Original article

Significance of HbA1c in Monitoring Diabetes at the Public Hospital, Guyana

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Abstract

Aim: To determine the prevalence of baseline/mean HbA1c among patients with suspected diabetes using Bio-Rad for the first time at a public hospital in Guyana.

Methods: A retrospective, laboratory-based, descriptive study examined 1,547 diabetic patients who underwent repeat HbA1c testing at a public hospital laboratory in Guyana between 2010 and 2014. All statistical analyses were performed using SPSS 21.0, JMP and Microsoft Excel. Distributions were used to show frequencies, the bivariate fit test was done to achieve correlations and significance, the χ2 test was used to compare the differences in proportions and ANOVA was used for differences in mean differences.

Results: A total of 1,547 patients were identified for the study. Mean age and standard deviation (SD) was 59.9 ± 11.47 (95% CI 59.3 - 60.4). Mean value for test 1 HbA1c was 9.2 ± 2.7 (95% CI 9.1-9.3), test 2 HbA1c recorded 9.1 ± 2.5 (95% CI 8.9-9.2), test 3 HbA1c was 9.6 ± 2.6 (95% CI 9.3-9.9) and test 4 HbA1c recorded a mean of 9.6 ± 2.6 (95% CI 9.0-10.2).

Conclusions: The mean HbA1c of the diabetic population was observed to be higher than the baseline in all tests.

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Introduction

Diabetes mellitus is defined by the World Health Organization (WHO) as a chronic disease caused by inherited and/or acquired deficiency in the production of insulin by the pancreas (1). It is estimated that 39 million people are living with diabetes in the North America and the Caribbean (NAC) region (2). In 2014, there were 61,800 cases of diabetes in Guyana and diabetes was the cause of 1,025 deaths in adults aged 20–79. The International Diabetes Federation (IDF) also estimated that there are about 15,400 undiagnosed cases of diabetes (3). With the prevalence of diabetes increasing at an alarming rate both nationally and internationally, diabetes-related complications and deaths tend to increase as well (4-8). It is therefore critical to maintain good glycemic control to keep diabetes in check and reduce diabetes-related complications (9).

HbA1c has been recommended as a test option for the diagnosis of diabetes by both the American Diabetes Association (10) and the World Health Organization (WHO) (11). Both organizations advised that after a result consistent with the diagnosis of diabetes (≥ 6.5% (48 mmol/mol), testing of HbA1c levels should be repeated in asymptomatic patients within 2 weeks to rule out the rare occurrence of a sample being mislabeled. Not much research has been conducted in the area of repeat testing of HbA1c; however, Driskell et al. (2014) stated that “the optimal testing frequency required to maximize the downward trajectory in HbA1c was four times per year, particularly in those with an initial HbA1c of ≥7% (≥53 mmol/mol), supporting international guidance. Testing 3-monthly was associated with a 3.8% reduction in HbA1c compared with a 1.5% increase observed with annual testing; testing more frequently provided no additional benefit. Compared with annual monitoring, 3-monthly testing was associated with a halving of the proportion showing a significant rise in HbA1c (7–10 vs. 15–20%)” (12). The authors concluded that monitoring frequency is associated with a significant detrimental effect on diabetes control and that to achieve the optimum downward trajectory in HbA1c, monitoring frequency should be quarterly.

There are also reports that suggest that guidelines for testing HbA1c are not necessarily being followed (13-15). This study therefore evaluated for the first time the baseline/mean HbA1c (mmol/mol) among the Guyanese population and aims to determine if a standard international algorithm has been followed in regard to repeat testing of patients with suspected diabetes and of undiagnosed/high-risk population.

Methods

This was a laboratory-based retrospective study conducted between 2010 and 2014 at a level III public hospital in Guyana. All patients who had already performed the HbA1c test to screen for diabetes and those who had complete information were included in the study. Any patient who did not follow the HbA1c algorithm was excluded. Inappropriate ordering of tests was defined as any order for testing a given patient occurring more than 3 months after the previous order. Bio-Rad D-10 was used to monitor HbA1c at the public hospital. Bio-Rad D-10 utilizes the principle of High Performance Liquid Chromatography (HPLC) to determine the percentage of HbA1c. Permission to conduct this research was obtained from the Ethics Committee under the Ministry of Health, Guyana, and from the Director of Medical Services of the public hospital.

