ≥7.0 mmol/l, if 2-hour plasma glucose level during OGTT was ≥11.0 mmol/l, or if HbA1c ≥ 6.5%.

#### Results

The prevalence of newly diagnosed diabetes was 14.3% (11.7% age standardized) (women=15.4%; men=11.8%). The prevalence rates were underestimated using FPG criteria, but overestimated when using the HbA1c. The AUC (area under the receiver-operator characteristics curve) was highest for FPG (.879), HbA1c (.855), then anthropometry measures (BMI=.621; waist circumference=.627). For diabetes, at levels ≥6.3, the discriminant ability (DA) of HbA1c was highest (79%), while a cut-point of ≥5.5mmol/l for FPG yielded a DA=81.5% (82% sensitivity; 81% specificity); there was a low level of agreement between the FPG (Kappa = .506), HbA1c (Kappa = .537), and the OGTT. Age- and sex-adjusted independent determinants of diabetes using stepwise backward logistic regression were age, triglyceride levels and a positive family history for diabetes.

#### Conclusion


#### Keywords

Diabetes; HbA1c; Asian Indians; Fasting Plasma Glucose; OGTT

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in African Americans compared with non-Hispanic Whites, which was attributed to variations in glycemic control.\textsuperscript{13} In contrast, a review of 25 studies showed the same diagnostic value for diabetes in Eastern and Western populations,\textsuperscript{14} highlighting the lack of agreement on the usefulness of HbA1c as a screening tool.\textsuperscript{12}

Recently, anthropometric indices such as the body mass index and waist circumference measurements have been found to be useful in cardiovascular risk stratification, particularly for diabetes,\textsuperscript{15} but these measures have not been tested for the detection of diabetes, especially in Indian Asians. In our study, we determined the prevalence of undiagnosed diabetes among Asian Indians in the cadastral district of Phoenix, north of Durban and we examined the predictive accuracy of glycemic and anthropometric measures in the detection of undiagnosed diabetes in this group.

**METHODS**

This study used data from the Phoenix Lifestyle Project (PLP), which was a cross-sectional survey of risk factors among 1,428 randomly selected participants between the ages of 15 and 64 years in the district of Phoenix, north of Durban. Detailed methodology has been described previously.\textsuperscript{6} Briefly, after informed consent was taken, blood samples were collected to measure plasma glucose, serum insulin and serum lipids (LDL calculated using Friedwald equation) following an overnight fast. For our study, we selected all participants from the PLP without known diabetestes who had undergone a two-hour oral postprandial glucose tolerance test (OGTT). Diabetes was diagnosed according to the American Diabetes Association criteria\textsuperscript{16} as follows: FPG ≥7.0 mmol/l/126.0mg/dL, or 2 hour plasma glucose level during OGTT ≥11.0 mmol/l/198.19mg/dL, or HbA1c ≥ 6.5%. Since the OGTT is an early marker for impaired glucose homeostasis, as well as a sensitive indicator for the risk of diabetes development,\textsuperscript{8} it was used as the reference for comparison with the FPG and HbA1c for the detection of previously undiagnosed diabetes.

**Statistical Analysis**

Statistical analysis was performed using SPSS statistical package (v24.0). Baseline characteristics of study participants are presented as mean and standard deviation (SD). The prevalence and 95% CIs for undiagnosed type 2 diabetes (DM), IFG and IGT were determined for the entire population, as well as in subgroups according to age and sex. Comparisons of the prevalence rates and patient characteristics across glucose tolerance categories were performed using chi-squared tests and one-way ANOVA. The prevalence of diabetes was age-standardized using the WHO standard world population distribution.\textsuperscript{17}

Receiver operating characteristic (ROC) curves were constructed to calculate sensitivity, specificity, and predictive values determined at different cut-off values for HbA1c, FPG, waist circumference (WC) and body mass index (BMI) for the diagnosis of diabetes. The Kappa coefficient was used to test for agreement between HbA1c, OGTT, WC and BMI-based diagnosis for diabetes and the OGTT. P <.05 were considered statistically significant.

**RESULTS**

Complete datasets were available for 1,378 of the 1,428 participants in the PLP. Of these, 1,076 participants were not previously diagnosed with diabetes, and underwent the OGTT. Of these, 154 (14.3%) were classified as having diabetes by the OGTT and comprised our study group. The group was compared to the remaining 922 (85.7%) participants without diabetes according to the OGTT.

