Diabetes & Metabolic Syndrome: Clinical Research & Reviews 13 (2019) 2080–2085

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

Does reviewing fasting plasma glucose results patterns before glycosylated hemoglobin testing in type-2 diabetic patients lead to better testing decision?

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ARTICLE INFO

Article history:
Received 28 March 2019
Accepted 21 April 2019

Keywords:
Fasting plasma glucose
Glycosylated hemoglobin
Type-2 diabetic patients

ABSTRACT

Aims: Glycosylated hemoglobin (HbA_{1c}) test for blood glucose control in type-2 diabetic patients is recommended at least once annually under the guidelines of the Thai National Health Security Office (NHSO) benefits coverage. With limited resources and capability for HbA_{1c} testing in most primary-care providers, this study explored patterns of fasting plasma glucose (FPG) tests for proper timing of HbA_{1c} test would increase value of the money spent.

Methods: A retrospective review of laboratory findings of 4906 type-2 diabetic outpatients in two university hospitals in Thailand was conducted. Percentages of discordant results between the indexed FPG and HbA_{1c} tests were compared between the patient groups with different FPG patterns before HbA_{1c} testing and the control group of randomly selected cases.

Results: Having HbA_{1c} tested after two and three consecutively normal FPG tests (OO and OOO patterns) were found to have significantly less discordance than the control group (−9.6% and −15.7%). HbA_{1c} testing after two abnormal and one normal consecutive FPG tests (XXO pattern) gained the discordant results by 24.8%.

Conclusions: Some FPG patterns were more predictive of HbA_{1c} findings than focusing on one-time FPG results. Reviewing and recognizing certain patterns of FPGs prior to taking HbA_{1c} tests can lead to better HbA_{1c} testing decision than randomly prescribing the tests.

1. Introduction

Diabetes Mellitus (DM) is a worldwide challenge recognized by World Health Organization (WHO). In 2014, the prevalence of DM in adult population was 8.5%, there were 422 million adults with DM and the top two regions were the Western Pacific region (131 million people) and the South-East Asia region (96 million people) [1]. In Thailand, the prevalence of DM increased from 7.8% in 2009 to 9.9% in 2014 and the proportions of undiagnosed DM increased from 46.1% to 51.2% among men and 23.3% to 41.3% among women [2]. In 2015, 80.8% of diabetic patients received glycosylated hemoglobin (HbA_{1c}) testing at least once a year, only 36.3% and 38.2% of patients met the glycemic goal of HbA_{1c} less than 7% (<53 mmol/mol) and fasting plasma glucose (FPG) 70–130 mg/dL (3.9–7.2 mmol/L), respectively [3].

Although FPG and HbA_{1c} are both used as measurements for DM control [4], the results of FPG and HbA_{1c} may not always agreeable in diagnosing and monitoring DM control [5–11]. The guideline for DM treatment used by the Thai Universal Coverage Scheme (UCS) in Thailand recommends that HbA_{1c} test should be conducted at least once a year [12]. However, due to limited capitation budget each healthcare provider has, the HbA_{1c} test is not routinely performed. The cost per unit of HbA_{1c} test is US$ 4.69 which is more expensive than the cost of FPG (Strip test) of only US$ 1.25. As the HbA_{1c} test must be tested in a standard laboratory, health care facilities, especially health centers and some small community hospitals in rural areas may not have the required capacity. Specimens for the test must be sent to the provincial general of tertiary-care hospitals. According to personal communication with some rural physicians, it seems to be a common practice that they consider HbA_{1c} when they suspect that patients with normal FPG results might Play

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https://doi.org/10.1016/j.dsx.2019.04.030
1871-4021/

Game by controlling food and sugar intake a few days prior to physician visits. Over-testing of HbA_{1c} could lead to inefficient use of resources for diabetic care [13]. HbA_{1c} testing for all Thai DM patients may cost up to US$ 19.72 million (1 US$ = 32 THB) annually. Therefore, this study aims to find out whether reviewing patterns of more commonly used FPG testing before decisions to go for HbA_{1c} tests could lead to different conclusions about patients' glycemic control, comparing to randomly ordering the test. Better informed decisions to order, or not to order HbA_{1c} test would add more value to the resources spent on DM care.

