

Communication- Chemical Pathology

Improving the diagnosis of Diabetes mellitus: Experience from a tertiary care hospital

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Introduction

Diabetes mellitus is a syndrome of chronic hyperglycaemia due to relative insulin deficiency, resistance or both (1).

It is estimated that diabetes mellitus will affect 220 million world-wide by the year 2020 (1). The latest figures (2005/2006) for Sri Lanka indicate a prevalence of 16.4% in the urban sector and 8.7% in the rural sector (2). It is expected to affect 0.6 million by 2025 (3).

Although it is a disease associated with a hormone, the classical tool for its detection has been the biochemical demonstration of an elevated level of plasma glucose.

The WHO has recommended cut-off values for plasma glucose levels under standard conditions, for the diagnosis of diabetes mellitus.

The WHO criteria for diagnosis of diabetes are dependent on 2 laboratory investigations:

- Fasting plasma glucose (FPG)
- 2-hour oral glucose tolerance test (OGTT)

Based on these tests, 3 groups of patients are

identified. They are:

- Diabetes is likely (FPG >7.0 mmol/L or 2-hour OGTT >11.1 mmol/L)
- Diabetes is unlikely (FPG <5.6 mmol/L and OGTT <7.8 mmol/L)
- Diabetes is uncertain (FPG 5.6 – 6.9 or 2-hour OGTT 7.8 – 11.1 mmol/L).

This last group includes patients having impaired fasting glycaemia (IFG) or impaired glucose tolerance (IGT), also called Pre-diabetes (4).

The American Diabetes Association (ADA) particularly considers that patients with values >5.6 mmol/L have impaired fasting glycaemia and need to be followed up (5), whereas the set cut-off for IFG according to WHO criteria are values >6.1 mmol/L, requiring an OGTT.

In our laboratory, 400 plasma glucose estimations are performed daily, collected into fluoride-oxalate tubes prepared in-house. The indications for these tests include, confirmation of a clinical suspicion of diabetes, follow-up of known diabetics including management of complications, exclusion of diabetes before proce-

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dures, and opportunistic screening for diabetes. Nowadays, a large chunk of this workload is justified by opportunistic screening, given the WHO warning that South-East Asia would experience a spectacular rise in the incidence of diabetes, and Sri Lanka being part of it.

The WHO describes two criteria for the diagnosis of diabetes, and advises that those who have impaired fasting plasma glucose (6.1 – 6.9 mmol/L) should proceed to the second diagnostic test which is the OGTT. According to the National Guidelines formulated in 2007 in Chemical Pathology, with the concurrence of the physicians and endocrinologists, FPG values of 5.6 – 6.9 mmol/L are identified as IFG, warranting an OGTT(6).

However, in our experience, we found that clinicians' requests for the OGTT were very few and actually dwindling compared to a decade ago. This prompted us to make the most of the first screening test which is the FPG, and follow up those with IFG, by performing an OGTT at the laboratory level. We realized that we could boost the diagnostic services by conducting the OGTT ourselves as it would reveal those patients who either have IGT or diabetes based on their inability to handle a glucose load appropriately, and would otherwise have been missed, at least until their FPG reached 7.0 mmol/L much later.

Identifying the patients who need an OGTT

We screened all the FPG results sent to us from the wards and clinics. For those found to have FPG values between 5.6 – 6.9 mmol/L (IFG by ADA criteria) a comment suggesting an OGTT was included. We requested that the patients be sent to the laboratory to get an appointment, on discharge from the hospital. The response from the ward staff was poor. It seemed that advice on life-style modification was all that was required for those with IFG in a busy medical ward of a tertiary care hospital, having a heavy turnover of patients.

