January 2018 Edition no. 46

AMPATHCHAT

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Screening and diagnosis of Diabetes Mellitus using glucose testing

Epidemiology of diabetes

Diabetes is a major health burden that affected approximately 8.8% or 415 million people worldwide in 2015 according to the International Diabetes Federation (IDF). The incidence of diabetes has also shown a dramatic increase in rural Africa, and is now considered a major non-communicable disease in Sub-Saharan Africa (SSA).[1]

The South African National Health and Nutrition Examination Survey (SANHANES) 2012 estimated that the national prevalence of diabetes (based on HbA1c) in persons older than 15 years is 9.5%, with 45% being previously undiagnosed and the highest prevalence being found in Asian Indian and Mixed Ancestry (coloured) populations.[2] The rising prevalence of obesity is one of the most important modifiable risk factors driving the diabetes epidemic.

Screening and diagnosis of diabetes and intermediate hyperglycaemia

The diagnosis of diabetes can be made by using a combination of glucose-based tests and HbA1c as set out in the 2012/17 guidelines of the Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA)[3] and summarised in Table 1.

Table 1: Diagnostic criteria for diabetes and intermediate hyperglycaemia

	Plasma glucose (PG) (mmol/l)			HbA1C (%)
	Fasting		OGTT 2 hr PG	
Normal	<6.1	And	<7.8	
Pre-diabetes (intermediate hyperglycaemia)				
Impaired fasting glycaemia	6.1–6.9		<7.8	
Impaired glucose tolerance	<7.0		7.8–11.0	
Diabetes	≥7.0	And/Or	≥11.1	And/Or ≥6.5

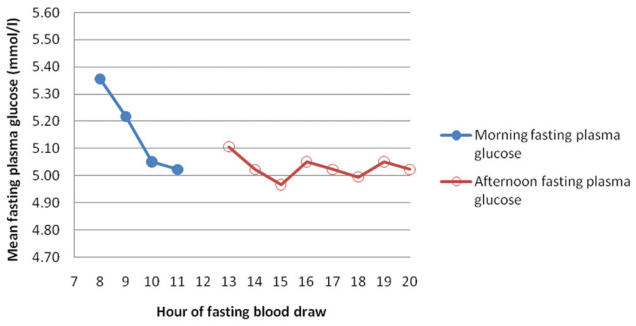
- **No one test is preferred above another.** It is, however, well known that the 2-h plasma glucose (PG) value following an oral glucose tolerance test (OGTT) will diagnose more people with diabetes compared to the fasting glucose value or HbA1c.
- **In a patient with symptoms of hyperglycaemia** (polyuria, polydipsia, blurred vision, weight loss) or **metabolic decompensation** (diabetic ketoacidosis or non-ketotic hyperosmolar state), a **single abnormal test** (including a random glucose) **confirms** the diagnosis of diabetes.
- **In asymptomatic patients,** the diagnosis should be confirmed by **repeat testing** of preferably the same test on a separate day within a two-week period. However, if both a glucose-based test and HbA1c test are measured and both are diagnostic of diabetes, the diagnosis is confirmed.
- **If the diagnosis of diabetes is not confirmed** by the repeat test, institute lifestyle changes and re-test in three to six months.
- **Hyperglycaemia detected under acute infective, traumatic, cardiovascular or other stressful conditions**, including corticosteroid therapy, may be transitory, and should be **confirmed after resolution of the acute condition.**
- **HbA1c can be used for diagnosis of diabetes** provided that the method is certified by the National Glycohaemoglobin Standardisation Program (NGSP) and controlled by stringent quality assurance procedures, as is the practice within Ampath. Any conditions precluding accurate measurement of HbA1c or affecting its interpretation should be excluded, including haemoglobinopathies (Hb-variants and thalassaemias), or other conditions affecting the red cell turnover and/or glycation rate, for example, iron or vitamin B12 deficiency, erythropoietin therapy, haemolytic conditions (malaria, autoimmune disease or anti-retrovirals), recent blood loss or transfusion, splenomegaly, splenectomy, pregnancy, chronic liver disease or renal failure, and alcoholism.
- **An HbA1c of 6.5% is recommended** as the diagnostic cut-point for diabetes. A value of less than 6.5% does not exclude diabetes diagnosed using glucose tests. In individuals with HbA1c values close to the diagnostic cut-point (6.0 to 6.4%), a glucose-based measurement is recommended.
- **Point-of-care testing of glucose or HbA1c** should not be used for the diagnosis of diabetes.
- **Impaired fasting glycaemia (IFG)** and **impaired glucose tolerance (IGT)** are **categories of intermediate hyperglycaemia regarded as modifiable risk factors** used for identification of patients with an increased risk for future diabetes and cardiovascular disease. **The diagnosis of** IFG or IGT should be confirmed by 2 consecutive tests.
- **Screening for type 2 diabetes:**
  - Screen all overweight adults (BMI > 25 kg/m^2 or > 23 kg/m^2 in Asian Indians) at any age if at least one risk factor is present for diabetes (including physical inactivity, hypertension, a first-degree relative with diabetes, dyslipidaemia, polycystic ovarian syndrome, Asian