2. Methods

2.1. Design and settings

We conducted a retrospective medical record review of laboratory findings of type-2 diabetic outpatients using the secondary databases in two university hospitals in Thailand, one in Bangkok and the other in the northern part of the country.

2.2. Study sample

The study sample included 4906 type-2 diabetic outpatients of the two university hospitals in the fiscal year 2012 (1 October 2011–30 September 2012) selected by the following inclusion and exclusion criteria.

Inclusion Criteria were (1) type-2 diabetic outpatients whose age up to 18 years old (2) having regular visits for DM care in one month to four month intervals (3) having FPG tests in all of those visits and (4) having HbA_{1c} test at least once in the year.

Exclusion Criteria were (1) having FPG tests more than four times in a month (2) having HbA_{1c} tests more than four times in the year and (3) pregnant patients.

The subjects were selected to be the pattern groups and the control group.

2.2.1. The pattern groups

We selected 30 pattern groups to represent different patterns of FPG. The FPG patterns included FPG results from four visits (time t-1, t-2, t-3 and t-4, respectively) before the indexed HbA_{1c} test (time t_0) as shown in Fig. 1. Each pattern group must have a regular interval of FPG test which may be every month, every two months, every three months, every four months or month-mixed.

2.2.2. The control group

The control group comprised 379 patients selected by simple random sampling with replacement from the secondary databases in two university hospitals. Using proportion of hospital 1 to hospital 2 there were 38.83% (147 patients) to 61.17% (232 patients) without considering FPG patterns before HbA_{1c} test. The results found that abnormal FPG but normal HbA_{1c} was higher than normal FPG but abnormal HbA_{1c} (42.5% vs 29.7%).

2.3. Observation and measurement

The outcome of interest was discordance between FPG and HbA_{1c} test findings.

To resemble the practice of decision making in ordering the HbA_{1c} test, the discordant outcome in the pattern groups were indicated by discordant results between the FPG test at the time t-1 visit (indexed FPG) and the HbA_{1c} test at the time t_0 visit (indexed HbA_{1c}). The random HbA_{1c} tests in the control group, the outcomes of both FPG and HbA_{1c} were determined at the time t_0 visit i.e. (1) abnormal FPG but normal HbA_{1c}, or (2) normal FPG but abnormal HbA_{1c}. Based on the Standards of Medical Care in Diabetes 2018 by American Diabetes Association (ADA) [14], the normal ranges of FPG and HbA_{1c} were set as follows:

- Adolescents aged 13–19 years old: FPG 90–130 mg/dL (5.0–7.2 mmol/L); HbA_{1c} less than 7.5% (<58 mmol/mol)
- Adults aged 20–64 years old: FPG 80–130 mg/dL (4.4–7.2 mmol/L); HbA_{1c} less than 7% (<53 mmol/mol)
- Older adults aged 65 years old up: FPG 90–130 mg/dL (5.0–7.2 mmol/L); HbA_{1c} less than 7.5% (<58 mmol/mol)

The FPG patterns were considered from regular interval visits between FPG at time t-1 and t-2 visit, time t-2 and t-3 visit, time t-3 and t-4 visit which regular interval visits were as follows:

- A monthly visit which had an interval visit within 21–35 days
- Every two months visit which had an interval visit within 49–63 days
- Every three months visit which had an interval visit within 77–91 days
- Every four months visit which had an interval visit within 105–119 days
- Month-mixed visit which had an interval visit different from regular interval within one month, more or less (21–35 days)

In case patient had more than one HbA_{1c} test in a year, the latest test was assigned as the indexed HbA_{1c} test.

2.4. Data analysis

We performed the data cleaning by checking accuracy and completeness of databases without the repetition of patients' data. The pattern groups and the control group were analyzed by using descriptive statistics included percentages, mean and standard deviation (SD). The percentages of indexed FPG-HbA_{1c} discordant results were calculated with the numbers of discordance between the indexed FPG and HbA_{1c} results divided by the numbers of patients in each group. The percentage differences of indexed FPG-HbA_{1c} discordant results between the pattern groups and the control group were analyzed by using Two-sample test of proportions. All statistical analyses were conducted using STATA software version 12.