Data analysis

The data collected from the database were first entered into a spreadsheet using Microsoft Excel. All statistical analyses were performed using SPSS 21.0, JMP and Microsoft Excel. Distributions were used to show frequencies, the bivariate fit test was done in order to achieve correlations and significance, the χ2 test was used to compare the differences in proportions and ANOVA was used for differences in mean differences. A p-value of < 0.05 was used to show significance.
Results

A total of 1,547 eligible patients were selected for the study from the database of the GPHC medical laboratory. The patient population analysis had the following baseline characteristics: mean age was 59.9 ± 11.5 years (95% CI 59.3 - 60.4). 5% of the patients were between the ages of 21 and 40, 41% were between the ages of 41 and 60 and 54% were between the ages of 61 and 90.

Figure 1 shows the HbA1c percentage in test 1, the maximum, median and minimum values of 19.2%, 8.9% and 4.2% respectively and a mean and standard deviation of 9.2 ± 2.7. For the HbA1c percentage in test 2, the maximum, median and minimum values were 18.5%, 8.7% and 4.0% respectively, with a mean (SD) of 9.1 ± 2.5. For test 3, 396 patients were tested with the maximum, median and minimum values of 19.7%, 9.4% and 41% respectively, and a mean (SD) of 9.6 ± 2.6. Only 82 patients were tested for a fourth time, with the maximum, median and minimum values of 15.1%, 9.2% and 5.2% respectively, and a mean (SD) of 9.6 ± 2.6 (Figure 1).

Figure 1. Distribution of HbA1c test results

The mean HbA1c ± standard deviation (SD) of all tests is shown in Table 1. Test 1 had a mean of 9.23 ± 2.6 (95% CI 9.1 - 9.4). Test 2 had a mean of 9.08 ± 2.5 (95% CI 8.95 - 9.20). Test 3 had a mean of 9.59 ± 2.6 (95% CI 9.34 - 9.85) and Test 4 had a mean of 9.59 ± 2.6 (95% CI 9.01 - 10.17).
Table 1. Mean ± SD of HbA1c in regard to gender

<table>
<thead>
<tr>
<th>HbA1c</th>
<th>Male Mean ± SD</th>
<th>95% CI</th>
<th>Female Mean ± SD</th>
<th>95% CI</th>
<th>Total Mean ± SD</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test 1</td>
<td>8.9 ± 2.7</td>
<td>8.7-9.2</td>
<td>9.4 ± 2.6</td>
<td>9.5-9.2</td>
<td>9.2 ± 2.7</td>
<td>9.1-9.4</td>
</tr>
<tr>
<td>Test 2</td>
<td>8.7 ± 2.4</td>
<td>8.5-8.9</td>
<td>9.2 ± 2.6</td>
<td>9.4-9.1</td>
<td>9.1 ± 2.5</td>
<td>8.9-9.2</td>
</tr>
<tr>
<td>Test 3</td>
<td>9.2 ± 2.5</td>
<td>8.7-9.7</td>
<td>9.8 ± 2.6</td>
<td>9.5-10.1</td>
<td>9.6 ± 2.5</td>
<td>9.3-9.8</td>
</tr>
<tr>
<td>Test 4</td>
<td>8.8 ± 2.5</td>
<td>7.8-9.8</td>
<td>9.9 ± 2.7</td>
<td>9.3-10.7</td>
<td>9.5 ± 2.6</td>
<td>9.0-10.2</td>
</tr>
</tbody>
</table>

The correlation analysis between each test is shown in Figure 2. The correlation between Test 1 and Test 2, Test 3 and Test 4 was 0.64 (95% CI 0.61-0.67), 0.58 (95% CI 0.50-0.64) and 0.66 (95% CI 0.52-0.77), respectively. The correlation between Test 2 and Test 3 was 0.64 (95% CI 0.57-0.69), and the one between Test 2 and Test 4 was 0.66 (95% CI 0.51-0.76). The correlation between Test 3 and Test 4 was 0.64 (95% CI 0.49-0.75).

