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General Practitioners,
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Re: Diabetes Diagnosis

Dear Colleague

Diagnosis of diabetes has been dependent on glucose tests for a number of years and case finding relied on fasting glucose values, augmented by oral glucose tolerance testing (OGTT) if fasting glucose levels were abnormal.

A World Health Organisation (WHO) consultation has concluded that glycated haemoglobin (HbA1c) can be used to diagnose diabetes. The rationale for this is the observation that the cut off point of 48mmol/mol (6.5%) correlates with the significant increase in risk for the development of diabetic retinopathy and the correlation is stronger than that for fasting plasma glucose.

It is now recommended to use HbA1c rather than fasting or random glucose testing or OGTT to diagnose diabetes in patients who you suspect in having the condition. Random glucose testing is rarely helpful unless the patient is symptomatic and should be discouraged.

HbA1c \geq 48mmol/mol, on two occasions in asymptomatic individual, diagnoses diabetes. If symptomatic, a single test will suffice. Diagnostic criteria are outlined in attached Swindon diabetes diagnosis guideline, which has been developed recently. A second HbA1c test would usually be taken 2-4 weeks after the first test in asymptomatic patient to confirm diabetes diagnosis. **Please note the repeat HbA1c sample must be sent with clinical detail (e.g. “repeat HbA1c to confirm diagnosis of diabetes”), as repeats within 60 days may be rejected by the GWH laboratory and also to alert the lab paying attention to the sample received for possible abnormal haemoglobins.**

There are some potential problems with using HbA1c to diagnose diabetes. HbA1c reflects prevailing glycaemia over the preceding two or three months, so may not be elevated if glucose levels have risen acutely, or where there is abnormal haemoglobin metabolism. Clinicians need to be aware of certain clinical situations where HbA1c may not be suitable for diagnostic use in diabetes, and where glucose tests must be undertaken (see guideline).

Most haemoglobin traits do not affect the level of HbA glycation or its analytical quantitation. In particular, Sickle Cell trait and HbA/HbC, HbA/HbD, HbA/HbE heterozygotes do not interfere with HbA1c analysis and the result is valid. Thalassaemia α and β do not interfere with HbA1c analysis and the result is valid. Rarer haemoglobinopathies including homozygous sickle cell and complex thalassaemia/haemoglobinopathy heterozygotes may interfere and blood glucose/OGTT are advised.

Most abnormal haemoglobins will be picked up by standard HbA1c assays, but a frequently encountered important clinical situation in which HbA1c may be raised is in the presence of iron deficiency anaemia (haemoglobin under 10 g/dl). The WHO guideline does not suggest undertaking a full blood count in all patients undergoing HbA1c testing to diagnose diabetes.

Other factors influencing HbA1c include carbamylated haemoglobin (seen in end stage renal failure) which increases HbA1c, as does hypertriglyceridaemia and hyperbilirubinaemia. Anti-retroviral therapy, pregnancy and chronic liver disease all modestly lower HbA1c.

Glucose tests and HbA1c may detect different populations of people with diabetes, with many studies showing significant discordance between glucose and HbA1c tests. Some ethnic groups have modestly higher HbA1c (eg. black African/Caribbeans and South Asians by around 0.4%).

Some studies suggest that HbA1c is a more specific, but less sensitive test for diagnosis of diabetes, therefore potentially missing some patients with diabetes diagnosed on glucose tests. Other studies suggest that in some ethnic groups, especially South Asians, HbA1c may increase the diagnosis of diabetes. Proponents for the test, however, suggest that **HbA1c of 48 mmol/mol is the level at which risk for complications rises and HbA1c is a better predictor of CVD events than glucose tests**. Hence this level is one at which intervention to improve glycaemia might be instituted.

HbA1c has been used for population based screening for diabetes in some studies. When compared to the OGTT, the performance of HbA1c ≥ 48 mmol/mol for T2D diagnosis is variable, and may be influenced by ethnicity. For population based screening of diabetes, a more cost effective and efficient option is to undertake screening using a risk score to identify people at high risk of developing diabetes followed by the use of HbA1c to identify diabetes in people found to be at high risk.

The attached Swindon Diabetes Diagnosis guideline is the first locally developed diabetes guidelines. We are currently in process of development of local guidelines on lipid and blood pressure management in diabetes along with anti-diabetes therapies in T2DM, painful diabetes neuropathy etc.

I hope the guideline would be useful for your practice. Should you have any questions or comments please do not hesitate to contact me.

With kind regards

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Enc: Swindon Diabetes Diagnosis Guideline