The prevalence of newly diagnosed diabetes (Table 1) was higher in women compared with men (15.4% vs 11.9%). Newly diagnosed diabetestes had higher BMI (29.4±5.8 vs 27.1±6.5) and waist circumference levels (97.4±15.2 cm vs 91.3±15.0 cm), as well as higher levels of blood pressure and biochemical parameters. They also had a higher prevalence (78.4% vs 60.6%) of positive family history for diabetes (P<.001). There was a preponderance of both abdominal and generalized obesity in diabetestes (71.4%) and to a lesser degree in those classified without diabetes (54.7%).

The prevalence of newly diagnosed diabetes was age-standardized to 11.7% (Table 1). There was a marked increase in the crude prevalence of newly diagnosed diabetes from 3.1% in the first decile (15-24 yr) to 22.1% in the fifth decile (55-64 yr) (P trend <.001). These prevalences were underestimated using FPG (4.6%), but overestimated when using the HbA1c ≥ 6.5% (14.9%)(Table 1) when com-
pared with the OGTT. The crude prevalence increased to 20.6% when the HbA1c and the fasting plasma glucose were combined, and this further increased to 23.9% (n=257) when the three tests were combined.

A low level of agreement between the fasting plasma glucose and the OGTT as well as between the HbA1c and the OGTT for the diagnosis of diabetes was observed (Kappa = .506, OR=.103; CI .8, .13 and .537,OR =.09; .07, .13). Only 39.6% of participants with FPG ≥7.0mmol/l (126.0 mg/dL) were classified as diabetic by the OGTT. In contrast 72.7% of individuals with HbA1c ≥6.5% were classified diabetic by the OGTT. Taken together, the HbA1c and FPG over-diagnosed diabetes two-fold (n=308). There was .8% and 10.7% discordance in FPG and HbA1c with the OGTT, respectively in those participants classified without diabetes.

The ROC curves using the OGTT as a reference for the diagnosis of diabetes (Figure 1) indicated the highest area under the curve for FPG (.879), followed by the HbA1c (.855), while the anthropometric measures had

<table>
<thead>
<tr>
<th>Table 1. Baseline characteristics of participants without known diabetes by glycemic status using the OGTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=1076</td>
</tr>
<tr>
<td>Diagnosis by FPG (≥7.0 mmol/l)(126.0 mg/dL)</td>
</tr>
<tr>
<td>Diagnosis by HbA1c (≥ 6.5%)</td>
</tr>
<tr>
<td>Diagnosis by FPG (≥7.0 mmol/l)(126.0 mg/dL) + HbA1c (≥ 6.5%)</td>
</tr>
<tr>
<td>Diagnosis by FPG+HbA1c+OGTT</td>
</tr>
<tr>
<td>Oral glucose tolerance test (≥11.0 mmol/l)(198.19 mg/dL)</td>
</tr>
</tbody>
</table>

Males, n=326, 30.1%
Females, n=750, 69.7%
Age<sup>a</sup> 40±14 49±10 <.001 (trend)
15-24, n=123 118(96.9) 5(3.1) <.001 (trend)
25-34, n=151 141(93.4) 10(6.6) <.001 (trend)
35-44, n=249 222(89.1) 27(10.9) <.001 (trend)
45-54, n=320 261(81.5) 59(18.5) <.001 (trend)
55-64, n=240 187(77.9) 53(22.1) <.001 (trend)
BMI, kg/m<sup>2</sup> 27.1±6.5 29.4±5.8 <.001
Waist circumference, cm 91.3±15.0 97.4±15.2 <.001
Mean systolic BP, mm Hg 129.8±19.7 139.6±20.6 <.001
Mean diastolic BP, mm Hg 80.1±12.1 85.3±12.4 <.001
FPG, mmol/l 5.0±.7 7.7±3.2 <.001
FPG, mg/dL 90.0±12.6 136.6±57.6 <.001
Two-hour glucose, mmol/l 6.8±1.8 15.6±4.5 <.001
Two-hour glucose, mg/dL 122.4±32.4 280.8±81.0 <.001
HbA1c (%) 5.9±.8 7.8±2.1 <.001
Total cholesterol, mmol/l 5.2±1.1 5.7±1.1 <.001
Total cholesterol, mg/dL 200.77±42.47 220.08±42.47 <.001
Triglycerides, mmol/l 1.5±3.1 2.1±1.3 .020
Triglycerides, mg/dL 132.74±274.3 185.8±115.04 .020
HDL, mmol/l 1.33±0.5 1.27±.3 .05
HDL, mg/dL 51.35±19.31 49.03±11.58 .05
LDL cholesterol, mmol/l 3.29±1.0 3.5±1.1 <.001
LDL cholesterol, mg/dL 127.03±38.61 135.14±42.47 <.001
Smoker 205(31.4) 36(23.5) <.001
Hypertension 152(23.3) 68(44.4) <.001
Positive family history of diabetes 559(60.6) 117(78.4) <.001

