Laboratory Interpretation for Diagnosis and Monitor of Diabetes

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Abstracts

Background: Laboratory interpretation for diabetes involves a comprehensive approach to diagnosing, distinguishing between subtypes, and monitoring the disease. Key laboratory tests include glucose measurements, hemoglobin A1c (HbA1c), and insulin and C-peptide levels assessments. These tests are crucial for both initial diagnosis and ongoing management of diabetes. Interpreting these tests requires understanding their limitations and the context in which they are used. Aim: an overview of laboratory interpretation related to the diagnosis of diabetes. Method: The PubMed and Google Scholar search engines were the main databases used for the search process, with articles collected from 1980 to 2024. Conclusion: Laboratory interpretation for the diagnosis of diabetes involves a comprehensive evaluation of various biomarkers to confirm the presence of the disease and differentiate between its types. Key laboratory tests include measurements of glucose levels, hemoglobin A1c (HbA1c), and other specific markers such as C-peptide and autoantibodies. These tests are crucial for accurate diagnosis, prognosis, and management of diabetes.

Keywords: Fasting Blood Glucose Test, Oral Glucose Tolerance Test, Random Plasma Glucose, HbA1c, Fasting Insulin Test, postprandial insulin test, C-peptide, Ketone testing.

1. Introduction

Laboratory testing for diabetes presents several challenges and limitations that can significantly impact diagnosis and management. One major issue is the requirement for fasting before testing, which typically necessitates an 8-10 hour period without food. This requirement can be a barrier for many patients, potentially leading to missed or delayed testing opportunities. (1) Additionally, variability in test results can arise from differences in laboratory equipment, techniques, and standards, complicating the diagnostic process. Such variability can lead to inconsistent results, making it difficult for healthcare providers to assess accurately. Moreover, patient compliance plays a crucial role in the effectiveness of diabetes testing. Non-compliance with fasting or multiple visit protocols can undermine the reliability of test outcomes, further complicating diabetes management. (2, 3) Human error during sample collection also contributes to laboratory testing's limitations, as improper handling can affect the accuracy of results. Finally, the cost of diabetes-related laboratory tests varies widely, ranging from 5 to over 200, which can deter patients from seeking necessary testing. These factors collectively highlight the need for improved standardization in testing protocols and enhanced patient education to address compliance issues, ultimately aiming to improve the accuracy and accessibility of diabetes testing.

Blood Glucose Testing

- Fasting Blood Glucose Test

The Fasting Blood Glucose Test (FBGT) is a critical diagnostic tool for identifying diabetes mellitus. It measures blood sugar levels after fasting for at least 8 hours, with a diagnostic cutoff established at 126 mg/dL (7.0 mmol/L). The American Diabetes Association (ADA) emphasizes the importance of fasting plasma glucose (FPG) levels over the oral glucose tolerance test (OGTT) for diagnosing diabetes. However, the 75-gram glucose tolerance test (GTT) remains the international standard for assessing diabetes. According to the World Health Organization (WHO), the threshold values for diagnosing diabetes include a fasting blood glucose level of 6.7 mmol/L and a post-glucose load level of 11.1 mmol/L. In addition to traditional FPG testing, fasting capillary blood glucose (FCG) measurements have shown high concordance with FPG levels, making them a viable screening method, especially in low-resource settings. (4, 5) While the 100-g, 3-hour OGTT is still considered the gold standard for diagnosing gestational diabetes mellitus (GDM), the ADA has also recommended using a 2-hour, 75-g OGTT. (6)

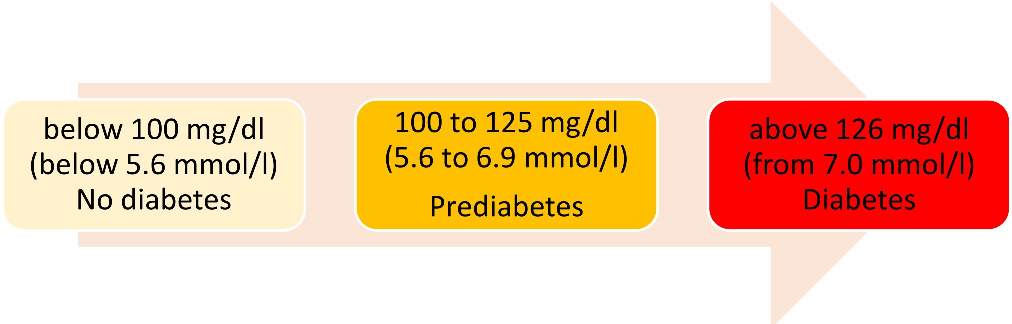

Figure 1: Normal Ranges and Reference Values in Fasting Blood Glucose Test.

