

Raising Question Marks: Diagnostic anomalies with standard Oral Glucose Test



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Editorial

Since the 17th century when Thomas Willis described diabetic urine as “wonder Tolerance fully sweet” like sugar or honey, which paved way for future diagnostic methodologies for diabetes. Since then diabetes diagnostics over the last century had witnessed multi-step evolution from urine glucose analysis, to oral glucose tolerance test, and introduction of glycated hemoglobin. Urine glucose analysis by means of acid hydrolysis was started was introduced by Karl Trommer, in 1841, which is considered as a landmark milestone in the laboratory diagnostics [1]. It was in 1923 when the first use of oral glucose tolerance test was first introduced in literature [2]. Overtime the test, albeit in modified version of OGTT were also adopted for diagnosing gestational diabetes mellitus (GDM). With further refinements in biotechnology, improved understanding of insulin-glucose dynamics including peak glucose appearance timings, wider population data availability and addressing laboratory related accuracy and imprecision issues the relevant authorities were able to further standardize the diagnostic criteria glucose tolerance analytical aspects [3]. However, the clinical practice experience and review of contrasting data on the subject highlights various shortcomings and areas needed to be improved for oral glucose tolerance tests for improved patient outcomes.

Current day laboratory diagnostics relies heavily on glucose load testing as the core behind which the diagnosis revolves. However, the laboratory experience suggest multiple technical issues which need to be over taken before execution of a sound oral glucose tolerance test which question the methodology and need to up gradation for diagnosing diabetes mellitus in a more feasible and precise manner [4,5]. Clinical experience suggests a glucose load of 75 gram may not be sufficient for obese subjects

and may be exuberant to result in false negative and false positive case scenario thus questioning the utility of fixed dose (75 gram) testing. There is some data which indirectly confirms the role of obesity as a confounding factor in the diagnosis of diabetes mellitus [6]. Furthermore, gastrointestinal absorption rates may vary between subjects due to disease or simply vary due to differential physiology affecting glucose insulin absorption rate based models which could again mislead the diabetes diagnosis. These factors does affect the credibility of use of oral glucose tolerance test as a “gold standard” [5]. Apart from the assumptions of appropriate patient preparation in routine clinical setting, the wait time to completely conduct a test and glucose loading related time and absorption variables it can easily be conceived that an oral glucose tolerance may not be the so termed “gold standard” in routine non-standardized hospital settings. These variables have been discussed by Khalafallah et al. [7].

In a recent study from Western Australia from the authors demonstrated that the GDM screening by OGTT was found to be inadequate for many subjects [8]. A deeper dissection of the pattern of post-glucose loading glucose concentration by Cheng et al identified two patters as monophasic or multiphasic, where subjects with former pattern were identified as more insulin resistant with impaired beta-cell dysfunction [9]. Huo et al, [10] have identified glomerular filtration rates may result in fluctuations of 2-hour readings more after glucose loading. Several other factors related to metabolism also contribute towards final appearance of results in any kind glucose loading tests [11]. A recent study among 5687 subjects highlighted the role of SGLT1 receptors in glucose absorption, indicating that people with missense mutation of SGLT1 receptor are bound to absorb less

glucose with less obesity, diabetes and ultimately lower incidence of cardio-metabolic side effects [12].

Another debate emerged with introduction of HbA1c as an investigation for diabetes diagnosis. HbA1c with time has matured into a clinically robust and precise biomarker to assess glycemic status without medical fasting prerequisite or major variation. Alongside it has also climbed upstairs in terms of accreditation status like National Glycohemoglobin Standardization Program (NGSP) and earned recommendations for use as a diagnostic and diabetes biomarker in various clinical guidelines [13,14]. However, it still suffers from issues like race and gender, selection of NGSP technique, effect of hemoglobinopathies and conditions affecting blood cells like iron deficiency anemia [15].

In summary the laboratory experts and physicians dealing with diabetes in any capacity need to appreciate the aforementioned technical and non-technical issues associated with oral glucose loading testing. Researchers involved in diabetes diagnostics need to evaluate newer biomarkers for appropriate diagnosis of diabetes mellitus. Molecular diagnostics may be another horizon for future researchers which may promise something more precise and accurate to emerge as a next-generational diabetes biomarker.

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