2.5. Ethics approval

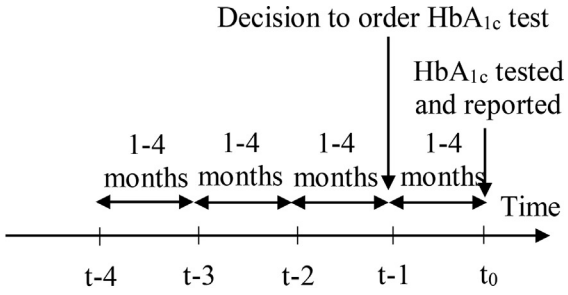
The study protocol was approved by the Institutional Review Board, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand (IRB no. 524/58). As all of data in the study were secondary database, the written informed consent was impossible. The data were used with the permission of the two university hospitals.

3. Results

General characteristics of the study sample were described in Table 1 which tended to be female (55.8%), age less than 65 years old (58.9%), having been treated for DM with drugs only (85.3%) and having FPG tests every three months (57.7%).

The control group, randomized proportionally from the study sample of the two hospitals, comprised 379 patients. There were 59.1% female, 44.9% age 65 years up and 84.7% having been treated for DM with drugs only.

Although the study sample had 1388 patients with available FPG results at time t-1, there were 529 patients with available FPG results at time t-1 and t-2, and 188 patients with available FPG results at time t-1, t-2 and t-3. However, there were only 26 patients with available FPG results at time t-1, t-2, t-3 and t-4. Therefore, an



The pattern groups	Visit				
	t-4	t-3	t-2	t-1	t_0
	FPG results before HbA_{1c} test				HbA_{1c}
The FPG tests had regular interval visit which can be every month, every two months, every three months, every four months or month-mixed.					
1.0 The previous FPG patterns 1 time				O	X
1.1				X	O
2.0 The previous FPG patterns 2 times			O	O	X
2.1			X	O	X
2.2			X	X	O
2.3			O	X	O
3.0 The previous FPG patterns 3 times		O	O	O	X
3.1		X	O	O	X
3.2		O	X	O	X
:				:	
3.7		O	O	X	O
4.0 The previous FPG patterns 4 times	O	O	O	O	X
4.1	X	O	O	O	X
4.2	O	X	O	O	X
4.3	O	O	X	O	X
:				:	
4.15	O	O	O	X	O

Note: O, normal result; X, abnormal result.

Fig. 1. The pattern groups analysis.

analysis on the patterns with four FPG tests before HbA_{1c} were excluded. The distribution of FPG patterns by groups were shown in Table 2 which were noted as the following:

1) The FPG patterns with abnormal FPG at time t-1 (X = 40.3%, XX = 39.1%, XXX = 42.6%) had a higher chance to be normal HbA_{1c} tests than normal FPG at time t-1 change to abnormal HbA_{1c} tests (O = 28.5%, OO = 20.1%, OOO = 14.0%).
2) The patients with abnormal FPG at time t-1, having normal FPG at time t-2 and/or t-3 would likelihood increase the finding of normal HbA_{1c} tests (OOX = 64.3%, OX = 51.2% vs X = 40.3%).
3) The patients with normal FPG at time t-1, having abnormal FPG at time t-2 and/or t-3 would possibly increase the finding of abnormal HbA_{1c} tests (XXO = 54.5%, XO = 35.7% vs O = 28.5%).

The percentage differences of indexed FPG-HbA_{1c} discordant results between the pattern groups and the control group were

Table 1
General characteristics of type-2 diabetic outpatients.