- Oral Glucose Tolerance Test

The Oral Glucose Tolerance Test (OGTT) is a critical diagnostic tool for identifying diabetes and prediabetes, particularly in pregnant women and those with gestational diabetes. The test evaluates carbohydrate metabolism and is especially relevant in the third trimester of pregnancy, where it helps diagnose gestational diabetes using the criteria established by O'Sullivan and Mahan (1964).(7) For women diagnosed with gestational diabetes, a postnatal OGTT is performed six weeks after delivery to detect any persistent glucose intolerance, which is crucial for managing long-term health risks. (8) The OGTT involves administering a specific oral glucose solution designed to empty rapidly from the stomach, minimizing discomfort and ensuring reproducibility of results. (9) This rapid absorption is essential for accurately differentiating between nondiabetic and diabetic subjects, thereby enhancing diagnostic precision. Furthermore, the OGTT is instrumental in identifying individuals with impaired glucose tolerance, a precursor to type 2 diabetes. Studies indicate that a significant percentage of patients with prediabetes exhibit abnormal glucose levels during the OGTT, highlighting its importance in early detection and intervention. (10) Overall, the OGTT is a vital method for assessing glucose metabolism, guiding treatment strategies, and preventing the progression of diabetes in at-risk populations.

Table 1: Normal Ranges and Reference Values in Oral Glucose Tolerance Test.

Specimen	Serum	Whole blood or capillary
Fasting	105 mg/dl	90 mg/dl
1 hour	190 mg/dl	170 mg/dl
2 hour	165 mg/dl	145 mg/dl
3 hour	145 mg/dl	125 mg/dl

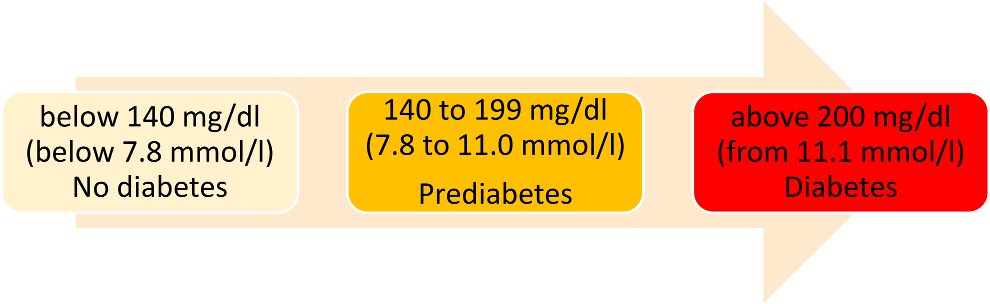

Figure 2: Normal Ranges and Reference Values in Oral Glucose Tolerance Test.

- Random Blood Glucose Test

The Random Plasma Glucose Test is a critical diagnostic tool for identifying diabetes, particularly when a random plasma glucose level of 200 mg/dL (11.1 mmol/L) or more is observed. (6) This test is especially relevant in the context of gestational diabetes, where specific cut-off levels are established to determine the need for further testing. For instance, women with a random blood glucose concentration exceeding 6.1 mmol/L within two hours of their last meal or 5.6 mmol/L more than two hours after being referred for a fasting blood glucose measurement. Normal glucose levels for a random test are typically below 200 mg/dL, with elevated levels indicating potential diabetes. However, the reliability of random blood glucose measurements as a screening procedure during the early part of the second trimester has been questioned, as they may not consistently detect all cases of gestational diabetes. (11) Fingerstick testing has been employed in various studies to enhance the accuracy of diabetes screening. This method allows for convenient blood sample collection using glucometers. This method has been recognized as a feasible approach to identifying abnormal glucose levels in community dental practices, highlighting the growing need for effective diabetes screening. (6) While the Random Plasma Glucose Test is a valuable tool, it should be complemented with additional testing methods to ensure comprehensive diabetes assessment.

