

Received: 2018.05.18
Accepted: 2018.06.25
Published: 2018.10.16

Appropriateness of Using Tests for Blood Glucose and Diabetic Complications in Clinical Practice: Experiences in a Hospital in Thailand

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Source of support: None

Background: This study aimed to evaluate how the tests for blood glucose (BG) and diabetic complications have been utilized in a hospital in Thailand.

Material/Methods: Patient medical records having the results of BG, HbA_{1c} and/or urine microalbumin presented and the records of DM patients having the results of serum lipids, serum LDL-C, and/or serum creatinine presented were selected. The data of diagnosis, ordered tests, and testing results in these records were extracted for evaluation.

Results: This study recruited 1066 patients diagnosed with DM and 3081 patients diagnosed with other diseases. Point-of-care testing (POCT) for BG was repeatedly used in 371 non-DM cases; most of its results were normal. The results of BG and HbA_{1c} were often used together. There was a good relationship between them, and these test results indicated poor glycemic control in 58% of DM cases. In non-DM cases, the test results agreed, indicating normoglycemia in 17.32%, pre-diabetes in 20.47%, and diabetes in 21.78%. To prevent diabetic nephropathy, serum creatinine was frequently used, whereas urine microalbumin, the recommended test, was underutilized. The result of LDL-C from both direct measurement and calculation were used; however, based on the same guidelines, the results of measured LDL-C indicated risk of cardiovascular diseases in a higher percentage of DM cases than did the results of calculated LDL-C.

Conclusions: The use of POCT for BG in hospitalized patients may be inappropriate. The utilization of urine microalbumin should be promoted to effectively prevent diabetic nephropathy.

MeSH Keywords: **Creatine • Diabetes Complications • Hemoglobin A, Glycosylated • Point-of-Care Systems**

Full-text PDF: <https://www.medscimonit.com/abstract/index/idArt/911216>



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Background

Diabetic mellitus (DM), particularly type 2 DM, is one of the most common chronic diseases worldwide [1–3]. The test for blood glucose (BG) is generally used for diagnosis DM. In ill patients, the test is utilized for detecting hypo- and hyperglycemia, and for close BG monitoring, a point-of-care testing (POCT) for BG has been recommended and applied in most hospitals [4], including in this hospital. To prevent diabetic complications associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, heart, and blood vessels in DM patients [5], the test for hemoglobin A_{1c} (Hb A_{1c}) was recommended for monitoring long-term glycemic control and serum lipids, as well as urine microalbumin, were recommended for detecting and preventing some diabetic complications [6]. The inappropriate use of laboratory tests can lead to unnecessary expense and some undesirable consequences, such as unnecessary patient inconvenience from waiting and specimen collection, increasing turnaround time, and increasing chance of getting a false-positive result, over-diagnosis, and over-treatment [7–9].

As previously reported, the use of laboratory tests may differ by region and geography [10,11]. The issue of inappropriate laboratory utilization is receiving increasing attention internationally due to pressure to reduce healthcare spending [12]. This study aimed to evaluate how the laboratory tests for BG and diabetic complications have been utilized in a hospital in Thailand and to determine whether the tests were used appropriately based on the medical necessity accordingly to the recommended clinical guidelines for a particular test.

Material and Methods

This study was conducted at the HRH Princess Maha Chakri Sirindhorn Medical Center, Nakhon Nayok, located in the central region of Thailand near Bangkok. The project was approved by the Srinakharinwirot University Ethics Committee for Human Research. Medical records of patients admitted from 2014 to 2016 were randomly collected using a systematic sampling method. From the collected records, only those having the results of BG, HbA_{1c}, and/or urine microalbumin presented and the records of DM patients having the results of serum lipids, serum LDL-C, and/or serum creatinine presented were recruited. The data on diagnosis, tests ordered, and testing results in these records were extracted anonymously for evaluating the utilization of these tests. Statistical analyses were performed using Microsoft Excel 2007 (file version 12.0.6665.5003). Linear regression analysis with the significance level of 0.05 was used to determine relationships between the results of BG and HbA_{1c} and between the results of urine microalbumin and serum creatinine.

Results

Case information

The total number of 4147 cases were recruited; 1066 cases were diagnosed with DM (DM cases) and 3081 cases were diagnosed with other diseases (non-DM cases).

Blood glucose

The results of BG were reported in 921 DM cases and 1788 non-DM cases. They were interpreted according to the standard guidelines [13, 14]. As presented in Table 1, the BG results were used to diagnose DM in non-DM cases and to detect hypoglycemia and hyperglycemia in DM and non-DM cases.

The results of BG from POCT were reported in 81 DM cases; its result was reported as a single test utilized in 88.89% of them. In contrast, the test was repeatedly utilized in 371 non-DM cases; 2–21 results per day (mean \pm SD=3.74 \pm 2.00 results/day). As shown in Table 2, close BG monitoring in DM cases led to prompt treatment at least once in all 9 cases, but in non-DM cases, repeated BG measurements detected hypoglycemia and/or stress-induced hyperglycemia at least once only in 28%.

