Diagnosis of Dysglycemia in Diabetic Patients in Primary Health Care

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Authors’ contributions
This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT
An early diagnosis of diabetes is a cornerstone for achieving the best prognostic outcomes. The potential complications take time to develop. For this reason, diabetic patients, especially type 2 are usually diagnosed with the disease after complications have been arisen. Dysglycemia is a term that has been used to describe the fluctuations in the plasma glucose levels, including the

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1. INTRODUCTION

According to previous estimates from the United States, 30 million patients have been diagnosed with diabetes mellitus in 2015. On a global level, evidence shows that 415 million patients have been previously diagnosed with DM up to the same year, and projections even suggest that around 642 million cases are expected within the next two decades [1]. Two major types of DM commonly affect patients and impact their quality of life. These include type 1 and type 2 DM. However, the diagnosis, pathophysiology, and management of both types differ from each other.

A study has shown that the usual start of T1DM is during childhood in which patients suffer from absolute insulin insufficiency and they have to continue receiving exogenous insulin therapy for the rest of their lives. On the other hand, patients with T2DM, also know as the late-onset type is mainly affects the elderly. The study has found that patients suffer from a state of insulin resistance and irrespective of the insulin levels in their plasma, however, insulin deficiency can develop over time [2]. Inappropriate management of these types can significantly increase the risk of developing serious complications, which are mainly attributable to the subsequent increase in the blood glucose levels, leading to both acute and chronic complications that might even lead to mortality. Several organs can be impacted by uncontrolled diabetes and fluctuating blood glucose levels. Among the commonly reported organs, the renal, cerebral, eyes, nerves, and cardiovascular-related organs have been reported to be associated with the most serious complications. Besides, death secondary to diabetes has been marked as the most common cause of worldwide mortalities as a result of kidney failure, amputations, and cardiovascular complications [3-5]. Therefore, management of diabetes should be appropriately conducted to enhance treatment compliance and to increase the frequency of adequate blood glucose monitoring.

An early diagnosis of diabetes is a cornerstone for achieving the best prognostic outcomes. However, diabetic patients, especially type 2, are not usually diagnosed with the disease after complications have been arisen because diabetic complications usually take time to develop [6-8]. Therefore, routine check-ups of plasma glucose are encouraged for patients at risk. Dysglycemia is a term that has been used to describe the fluctuations in plasma glucose levels, including the high (hyperglycemia) and low (hypoglycemia) levels, and can also refer to impaired glucose tolerance (IGT) or impaired fasting glucose (IFG) [9]. Many modalities have been developed to assess plasma glucose levels. Studies have shown that advantages and disadvantages are reported for each modality when assessing dysglycemia and screening for diabetes. [10-15]. The aim of this study is to discuss the previously reported diagnostic approaches of dysglycemia among diabetic patients according to the existing published studies in the literature.

2. LITERATURE REVIEW

The present section discusses some of the modalities and tools that have been recently reported in the literature about the proper diagnosis of dysglycemia and glucose abnormalities in patients with diabetes. Previous investigations have reported the limitations and advantages of previous modalities [11-12]. The assessment is based on developing assessment risk scores, in addition to the routinely done tests.
such as random blood glucose, urine glucose levels, fasting plasma glucose, oral glucose tolerance test (OGTT), glycated hemoglobin levels (HbA1c), and serum levels of fructosamine.

2.1 Urine and Random blood Glucose Levels

Previous studies have reported that the positive predictive value for urine glucose levels in diagnosing diabetes and dysglycemia is variable being 11-37%, while the sensitivity for the same test has also been previously estimated to be hugely variable, ranging between 16% and 64% [11]. Therefore, it has been suggested that urine testing to detect dysglycemia is a poor tool that should not be routinely done as many patients with dysglycemia and/or diabetes would be misdiagnosed and this is based on the sensitivity results of the modality. Similarly, studies were against using random blood glucose levels in screening for dysglycemia and diabetes because of the poor performance of the modality [12]. This was indicated by previous large comparative studies. For instance, Ziemer et al. [16] reported that at a cutoff ≥of 6.9 mmol/L for the random blood glucose levels, the specificity and sensitivity of diagnosing diabetes were 93% and 41%, respectively, and when diagnosing dysglycemia, the sensitivity and specificity were 23% and 94%, respectively. Another previous investigation also validated the random blood glucose assessment against OGTT and reported that an estimated cutoff of ≥7.2 mmol/L was associated with the estimated sensitivity and specificity rates of 63% and 87%, respectively [17].