Hemoglobin A1c (HbA1c) Test

The Hemoglobin A1c (HbA1c) test is crucial for diagnosing and monitoring diabetes, particularly type 2 diabetes. It measures the average blood sugar levels over the past two to three months, providing insights into long-term glucose control. The proposed diagnostic cut-off for HbA1c is 6.5%, which aligns with the criteria for identifying diabetes. This test has been shown to have a slightly higher ability to discriminate type 2 diabetes compared to fasting plasma glucose (FPG) tests. However, its adoption varies across countries due to a lack of consensus on cut-off points. (12, 13) Recent advancements in testing methods, such as the immunoturbidimetric assay, have improved the quantitative measurement of HbA1c. This assay effectively measures HbA1c without interference from other hemoglobin variants, making it a reliable option for diabetes monitoring. The immunoturbidimetric assay is performed on clinical chemistry analyzers, enhancing the accuracy and efficiency of HbA1c testing in clinical settings. (14) The HbA1c test is a vital component in the diagnosis and management of diabetes, with established cut-off values and improved testing methodologies that support its clinical utility. As diabetes prevalence rises, the importance of accurate and accessible HbA1c testing cannot be overstated.

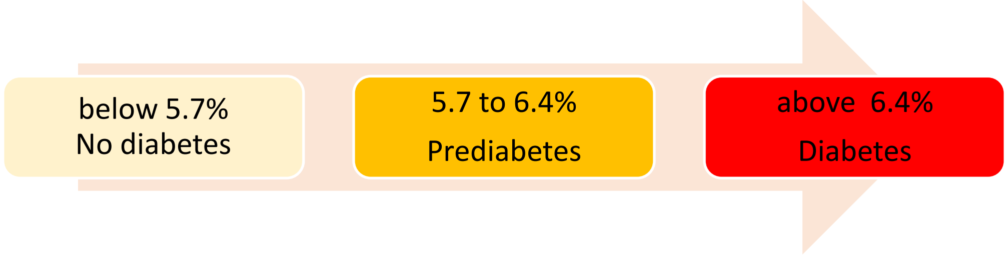

Figure 3: Normal Ranges and Reference Values in Hemoglobin A1c (HbA1c) Test.

Insulin Level Testing

- Fasting Insulin Test

The Fasting Insulin Test is a crucial early screening tool for diabetes and related metabolic disorders, particularly by measuring fasting serum insulin levels. Elevated insulin levels, known as hyperinsulinemia, are significant risk factors for non-insulin-dependent diabetes, cardiovascular disease, and hypertension. The IMx-Abbott kit is commonly employed for this test, providing a specific measurement of serum insulin without cross-reacting with proinsulin, thus enhancing the accuracy of the results. In a study involving 4,032 men and women aged 30 to 64, fasting insulin concentrations were assessed, revealing median values of 5.9 microU/ml for men and 5.4 microU/ml for women, with notable differences across age groups. These reference values are essential for interpreting test results, as they help identify individuals at risk of developing diabetes. (15) Furthermore, insulin resistance, characterized by the body's diminished response to insulin, plays a pivotal role in the progression of type 2 diabetes. It often precedes clinical hyperglycemia and is associated with various metabolic disorders. (16) Therefore, the Fasting Insulin Test not only aids in early detection but also provides insights into the underlying mechanisms of insulin resistance, which is critical for effective diabetes management and prevention strategies.

- Postprandial Insulin Test

The postprandial insulin test is a critical assessment for understanding insulin secretion and beta-cell function in diabetes management. This test measures plasma C-peptide levels after a meal, essential for evaluating the beta-cell reserve in diabetic patients. Specifically, postprandial plasma C-peptide levels can help identify those who may require insulin treatment, particularly in non-obese diabetic patients. Research indicates that a significant reduction in beta-cell reserve correlates with the duration of diabetes, leading to secondary failure in insulin production. For instance, patients exhibiting C-peptide delta values lower than 1.0 ng/ml are often identified as needing insulin therapy. Furthermore, the C-peptide/insulin molar ratio provides additional insights into the balance of insulin secretion relative to C-peptide levels, further elucidating beta-cell function. (17) The insulin response to meals is also crucial, reflecting how effectively the body can manage glucose levels post-consumption. Elevated insulin responses are typically observed after carbohydrate-rich meals, which can influence overall metabolic control. (18) Thus, the postprandial insulin test, alongside the assessment of postprandial glucose levels, is a vital tool in diagnosing and managing diabetes, allowing for tailored treatment strategies based on individual beta-cell function.

Table 2: Normal Ranges and Reference Values in Oral Glucose Tolerance Test.

