A Systematic Review comparing HbA1c to fasting plasma glucose and the oral glucose tolerance test in the diagnosis of type 2 diabetes mellitus in Adults.

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Background

The global prevalence of diabetes in 2014 was 9% in adults aged 18 years or more. About 387 million people globally had diabetes in 2014 and it is estimated that there will be a 55% rise to about 992 million by the year 2035. In 2012, about 1.5 million deaths were directly attributable to diabetes, and this rose to 4.9 million in 2014. About 80% of deaths due to diabetes occur in low and middle income countries. Diabetes has been projected to become the 7th leading cause of death by the year 2030. Type 2 diabetes (T2DM) accounts for 90% of the global prevalence of diabetes.

Non-modifiable risk factors for developing T2DM include age, sex, ethnicity, family history, gestational diabetes (GDM) and polycystic ovarian syndrome (PCOS). Its prevalence increases with age and in the United Kingdom, T2DM is three to four times more prevalent in people of south Asian, African and Caribbean roots. The modifiable risk factors include being overweight or obese, physical inactivity, sedentary behaviour, dietary factors, smoking, impaired glucose tolerance or fasting glycaemia, abnormal lipid profile, hypertension, inflammation and intrauterine factors. Being overweight or obese is the single most important predictor of developing T2DM.

About 50% of people with diabetes are undiagnosed. According to the WHO criteria for the diagnosis of T2DM, fasting plasma glucose (FPG) ≥ 7.0mmol/l (126mg/dl), random plasma glucose ≥ 11.1mmol/l or 2-hour plasma glucose (2H PG) ≥ 11.1 mmol/l (200mg/dl) is diagnostic of diabetes in a patient with symptoms. In 2011, the WHO added HbA1c ≥ 48mmol/mol (6.5%) as the recommended cut off point for diagnosing T2DM. A value of less than 6.5% does not exclude T2DM diagnosed using blood glucose tests and it should be repeated in asymptomatic patients.

A total of 2160 studies were retrieved and 1977 studies remained following the removal of duplicate studies. On screening of the titles and abstracts, 62 studies were found to be eligible. A total of 24 studies were included in this systematic review following the review of the full articles.

Method

Ovid Medline, EMBASE, Cochrane databases of systematic reviews, Database of reviews of abstracts and extracts, PubMed and CINAHL Plus were searched.

Selection criteria

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
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<tbody>
<tr>
<td>• Comparison of HbA1c to FPG or OGTT to make T2DM diagnosis</td>
<td>• Age less than 18 years</td>
</tr>
<tr>
<td>• More than 18 years old</td>
<td>• Type 1 diabetes</td>
</tr>
<tr>
<td>• Published after 2011</td>
<td>• Acute illness</td>
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</table>

Conclusion

This systematic review shows that the prevalence of type 2 diabetes mellitus varies depending on the diagnostic criteria used and on the characteristics of the population being studied. These characteristics include the sex, age, ethnicity, overweight/obesity, family history of T2DM, history of GDM or PCOS.

This review shows that HbA1c captures different groups as having T2DM in comparison to the blood glucose tests. One study found a tripling of the prevalence of T2DM based on HbA1c and this was mainly in older people, people in lower socio economic class and in rural areas. Of these, 40% were found to have normal FPG. Another study found that nearly 50% of individuals with HbA1c ≥ 6.5% were not classified as having T2DM based on FPG alone. A study examining the effect of age on HbA1c found that its levels increased by 0.1% per decade in people with normal glucose tolerance and by 0.07% in those with impaired fasting glycaemia or impaired glucose tolerance.

Prevalence of T2DM:

• In comparison to FPG, ten studies reported a higher prevalence whilst six studies reported a lower prevalence to be lower based on the HbA1c criterion. In one study prevalence was comparable for either method.

• In comparison to OGTT criterion, prevalence was lower using the HbA1c criterion in all but one study where the prevalence was comparable. In two studies, those who had T2DM based on OGTT results, half of them were detected by HbA1c.

• Measures of performance of HbA1c ≥ 6.5% criteria as a diagnostic criteria for T2DM

The measures of agreement reported in this review were kappa (K), Pearson’s correlation coefficient (r) and the spearman’s correlation coefficient (R).

• Three studies reported a high degree of agreement, five studies reported moderate agreement and a third study reported poor agreement between HbA1c and the OGTT criterion.

• Nine studies reported values for Area under the Receiver Operating Characteristic curve (AROC) for HbA1c ≥ 6.5% and all the AROC values were more than 0.5 irrespective of the reference test used.

Prevalence of T2DM

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FPG</td>
<td>26.6-76</td>
<td>68-300</td>
<td>27-87</td>
<td>85-98</td>
</tr>
<tr>
<td>OGTT</td>
<td>16.7-62</td>
<td>62-100</td>
<td>42.6-65</td>
<td>41-78</td>
</tr>
<tr>
<td>FG/OGGT</td>
<td>30.7-73</td>
<td>62-799</td>
<td>58-63</td>
<td>80-98</td>
</tr>
</tbody>
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References