2.2 Fasting Plasma Glucose

Previous studies have also demonstrated that the validity of the fasting plasma glucose is poor in diagnosing the blood glucose fluctuations and hyperglycemia in regard to sensitivity.[12]. Kim et al. [18] concluded that the specificity and sensitivity of the fasting blood glucose levels were estimated to be 100% and 55.7%, respectively, for patients who were priorly diagnosed with diabetes using OGTT, considering that the cutoff level for the test is not less than 7 mmol/L. Moreover, they have reported that a cutoff for the fasting blood glucose test of >6.1 mmol/L was estimated to have rates of 85.2% and 88.5% for sensitivity and specificity. A previous study that was conducted on African American patients with diabetes and dysglycemia has reported that the fasting blood glucose levels were not adequately sensitive or specific as compared to the OGTT in the diagnosis of impaired glucose tolerance (IGT). Besides, the authors reported that a threshold of >5.6 mmol/L could attribute to only a 28.9% specificity rate in detecting the potential cases with IGT, as compared to the OGTT, which was associated with an 87.4% rate of detection and specificity [19]. Therefore, fasting blood glucose levels assessment should be considered with other assessment modalities for better detection and diagnosis of dysglycemia.

2.3 Glycated Hemoglobin

The American Diabetes Association (ADA) has recently recommended that HbA1c tests should be the standard tools for diagnosis of diabetes and dysglycemia when the estimated levels are ≥6.5% [20]. However, conflict about the validity of the modality can still be noticed among studies in the literature. Nevertheless, the ADA justified their suggestions by the previously proven solid correlation between HbA1c and blood glucose levels that might cause relevant complications, especially retinopathy, the strong association between the parameter and cardiovascular complications, in addition to the all-cause mortality among diabetic patients [21]. The recommendations of the ADA did not also define specific parameters to diagnose the IGT and IFG. It has been reported that an HbA1c level that ranges between 5.7-6.4% should be considered for close monitoring to avoid deterioration of these cases and prognosis to diabetes.

The specificity and sensitivity for the HbA1c threshold of ≥6.5% have been hugely variable among studies in the literature for diagnosing dysglycemia and diabetes. Some studies agreed with the ADA about this threshold and reported a significant correlation coefficient [22]. On the other hand, other investigations reported that glycated hemoglobin levels were less efficacious and valid than the OGTT according to the estimations from their population-based studies. Kramer et al. [23] reported that the sensitivity and specificity for HbA1c were 44% and 79%, respectively, for diagnosing dysglycemia and diabetes. Moreover, they reported that 85% of the patients who were diagnosed with having diabetes were assessed by the glycated hemoglobin levels as non-diabetic. The study has also furtherly showed the importance of OGTT in obtaining better diagnostic outcomes as they compared between the criteria by the ADA, which requires that diabetes and dysglycemia
should be diagnosed with fasting plasma glucose without OGTT as it was mentioned by the World Health Organization (WHO), which requires OGTT with fasting blood glucose to diagnose dysglycemia and diabetes, and reported the diagnostic rates for both criteria were 70% and around thrid, respectively, although both criteria depend on the same threshold for HbA1c [24]. Previous studies have demonstrated that ethnicity might play a significant role, affecting the prevalence rates of diabetes and dysglycemia. Studies have shown that the prevalence might be higher when using the hemoglobin levels as compared with fasting blood glucose and/or OGTT in the United States [25], while other investigations also reported that the prevalence might also be higher for hemoglobin as compared to OGTT alone in Greenland, English, Kenyan, and Australian population, and lower in Indian and Danish populations [26].