Figure 2. Correlation between individual HbA1c test values
Mean ± SD of each HbA1c test among male and female patients is shown in Table 2. Mean HbA1c was higher among females in all four HbA1c tests. Females were more at risk and all four tests indicated that females were above the baseline when compared to males (30.8% (2 5.86 and p < 0.05)).

<table>
<thead>
<tr>
<th>HbA1c &gt; Mean</th>
<th>Female</th>
<th>Male</th>
<th>P-value</th>
<th>RR (95% CI)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>N (%)</td>
<td></td>
<td></td>
<td>N (%)</td>
</tr>
<tr>
<td>Test 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>145 (9.4)</td>
<td>92 (0.1)</td>
<td>&lt; 0.05</td>
<td>1.13 (1.02-1.26)</td>
<td>237 (15.3)</td>
</tr>
<tr>
<td>Yes</td>
<td>906 (58.6)</td>
<td>404 (26.1)</td>
<td></td>
<td></td>
<td>1310 (84.7)</td>
</tr>
<tr>
<td>Test 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>147 (9.5)</td>
<td>85 (0.1)</td>
<td>&lt; 0.05</td>
<td>1.04 (0.99-1.08)</td>
<td>232 (15)</td>
</tr>
<tr>
<td>Yes</td>
<td>904 (58.4)</td>
<td>411 (26.6)</td>
<td></td>
<td></td>
<td>1315 (85.0)</td>
</tr>
<tr>
<td>Test 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>27 (6.8)</td>
<td>15 (3.8)</td>
<td>&gt; 0.05</td>
<td>1.04 (0.96-1.13)</td>
<td>42 (10.5)</td>
</tr>
<tr>
<td>Yes</td>
<td>258 (64.7)</td>
<td>99 (24.8)</td>
<td></td>
<td></td>
<td>357 (89.5)</td>
</tr>
<tr>
<td>Test 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3 (3.7)</td>
<td>2 (2.4)</td>
<td>&gt; 0.05</td>
<td>1.03 (0.90-1.16)</td>
<td>5 (6.1)</td>
</tr>
<tr>
<td>Yes</td>
<td>53 (64.6)</td>
<td>24 (29.3)</td>
<td></td>
<td></td>
<td>77 (93.9)</td>
</tr>
</tbody>
</table>

The mean difference ± standard error (SE) change between two HbA1c tests is shown in Table 3. The duration between individual tests is shown in Figure 3. Mean duration between test 1 and test 2 was 16.14 ± 11.3 (95% CI 15.6-16.7), with the standard error of 0.28; for test 2 and test 3, it was 12.43 ± 8.83 (95% CI 11.6-13.3), with an SE of 0.44; for test 3 and test 4, it was 10.25 ± 8.8 (95% CI 8.32-12.2), with an SE of 0.96.

Figure 3. Duration and standard error between individual tests
Table 3. Correlation and mean difference between each test

<table>
<thead>
<tr>
<th>HbA1c</th>
<th>Mean difference</th>
<th>SE</th>
<th>95% CI</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test 1 - Test 2</td>
<td>-0.15</td>
<td>0.05</td>
<td>-0.26-0.04</td>
<td>0.64</td>
</tr>
<tr>
<td>Test 1 - Test 3</td>
<td>0.06</td>
<td>0.12</td>
<td>-0.17-0.29</td>
<td>0.57</td>
</tr>
<tr>
<td>Test 1 - Test 4</td>
<td>0.22</td>
<td>0.23</td>
<td>-0.25-0.68</td>
<td>0.67</td>
</tr>
<tr>
<td>Test 2 - Test 3</td>
<td>0.11</td>
<td>0.10</td>
<td>-0.10-0.32</td>
<td>0.63</td>
</tr>
<tr>
<td>Test 2 - Test 4</td>
<td>-0.23</td>
<td>0.24</td>
<td>-0.70-0.23</td>
<td>0.67</td>
</tr>
<tr>
<td>Test 3 - Test 4</td>
<td>-0.35</td>
<td>0.24</td>
<td>-0.83-0.12</td>
<td>0.65</td>
</tr>
</tbody>
</table>