A second strategy adopted was to reach the patient directly. To every FPG report having values in the IFG range, we attached a note addressed to the patient to come for further testing after convalescence. Here we found a set of eager patients who phoned us for appointments. Our laboratory medical officers interviewed them and rejected known diabetics and gave appointments for OGTT to the others one month after discharge from the hospital. This was to ensure that the patients had returned to normal daily activities and a normal carbohydrate diet (of at least 150g/day) before embarking on the OGTT which is best done as an outpatient. Although patients from distant towns were advised to go to their local physician, some preferred to come to our laboratory.

Glucose monohydrate load for OGTT: 82.5g (instead of 75g)

For the OGTT, the recommended glucose load is 75g of the anhydrous form. Traditionally in Sri Lanka, we have substituted glucose monohydrate which is freely available in the market in the solid form, without adjusting the weight. Even that amount was weighed in a crude balance by ancillary staff from the 100g packs the patients brought themselves. 82.5 g of the monohydrate form is the equivalent of the 75g anhydrous form. We ordered the glucose from the hospital pharmacy, in packs of 82.5g, weighed accurately. We expected this to reveal more diabetics failing to face the challenge of the larger glucose load used.

The patients were asked to come as out-patients after an overnight fast. Water was allowed to maintain normal hydration. Blood was collected for fasting plasma glucose into a fluoride-oxalate tube and tested immediately in an automated chemistry analyser which had undergone routine quality control procedures in the morning. Further testing was decided based on this second FPG result which was made available in 20 minutes. This avoided an unnecessary glucose load being given to any patient already recording a normal fasting value or one which is in the diabetic range. A glucose meter (glucometer) is a useful tool in this sense, but in any patient recording a value >7.0 mmol/L by

glucometer, a proper venous blood sample should be collected to confirm this result, while abandoning the OGTT. Glucometers are recommended for monitoring the blood glucose levels of known diabetics but not for diagnosis. In our protocol, we resorted to performing an accepted diagnostic test straight away as FPG.

This second FPG test allowed the patients to be re-classified into 3 categories as out-patients based on WHO recommendations outlined above. Those recording a fasting glucose level <5.6 mmol/L were discharged as normal, without further testing. Those with values >7.0 mmol/L were diagnosed as diabetes and referred to the diabetic clinic.

Only those with intermediate values of 5.6 - 6.9 mmol/L for the second time, were retained for the OGTT. They were asked to drink 82.5g of glucose monohydrate dissolved in about 300ml of water in approximately 5 minutes. The time on commencing the drinking was noted and a further blood sample collected for glucose estimation into fluoride-oxalate tubes in exactly 2 hours and analysed immediately. The patients were allowed to rest seated during this period and any nausea or vomiting recorded. Vomiting would nullify the test while an additional sample collected at 1 hour from those patients reporting nausea would facilitate interpretation of the results of the latter group. These adverse effects are often due to the

high osmotic activity of the glucose load and could be reduced by using a starch solution equivalent.

Patients undergoing OGTT were classified into 3 categories based on the 2-hour plasma glucose result.

- IFG only (<7.8 mmol/L)
- IGT (7.8 – 11.0 mmol/L)
- DM (>11.1 mmol/L)

All patients were issued a results sheet the same morning with interpretative comments and for those with pre-diabetes, re-screening in one year was recommended. All patients had their BMI measured and were advised on life-style modification during their 2 hour stay.

Recommendations

We decided to take an independent action on the FPG results of in-patients, in the form of follow-up testing. Our results showed that the procedure we adopted unmasked a great number of diabetics and pre-diabetics who would have otherwise been identified much later or even missed altogether. The correct, but greater glucose load too would have also helped in identifying them in considerable numbers. The initial FPG could not have predicted the correct outcome after convalescence, as the response could be variable. However, the yield of diabetic and prediabetic patients was considerable and therefore highly cost effective, justifying similar testing in other laborat-

ories too.

Pathologists could add value to the work done by the clinicians by performing OGTT in patients who require them. With the ability to provide prompt and reliable test results, the laboratory set up is ideally designed to avoid unnecessary OGTT too, as it is a cumbersome test for the laboratory and an unpleasant test for the patient in spite of the glucose being so sweet!

References:

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