A previous systematic review by Bennett et al. [27] analyzed the results of 63 studies to assess the sensitivity and specificity of the different HbA1c parameters and their ability to diagnose diabetes and dysglycemia. The authors reported that HbA1c levels between 5.8-6.3% usually have specificity and sensitivity rates of 66%-95%, and 97-98%, respectively. On the other hand, when the levels were 6.1-6.2%, it corresponded to the optimum sensitivity [27]. Previous studies have demonstrated that having HbA1c levels more than or equal to 6.1% might significantly correspond with estimated specificity and sensitivity rates of 97.4% and 63.2%, respectively [28]. The authors reported that these validity rates probably correlate with a 2-hour postprandial blood glucose level of 11.1 mmol/L, and the estimated parameters were obtained from a population that included 21% IGT individuals and 41% non-diabetic subjects [29]. Another pitfall for HbA1c assessments is that they might not differentiate between normoglycemia and undiagnosed diabetes, as a previous investigation showed that according to the fasting plasma glucose levels assessment, 60% of patients with diagnosed diabetes showed to have normal HbA1c levels [30].

The previous investigation reported that the sensitivity rate for HbA1c levels ≥5.8% to detect dysglycemia was 30%, and for ≥6.1%, the sensitivity is 50% for diagnosis IGT [31]. For detecting dysglycemia, a previous investigation also estimated the specificity and sensitivity rates for HbA1c levels ≥5.7% to be 73.9% and 59.4%, respectively [32]. Previous studies have also assessed the validity of using the area under the curve (AUC). A previous Indian investigation reported that HbA1c levels ≥5.6% was considered optimum for diagnosis of IGT, with an estimated AUC of 0.708 and 0.632 for IGT and IFG, respectively, according to the WHO criteria, and 0.708 for IFG according to the ADA criteria [33]. On the other hand, a previous Chinese investigation reported low values of AUC for HbA1c levels ≥5.6% in detecting IGT and IFG in female (AUC= 0.51) and male (AUC= 0.47) participants [34]. Based on these findings, previous studies have demonstrated that HbA1c levels assessment should be simultaneously conducted with the random and fasting blood glucose tests to decide which patients are required to perform an OGTT [18, 27, 35]. Moreover, HbA1c tests might not be affordable in some healthcare settings [17] although the unified recommendations about their abilities in predicting the long-term glycemic control [36-38].

Despite the selection of limitations in the study by Phillips et al. [39], the authors reported that the AUC for the 50-g oral glucose challenge test in detecting dysglycemia was 0.79 while it was 0.82 and 0.90 for dysglycemia or undiagnosed diabetes and undiagnosed diabetes, respectively. Capillary blood testing has also been previously reported in the literature to diagnose the state of dysglycemia and diabetes. A previous Australian investigation reported that the estimated AUC for the test to detect dysglycemia was 0.87, and 0.76 for fasting blood glucose and point-of-care, respectively [40]. Moreover, a previous investigation also reported that a cutoff point for the test of >6 mmol/L showed acceptable specificity (65.5-69.5%) and sensitivity (66.5-70.5%) rates for dysglycemia and diabetes diagnosis [41].

3. CONCLUSION

Our literature review has discussed the different assessment tools of dysglycemia in diabetic patients according to the previous investigations. We have discussed the 50-g oral glucose challenge test, HbA1c, fasting blood glucose, random blood sugar, and oral glucose tolerance tests in the assessment of the blood glucose fluctuating levels. Based on our findings, it is recommended that HbA1c levels assessment should be simultaneously conducted with the random and fasting blood glucose tests to decide which patients are required to perform an OGTT. Moreover, HbA1c tests might not be affordable in
some healthcare settings although they are important indicators of long-term glycemic control.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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