Indian or Coloured race, cardiovascular disease history, gestational diabetes or baby > 4 kg, previous IFG or IGT, other conditions associated with insulin resistance).
- Otherwise start screening at 45 years of age.
- Frequency for rescreening depends on the individual risk and can range from three months (obese patient with IGT and multiple risk factors) to three years (normal weight patient with no risk factors).
- The preferred screening test for high-risk patients is the OGTT as it is more sensitive and the only method to detect IGT.

The effect of diurnal variation on glucose

Fasting glucose levels are affected by the **duration of fasting** and the effect of **circadian rythmicity**, the latter being the predominant factor. Both **glucose** and insulin levels are **highest in the early morning**, showing a progressive decline after 09h00 and levelling off in the afternoon (refer to Figure 1). This pattern of diurnal variation is thought to be related to the increase in early morning cortisol concentration. Data from the US population-based Third National Health and Nutrition Examination Survey (1988–1994) has shown that if current diabetes diagnostic criteria are applied to patients tested in the afternoon, approximately half of all cases of undiagnosed diabetes may be missed.[4] Glucose levels are also affected by the duration of fasting, and show a significant decline after 12 hours, although this effect is smaller than the effect of circadian variation.[5]

Figure 1: Median plasma fasting glucose by hour of blood draw[4]



Glucose tolerance also shows **diurnal variation**, being decreased in the afternoon and evening.[5] Plasma glucose levels following a 75 g glucose load are generally 1.7–2.8 mmol/l higher in the afternoon or evening than when the test is performed in the morning, giving rise to the term "afternoon diabetes." This is thought to be due to decreased insulin sensitivity as a delayed effect of the morning cortisol peak.[6]

Collection requirements for fasting glucose and the OGTT:

Due to the importance of accurate diagnosis, it is crucial to pay attention to the following collection requirements for both fasting plasma glucose and the OGTT.
- Fasting glucose should be collected before 09h00.
- Duration of fasting: 8–12 hours.
- The OGTT should not be started after 09h00.

Other important factors to keep in mind when performing an OGTT:

- **Various drugs** can affect a patient's glucose status and details of current medication can be helpful in interpretation of the OGTT results. If possible, therapy with non-essential medication should be discontinued for a period of five times the drug's half-life.[7] Please refer to Table 2 for a list of the most commonly used drugs. Visit http://www.diabetesincontrol.com/drugs-that-can-affect-blood-glucose-levels for a more complete list.
- **Carbohydrate intake** of less than 150 g per day for several days before an OGTT can cause an abnormal result, as well as **physical inactivity**, for example, due to bed rest following an acute illness. An information leaflet is available providing patients with guidelines on adequate carbohydrate intake.

Table 2: List of medications that may influence blood glucose concentration in vivo[7]

Medication reported to elevate blood glucose concentration			
Acetazolamide (Diamox)	Imipramine (Tofranil)	Nicotine/Nicotinic acid	Propranolol (Inderal)
Chlorpromazine (Largactil)	Isoniazid	Nifedipine (Procardia)	Theophylline
Corticosteroids	Indomethacin	Phenazone (Antipyrine)	Thiazides
Ephedrine	Labetalol	Phenytoin (Epanutin)	Thyroid hormone
Furosemide (Lasix)	Levodopa	Prazosin (Minipress)	Triamterene
Medication reported to lower blood glucose concentration			
Asetylsalicylic acid	Ascorbic acid	Cimetidine (Tagamet)	Probenecid
Aminosalicylic acid	Atenolol	Clofibrate	Spironolactone
Amitriptyline (Tryptanol)	Biguanides (Metformin)	Ethanol	Sulphonylureas
Anabolic steroids	Cannabis	Oestrogens	
Agents reported to have a variable effect on blood glucose			
Caffeine	Lithium		

Conclusion

Due to the increasing frequency of diabetes and the importance of correct diagnosis of not only diabetes, but also pre-diabetes, it is paramount that the correct precautions are adhered to when collecting fasting glucose samples. It is of crucial importance to diagnose these conditions accurately for timely intervention and possibly prevention of progression to diabetes.

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