	Number (percentage) of study sample		
	Hospital 1 (n = 539)	**Hospital 2 (n = 849)**	**Total (n = 1388)**
Sex			
Male	275 (51.0)	339 (39.9)	614 (44.2)
Female	264 (49.0)	510 (60.1)	774 (55.8)
Age group			
18–64 years	344 (63.8)	474 (55.8)	818 (58.9)
65 years up	195 (36.2)	375 (44.2)	570 (41.1)
Mean age	60.7 (SD = 11.8)	62.8 (SD = 11.6)	62.0 (SD = 11.7)
Health Insurance			
Civil Servant	329 (61.0)	151 (17.8)	480 (34.6)
Universal Coverage	57 (10.6)	219 (25.8)	276 (19.9)
Social Security	153 (28.4)	225 (26.5)	378 (27.2)
Other	–	254 (29.9)	254 (18.3)
Treatment			
Drugs	538 (99.8)	845 (99.5)	1383 (99.6)
Drug only	488 (90.5)	696 (82.0)	1184 (85.3)
Drugs with insulin	50 (9.3)	149 (17.5)	199 (14.3)
Insulin only	–	1 (0.1)	1 (0.1)
No drugs	1 (0.2)	3 (0.4)	4 (0.3)
Interval of FPG test			
Monthly	89 (16.5)	56 (6.6)	145 (10.4)
Every 2 months	136 (25.2)	148 (17.4)	284 (20.5)
Every 3 months	256 (47.5)	545 (64.2)	801 (57.7)
Every 4 months	58 (10.8)	100 (11.8)	158 (11.4)

SD, standard deviation.

Table 2
Distribution of FPG patterns in the pattern groups.

Patterns of FPG tests before HbA_{1c} test (t-3←t-1)		**Number and percentage of FPG-HbA_{1c} discordant results**		
		n	**If HbA_{1c} at t_0 was …**	
			Abnormal	Normal
1.0	O	604	172 (28.5)	–
2.0	OO	154	31 (20.1)	–
2.1	XO	98	35 (35.7)	–
3.0	OOO	43	6 (14.0)	–
3.1	OXO	15	4 (26.7)	–
3.2	XOO	12	3 (25.0)	–
3.3	XXO	22	12 (54.5)	–
4.0	X	784	–	316 (40.3)
5.1	XX	197	–	77 (39.1)
5.2	OX	80	–	41 (51.2)
6.0	XXX	61	–	26 (42.6)
6.1	XOX	12	–	5 (41.7)
6.2	OXX	9	–	4 (44.4)
6.3	OOX	14	–	9 (64.3)

O, normal FPG; X, abnormal FPG.
FPG-HbA_{1c} discordant results were determined by normal FPG at time t-1 visit and abnormal HbA_{1c} at time t_0 visit or abnormal FPG at time t-1 visit and normal HbA_{1c} at time t_0 visit.

described in Table 3. The pattern groups with normal FPG at time t-1 and t-2 (OO pattern) and normal FPG at time t-1 to t-3 (OOO pattern) were found to have significantly less discordance than the control group (−9.6% and −15.7%). In addition, the pattern group with normal FPG at time t-1 together with abnormal FPG at time t-2 and t-3 (XXO pattern) was found significantly more discordance than the control group (24.8%).

4. Discussion

Based on the study findings, some patterns of FPG results prior to deciding to order HbA_{1c} tests were predictive of HbA_{1c} findings than random testing. Prescribing a HbA_{1c} test after seeing two and three consecutively normal FPG tests (OO and OOO patterns) were found to lead to significantly less discordant results than random test decisions, whereas ordering HbA_{1c} after two abnormal and one normal consecutive FPG tests (XXO pattern) showed more discordance. Moreover, taking HbA_{1c} test after certain FPG patterns, such as XO, OX and OOX patterns, were marginally discordant.

Our study found relatively high proportions of discordant HbA_{1c} results of 14.0%–54.5% given normal FPGs and 39.1%–64.3% when FPG was abnormal in comparison to 0.5%–5.6% and 0.7%–1.8% in some previous studies, respectively [5,7,8]. The considerable differences were mainly due to the different timing of how FPG and HbA_{1c} results were compared. Most previous studies compared the results at the same patient visits in order to examine the discordance for a purpose of DM diagnosis. The study in Zambia found weak positive correlation between HbA_{1c} and previous FPG while

Table 3
The percentage differences of FPG-HbA_{1c} discordant results between the pattern groups and the control group.