Specimen	Insulin level	Insulin level (SI units*)
Fasting	< 25 mIU/L	< 174 pmoL
30 minutes after glucose administration	30-239 mIU/L	208-1597 pmol/L
1 hour after glucose administration	18 -276 mIU/L	125-1917 pmol/L
2 hours after glucose administration	16-166 mIU/L	111-1153 pmol/L
≥3 hours after glucose administration	< 25 mIU/L	< 174 pmol/L
*SI unit: conversion units x 6.945		

C-Peptide Test

The C-peptide test is a crucial diagnostic tool for assessing insulin production by the pancreas, particularly in diabetes management. C-peptide, a 31 amino acid fragment released during insulin formation, is a reliable marker for endogenous insulin secretion, distinguishing between types of diabetes and guiding treatment strategies. (19, 20) Various methodologies exist for measuring C-peptide levels, including the traditional radioimmunoassay (RIA) and newer automated chemiluminescence assays, such as the LIAISON C-Peptid. The latter offers advantages in terms of speed and simplicity, being a non-radioactive, fully automated one-step process that correlates well with RIA results. (21) In clinical practice, C-peptide determination is essential for diagnosing diabetes subtypes, particularly in children, where it helps differentiate between type 1 and type 2 diabetes. C-peptide indicates endogenous insulin secretion, absent in patients relying solely on synthetic insulin. (20) Overall, the C-peptide test not only aids in diagnosing conditions like insulinoma and factitious hypoglycemia but also plays a vital role in monitoring beta-cell function in diabetic patients. Thus, it is an indispensable component of diabetes care, providing insights that inform both diagnosis and management.

Ketone Testing

Ketone testing is a critical component in the management of diabetes, particularly for preventing complications such as diabetic ketoacidosis (DKA). The primary methods for ketone testing include measuring blood β-hydroxybutyrate acid (β-HBA) and urine ketones. Blood β-HBA is a direct biomarker for assessing diabetic ketosis and DKA, with studies showing a positive correlation between blood β-HBA levels and blood glucose ($r = 0.34$, $P < 0.001$). The glucose-ketone meter is instrumental in quickly diagnosing these conditions, allowing for timely intervention in patients with severe hyperglycemia. Urine ketone testing is another valuable method, providing insights into the presence of ketones in the body. In cases where urine ketones are positive, a significant percentage of patients may still present with low blood β-HBA levels, indicating the need for comprehensive testing. (22) Additionally, using test strips for ketone bodies enhances the ability to monitor ketone levels effectively, essential for managing diabetes and related disorders. (23) Emerging methods, such as breath testing for ketones, offer a non-invasive alternative for monitoring ketone levels, showing high sensitivity and specificity. (24) Overall, integrating various ketone testing methods is crucial for effective diabetes management, enabling healthcare providers to promptly detect and address potential complications.

2. Conclusion

Laboratory interpretation for the diagnosis of diabetes involves a comprehensive evaluation of various biomarkers to confirm the presence of the disease and differentiate between its types. Key laboratory tests include measurements of glucose levels, hemoglobin A1c (HbA1c), and other specific markers such as C-peptide and autoantibodies. These tests are crucial for accurate diagnosis, prognosis, and management of diabetes. Overall, the OGTT is a vital method for assessing glucose metabolism, guiding treatment strategies, and preventing the progression of diabetes in at-risk populations. The HbA1c test is a vital component in the diagnosis and management of diabetes, with established cut-off values and improved testing methodologies that support its clinical utility. As diabetes prevalence rises, the importance of accurate and accessible HbA1c testing cannot be overstated. The postprandial insulin test, alongside the assessment of postprandial glucose levels, is a vital tool in diagnosing and managing diabetes, allowing for tailored treatment strategies based on individual beta-cell function. Overall, the C-peptide test not only aids in diagnosing conditions like insulinoma and factitious hypoglycemia but also plays a vital role in monitoring beta-cell function in diabetic patients. Thus, it is an indispensable component of diabetes care, providing insights that inform both diagnosis and management. Overall, integrating various ketone testing methods is crucial for effective diabetes management, enabling healthcare providers to promptly detect and address potential complications.

Author Contributions

Each author participates in the paper's editing, collects pertinent material, and approves the final submission to the journal. The corresponding author oversaw the first author's draft of the paper.

Conflict of Interest

The authors declare they don’t have any conflicts of interest.

Ethical Approval

Not Applicable

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