Of the 1,547 patients included in the study, for 828 (53.5%) patients, the HbA1c result decreased in test 2 when compared to test 1. Of the 396 patients who were tested for a third time, the HbA1c result decreased for 171 (43.2%) patients when compared to test 2. Of the 83 patients tested for a fourth time, 46 (56%) patients also experienced a decrease.

**Discussion**

The main outcome was the proportion of patients undergoing repeat HbA1c testing and the proportion of patients whose baseline HbA1c value decreased. This study used the HbA1c threshold for the diagnosis of diabetes (48 mmol/mol (6.5%)), according to the new diagnostic criteria for diabetes adopted by the American Diabetes Association (16).

This study represents the first attempt to review and analyze the HbA1c data of patients using Bio-Rad at the Georgetown Public Hospital Corporation. Older patients, between the ages of 61 and 90, represented the largest group (54%) in the diabetic population and female patients were above baseline HbA1c in more cases than male patients. A similar pattern has been noted in other studies, where female patients of all age groups and races were found to be at risk (17).

This study revealed that no standard guidelines were followed by the clinicians in terms of repeat testing intervals. There were many variations noted in regard to the duration between tests. Discordant HbA1c results have created confusion among the clinicians.Clinicians need to be aware that significant test-retest variation exists in HbA1c and is sometimes quite large (18). Mean HbA1c for all four tests was recorded above 9.0, which is much greater than the baseline value. Many studies have warned that HbA1c concentrations above 48 mmol/mol (6.5%) are risk factors for development of diabetic retinopathy, macrovascular outcomes and death (18-21).

The International Expert Committee (IEC) (24) and ADA (16) have proposed new diagnostic criteria for diabetes on the basis of HbA1c measurement, in which HbA1c of ≥ 6.5% is defined as diabetes. In the present study, an HbA1c level of 6.5% had a reasonably high specificity (99.1%) and low false-positive rate (0.9%) for the diagnosis of diabetes, which is in complete concordance with IEC and ADA recommendations.

Repeat testing showed a significant decrease in HbA1c levels in a portion of patients. A decrease in a follow-up test is favored because this is indicative of following proper treatment strategies and overall control of the patient’s diabetic condition. It is also understood that a decrease should not be expected in every case of repeat testing, since an increased value maybe be accounted for by a number of different reasons. Multiple factors affect the accuracy of HbA1c as an indicator of average
glucose concentration, including abnormal erythrocyte lifespan, assay-related artifacts, fast vs. slow glycosylation, ethnicity, pregnancy, use of drugs and acute illness. Different factors affect the validity of HbA1c, such as iron deficiency, altered hemoglobin structure, erythrocyte lifespan and interracial variability, age (the elderly and children), gender and pregnancy (25, 26).

It is a well-known fact that high levels of HbA1c are associated with an increased risk of atrial tachyarrhythmia and paroxysmal atrial fibrillation in patients with type 2 DM (27). Furthermore, it has been reported that an increase of 1% in HbA1c concentration was associated with roughly a 30% increase in all-cause mortality among diabetes patients (28). This shows that the proportion of HbA1c percentage increase is far too high and, as such, stricter measures should be implemented to reduce this percentage.

**Conclusion**

It is a fact that HbA1c is a test that is accurate and easy to administer for diagnosing diabetes, especially in low and middle income countries like Guyana. However, the mean HbA1c percentage of the diabetic population in Guyana was found to be 9.4%, which is far higher than ADA’s established HbA1c criteria for prediabetes and diabetes (5.7% and 6.5%). Therefore, the researchers recommend that strict guidelines be followed by physicians in regular and accurate testing of HbA1c.

**Acknowledgments**

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**References**