Hemoglobin A_{1c}

The results of HbA_{1c} were presented in 671 DM cases and 384 non-DM cases; 98.06% of DM cases and 99.22% of non-DM cases also had the BG results reported. The relationship between HbA_{1c} and BG was fairly good ($r=0.6999$ for all cases, $r=0.6631$ for DM cases, and $r=0.7264$ for non-DM cases). The HbA_{1c} result was interpreted according to previous recommendations [13,15]. Briefly, in DM cases HbA_{1c} results $\geq 6.5\%$ indicate uncontrolled DM, and in non-DM cases the HbA_{1c} results between 5.7% and 6.4% indicate pre-diabetes and HbA_{1c} $\geq 6.5\%$ indicates DM. As shown in Table 3, the results of BG and HbA_{1c} agreed, indicating poor glycemic control in 58.05% of DM cases and in non-DM cases the results of BG and HbA_{1c} agreed, indicating the same glycemic status in 59.57%.

Microalbumin

Urine microalbumin was utilized without serum creatinine in only 41 DM cases. It was utilized along with serum creatinine in 229 DM cases. Serum creatinine was utilized without microalbumin in 530 DM cases. Urine microalbumin was utilized in 150 non-DM cases; 46% of them were diagnosed with hypertension. The relationship between the results of urine microalbumin and serum creatinine was poor ($r=0.1463$ for all cases; $r=0.0714$ in DM cases, and $r=0.2417$ in non-DM cases). Because various cut-off values of serum creatinine are recommended [16–18], it was decided to use 88.4 μ mol/L as the cut-offvalue. The

Table 1. Number of cases based on their BG results.

BG results (mmol/L)	Number of cases (n (%))				Status
	DM cases		Non-DM cases		
<3.9	17	(1.85%)	11	(0.61%)	Hypoglycemia
3.9–5.6	67	(7.27%)	780	(43.62%)	Normoglycemia
5.7–6.9	224	(24.32%)	711	(39.77%)	Pre-diabetes
7.0–11.1	459	(49.84%)	237	(13.26%)	Diabetes
>11.1	154	(16.72%)	49	(2.74%)	Hyperglycemia/diabetes

Table 2. Abnormal BG result from repeatedly BG measurements.

Status	Number of DM cases (n (%))	Number of non-DM cases (n (%))
Total cases	9	371
Hypoglycemia detected	0	12 (3%)
Hyperglycemia detected	6 (67%)	86 (23%)
Hypo- and hyperglycemia detected	3 (33%)	8 (2%)

Table 3. Agreement between BG and HbA_{1c}.

BG (mmol/L)	Number of DM cases (n(%)) with HbA1C			Number of non-DM cases (n(%)) with HbA1C		
	<5.7%	5.7–6.4%	≥6.5%	<5.7%	5.7–6.4%	≥6.5%
<5.7	9 (1.37%)	20 (3.04%)	25 (3.80%)	66 (17.362%)	32 (8.40%)	10 (2.62%)
5.7–6.9	24 (3.65%)	69 (10.49%)	57 (8.66%)	53 (13.91%)	78 (20.47%)	25 (6.56%)
≥7.0	14 (2.13%)	58 (8.81%)	382 (58.05%)	5 (1.31%)	29 (7.61%)	83 (21.78%)

Table 4. Agreement between serum creatinine and random urine microalbumin.

Urine microalbumin	Number of DM cases (n (%))		Number of non-DM cases (n (%))	
	Creatinine ≤88.4 μmol/L	Creatinine >88.4 μmol/L	Creatinine ≤88.4 μmol/L	Creatinine >88.4 μmol/L
<30 mg/g creatinine	69 (30.13%)	41 (17.90%)	52 (40.94%)	34 (26.77%)
30–300 mg/g creatinine	44 (19.21%)	56 (24.45%)	20 (15.75%)	13 (10.24%)
>300 mg/g creatinine	5 (2.18%)	14 (6.11%)	3 (2.36%)	5 (3.94%)

results of random urine microalbumin were interpreted according to standard recommendations [13,14,19,20]; briefly its values between 30 to 300 mg/g creatinine indicate microalbuminuria and its levels >300 mg/g creatinine indicate overt- or macroalbuminuria or renal failure. As shown in Table 4, high serum creatinine concentrations without microalbuminuria were detected in 18% of DM cases and 27% of non-DM cases.

Serum lipids

At least 1 serum lipid testing result was reported in 640 DM cases; the results of lipid profile and LDL-C were reported in 48.59%, lipid profile in 26.25%, and LDL-C in 13.91%. LDL-C could be calculated (cLDL-C) from the results of other serum lipids using Friedewald’s formula [21]. Based on the standard guidelines [13,14,22], high risk of cardiovascular disease (CVD)

Table 5. Number of DM cases with hyperlipidemia.