Frequencies presented as n(%); data are mean values ±SD; BMI, body mass index
<sup>a</sup> WHO direct age standardization.
<sup>b</sup> P calculated using ANOVA

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lower AUCs (BMI=.621; waist circumference=.627). The established HbA1c cut-point of ≥ 6.5% yielded a sensitivity of 66% with a specificity of 90% for the diagnosis of diabetes (Table 2). A lower cut-point of ≥ 6.25% yielded a higher sensitivity of 75%, at the cost of a lower specificity, which fell to 80%. The discriminating capacity of HbA1c [(sensitivity + specificity)/2] was highest (78%) at levels ≥6.3%.

The optimal cut-point of ≥5.5mmol/l (99 mg/dL) for FPG for the diagnosis of diabetes yielded 82% sensitivity and specificity of 81% (discriminant capacity 81.5%). An FBG ≥7.0 mmol/l (126.0 mg/dL) improved specificity (99%), but had poor sensitivity (40%) and discriminant capacity (69.5%). Backward stepwise multiple logistic regression analysis (age and sex adjusted) (Table 3) for the risk of developing diabetes was performed (age, sex, mean diastolic blood pressure, BMI, waist circumference, total cholesterol, HDL and LDL cholesterol and triglyceride levels and a positive family history for diabetes adjusted for each other). Independent determinants of diabetes were age, mean diastolic pressure, BMI, triglyceride levels and a positive family history for diabetes. A one-unit increase in triglycerides (OR=1.5; CI 1.2,1.9; P<.001) was associated with a 1.5-fold risk for the development of diabetes. A positive family history almost doubled the risk of developing diabetes (OR=1.6; CI 1.09,2.34; P=.017).

**Discussion**

Using the OGTT, the prevalence of undiagnosed diabetes in this community was similar to the report by Herath et al in the Sri Lankan population (16.1%). The explanation for the high prevalence of undiagnosed diabetes is in marked contrast to Western series, which show much lower prevalence of approximately 2%. In addition, our data showed a higher prevalence in women (15.4%) and is at odds with studies that have reported a higher prevalence in men.

The HbA1c identified a substantial number (14.9%) of newly diagnosed diabetes patients in this study, and has also been reported in other studies of Asian participants. The literature cautions against the use of HbA1c for the diagnosis of diabetes, since this test has a low sensitivity and reliability for diagnosing diabetes or impaired glucose tolerance, particularly when considering other factors like sex, iron deficiency, smoking and alcohol consumption, and aging. These factors are of relevance in our study that had a preponderance of women, and suggests a role for ethnic-specific cut-points to accurately identify individuals with diabetes.

At levels of ≥5.5 mmol/l (99 mg/dL), FPG identified diabetes with
good sensitivity and specificity and a high discriminant capacity (81.5%). The Australian guidelines have recommended lower FBG cut points since this reduces the number of false negative individuals. Although FPG is reported to have lower intra-individual coefficients of variation than OGTT,27 the FPG detected fewer patients.28,29 The discordance may be attributed to FPG and OGTT glucose representing different entities in impaired glucose regulation and metabolism.20

Our study found that using a lower level than recommended by the ADA at ≥6.25% provided the most accurate measurement for diagnosing diabetes, and is consistent with a recommendation for lower thresholds in high-risk Arabic populations.29

The effects of anthropometry measures for cardiovascular risk stratification were attenuated when compared with measures of glycemia. However, our values were comparable to those of Hajiani-Tilaki.30

Our study identified age, obesity, a positive family history and diastolic blood pressure as independent determinants for diabetes mellitus, which is well-established in the literature. In addition, we also identified triglyceride levels as an independent predictor of diabetes. The contribution of triglycerides to the diabetic state has been previously reported,31 attributed to the fed/fasted state, insulin sensitivity, and lifestyle factors. The high free fatty acids derived from triglycerides is thought to diminish insulin sensitivity, increasing risk for diabetes mellitus.31

**Limitations**

Because of its cross-sectional nature, this study could not address causality, nor could future risk for diabetes be predicted. The study was skewed toward a predominance of women in the sample, a finding that has been observed in other similar studies conducted in South Africa. The hemoglobin in our participants was not measured; therefore, the influence on HbA1c levels could not be determined.

**CONCLUSION**

This study highlights the high prevalence of undiagnosed diabetes and shows that anthropometric measures had a low predictive accuracy for the detection of diabetes in a group of South African Asian Indians. Based on our findings, we recommend including the use of the OGTT for diagnostic confirmation of diabetes in this population and underscore the need for national surveillance data.

### Table 2. Sensitivity, specificity, positive and negative predictive values and discriminant ability of HbA1c and FPG for detecting diabetes as defined by the OGTT

<table>
<thead>
<tr>
<th>HbA1c (%)</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>PPV, %</th>
<th>NPV, %</th>
<th>Discriminant ability, %</th>
<th>FPG, mmol/l/ mg/dL</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>PPV, %</th>
<th>NPV, %</th>
<th>Discriminant ability, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥6.15</td>
<td>78</td>
<td>74</td>
<td>36</td>
<td>83</td>
<td>76.0</td>
<td>≥5.5/99.09</td>
<td>82</td>
<td>81</td>
<td>79</td>
<td>85</td>
<td>81.5</td>
</tr>
<tr>
<td>≥6.25</td>
<td>75</td>
<td>80</td>
<td>36</td>
<td>81</td>
<td>77.5</td>
<td>≥5.6/100.90</td>
<td>79</td>
<td>85</td>
<td>79</td>
<td>85</td>
<td>82</td>
</tr>
<tr>
<td>≥6.3</td>
<td>71</td>
<td>85</td>
<td>34</td>
<td>79</td>
<td>78.0</td>
<td>≥5.7/102.70</td>
<td>76</td>
<td>89</td>
<td>77</td>
<td>88</td>
<td>82.5*</td>
</tr>
<tr>
<td>≥6.4</td>
<td>69</td>
<td>87</td>
<td>32</td>
<td>78</td>
<td>78.0</td>
<td>≥5.8/104.50</td>
<td>73</td>
<td>90</td>
<td>73</td>
<td>90</td>
<td>81.5</td>
</tr>
<tr>
<td>≥6.5</td>
<td>66</td>
<td>90</td>
<td>30</td>
<td>77</td>
<td>78.0</td>
<td>≥5.9/106.30</td>
<td>70</td>
<td>93</td>
<td>70</td>
<td>92</td>
<td>81.5</td>
</tr>
<tr>
<td>≥7.0</td>
<td>40</td>
<td>99</td>
<td>40</td>
<td>99</td>
<td>69.5</td>
<td>≥7.0/126.13</td>
<td>40</td>
<td>99</td>
<td>40</td>
<td>99</td>
<td>69.5</td>
</tr>
</tbody>
</table>

PPV, positive predictive value; NPV, negative predictive value; discriminant ability = (sensitivity + specificity)/2

### Table 3. Multiple logistic regression for the risk of developing diabetes

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>1.04 (1.02,1.06)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Female</td>
<td>.75 (.484,1.16)</td>
<td>.204</td>
</tr>
<tr>
<td>Mean diastolic BP, mm Hg</td>
<td>1.01 (1.01,1.033)</td>
<td>.036</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>1.04 (1.004,1.08)</td>
<td>.031</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>.992 (.97,1.01)</td>
<td>.426</td>
</tr>
<tr>
<td>Total cholesterol, mmol/l; mg/dL</td>
<td>1.19 (1.87,1.62)</td>
<td>.276</td>
</tr>
<tr>
<td>Triglycerides, mmol/l; mg/dL</td>
<td>1.51 (1.2,1.89)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>HDL Cholesterol, mmol/l; mg/dL</td>
<td>.75 (.295,1.06)</td>
<td>.075</td>
</tr>
<tr>
<td>LDL, mmol/l; mg/dL</td>
<td>.853 (.618;1.18)</td>
<td>.334</td>
</tr>
<tr>
<td>Family history of DM</td>
<td>1.61 (1.09;2.27)</td>
<td>.017</td>
</tr>
</tbody>
</table>
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CONFIDENT OF INTEREST
No conflicts of interest to report.

AUTHOR CONTRIBUTIONS
Research concept and design: Prakashendra, Naidoo; Acquisition of data: Prakashendra; Data analysis and interpretation: Prakashendra, Naidoo; Manuscript draft: Prakashendra, Naidoo; Statistical expertise: Prakashendra, Naidoo; Acquisition of funding: Naidoo; Supervision: Naidoo

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