Criteria	Total ordered cases	Number of cases (n (%))
Cholesterol >5.18 mmol/L	485	118 (24.33%)
Triglycerides >1.70 mmol/L	556	217 (39.03%)
LDL-C >2.59 mmol/L	467	236 (50.54%)
cLDL-C >2.59 mmol/L	479	169 (35.28%)

in DM cases is indicated when their LDL-C values are >2.59 mmol/L. As presented in Table 5, the results of LDL-C >2.59 mmol/L were detected in 50.54% of DM cases, but the risk of CVD was detected in only 35.28% of them when the results of cLDL-C were used.

Discussion

The test for BG is traditionally used to diagnose DM, to monitor daily glycemic status in DM patients, and in critical ill or comatose patients it is necessary for identifying life-threatening hypoglycemia and stress-induced hyperglycemia [23–28]. Although hypo- and hyperglycemia were more often detected in DM cases than in non-DM cases, the POCT for BG was primarily utilized for close BG monitoring in non-DM cases and most of its results were normal. In this hospital, POCT devices were provided in the ward and they were simple to operate and gave results quickly; thus, they were used quite often by physicians and nurses. Additionally, as observed in this hospital, the POCT for BG was conducted as a single test used in some DM cases; it might be utilized for non-medical purposes such as to finish consultation, to reassure patients, or to meet patients' expectations. According to previous reports, finger-stick capillary BG measurement by use of a POCT device was not appropriate for BG monitoring in hospitalized patients because its results could deviate from the BG results from laboratory testing by up to 20% [25,29]. Unlike the laboratory testing, the POCT for BG is performed without daily internal quality control, the device is not routinely calibrated, and it can be operated improperly by untrained persons; thus, the BG results from POCT may not be accurate and reliable for managing an ill patient.

HbA_{1c} is a valuable diagnostic tool for monitoring long-term glycemic control in diabetes patients [13–15]. In this hospital, physicians preferred to use both BG and HbA_{1c} for this clinical purpose, as 2 values were in agreement, indicating poor glycemic control in 58% of DM cases. In non-DM cases, based on the 2011WHO guidelines [30,31], the result of HbA_{1c} was utilized for diagnosis DM and pre-diabetes. Likewise, for this clinical purpose, physicians in this hospital utilized both BG and

HbA_{1c} results, and the results indicated that both values identified the same glycemic conditions in 59.57% of non-DM cases.

Screening for microalbuminuria with a spot urine albumin/creatinine ratio has been recommended for identifying the early stages of diabetic nephropathy when physicians can manage to prevent the progression to renal failure [13,14,19]. Nonetheless, serum creatinine testing was performed for most DM cases in this hospital, possibly due to the physicians' familiarity with serum creatinine or their unfamiliarity with microalbumin. When used, urine microalbumin testing was often ordered along with testing for serum creatinine; however, its result had a poor relationship with the results of serum creatinine. High serum creatinine levels were found without microalbuminuria in 17.90% of DM cases according to a previous report [32]. Increasing serum creatinine with the absence of microalbuminuria might indicate an occurrence of acute renal failure, and the incidence of this condition in DM patients should be further studied. Although the number of factors influencing the concentration of serum creatinine was reduced by using calculated glomerular filtration rate, according to the 2002 Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines [33], changes in the value of GFR (e.g., serum creatinine) will indicate persistence of renal failure. To prevent the progression of early-stage diabetic nephropathy to renal failure, GFR as serum creatinine may not be sensitive enough. Urine microalbumin was recommended for monitoring the effectiveness of anti-hypertensive drugs and supporting the diagnosis of cardiovascular diseases [19,20]; therefore, the use of urine microalbumin in non-DM cases, particularly in hypertensive patients, might be a result of following these recommendations.

Serum lipid testing, specifically LDL-C, is recommended for preventing CVD in DM patients [22,23,34]. Low-density lipoprotein cholesterol or LDL-C can be directly measured (LDL-C) or traditionally calculated (cLDL-C) from the results of other serum lipids. Both LDL-C and cLDL-C are interpreted by the same guidelines; however, the percentages of DM cases with a high risk of CVD were different when utilizing results of LDL-C and cLDL-C. It is still unclear which LDL-C is more reliable [35]. New markers for more reliable estimation of CVD risk have been proposed, including sub-fractions of apolipoproteins [36], but these tests are still not available in most parts of the world [37], including in Thailand.

Conclusions

The use of tests for BG and diabetic complications in this hospital based on the standard guidelines of a certain test were mostly appropriate. The utilization of laboratory testing for BG is appropriate for hospitalized patients, as it is standardized and its result is more reliable than the BG result from POCT.

The use of BG and HbA_{1c} together in glycemic monitoring of DM patients and in diagnoses of diabetes and pre-diabetes seemed to be appropriate, since over half of their results agreed, indicating the same glycemic status. To prevent the progression of early-stage diabetic nephropathy to renal failure and to reduce the incidence of severe renal complication in DM patients, the use of urine microalbumin should be promoted in this hospital.

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Acknowledgements

I thank the director of HRH Princess Maha Chakri Sirindhorn Medical Center for her permission in accessing patients' medical records.

Conflicts of interest

None.