Patterns of FPG tests before HbA_{1c} test (t-3 ← t-1)		% FPG-HbA_{1c} discordance in the [pattern groups − control group]				*P* value
		If HbA_{1c} at t_0 was …		95% confidence interval of the difference		
		Abnormal	Normal	Lower	Upper	
1.0	O	−1.2	–	−8.9	6.5	0.759
2.0	OO	−9.6	–	−18.9	−0.3	0.046
2.1	XO	6.0	–	−5.7	17.7	0.309
3.0	OOO	−15.7	–	−28.1	−3.3	0.037
3.1	OXO	−3.0	–	−26.4	20.4	0.807
3.2	XOO	−4.7	–	−30.1	20.7	0.730
3.3	XXO	24.8	–	2.9	46.7	0.019
4.0	X	–	−2.2	−9.8	5.4	0.567
5.1	XX	–	−3.4	−13.0	6.2	0.487
5.2	OX	–	8.7	−4.2	21.6	0.184
6.0	XXX	–	0.1	−14.0	14.2	0.989
6.1	XOX	–	−0.8	−29.5	27.9	0.956
6.2	OXX	–	1.9	−31.3	35.1	0.910
6.3	OOX	–	21.8	−4.2	47.8	0.112

O, normal FPG; X, abnormal FPG.
FPG-HbA_{1c} discordant results were determined by normal FPG at time t-1 visit and abnormal HbA_{1c} at time t_0 visit or abnormal FPG at time t-1 visit and normal HbA_{1c} at time t_0 visit.

found moderate positive correlation between HbA_{1c} and current FPG ($r = 0.282$, $p = 0.001$ and $r = 0.385$, $p = 0.001$, respectively) [11]. As it is a common practice in rural settings in Thailand with limited resources that a HbA_{1c} test is not used as routine monitoring of blood sugar control in DM patients, our study tried to resemble physician practice in the field in which FPG results might be reviewed before HbA_{1c} tests were ordered. In addition, the discordant results may be a result of FPG and HbA_{1c} measurement variability [15]. Our study suggests that reviewing patterns of FPG tests prior to deciding to order HbA_{1c} tests instead of using a single FPG result should help reduce the effect of such variability.

It is worth noting that our findings disagreed with what we learned from our personal communication with some physicians in rural areas. They tended to order HbA_{1c} tests when they suspected that patients with normal FPG results might control food and sugar intake only for a few days before seeing their physicians. This patients' playing game with their physicians was also mentioned in another study in Thailand on DM screening which comparing fasting capillary blood glucose against HbA_{1c} and FPG against HbA_{1c} [16].

We recognize some limitations of our study. First, our database was limited to only a one-year period. It is recommended for a longer follow-up period in a future study so that more FPG patterns of more than three consecutive visits could be analyzed. Second, we did not exclude anemic patients from the study. Different types of anemia might falsely elevate or lower HbA_{1c} [17,18]. The structure of the databases did not permit us to examine anemic patients and to differentiate types of anemia. However, we believed that our approach to use comparisons between the pattern groups and the control group instead of a single-group study should reduce this confounding effect. Third, this study was based on the university hospitals databases because there were routine HbA_{1c} tests available for the comparisons. Generalization to other hospitals especially in small rural hospitals or primary care settings may need more studies. As suggested elsewhere, patients in rural areas might have poorer sugar control than those in urban areas [19]. Patients' dietary behaviors might be different. Although we could minimize the effect of game playing by reviewing FPG patterns from two or three consecutive visits, we would still recommend repeating a similar study in rural areas or in primary care settings before generalizing our recommendation.

In conclusion, given that availability of resources limited frequent HbA_{1c} monitoring for assessing sugar control, our findings indicate that reviewing FPG patterns before a HbA_{1c} test would be beneficial. Reviewing only the most recent FPG result before ordering HbA_{1c} seems inadequate. If possible, the review should include at least two or three consecutive FPG results prior to making decisions for HbA_{1c} test. Our study suggests that HbA_{1c} tests could be postponed if normal FPG were found two and three consecutive times. Based on the DM population of 4.2 million in Thailand [20] and the proportions of the FPG patterns found in our study, we might be able to add more value of the HbA_{1c} test worth US$ 6.37–10.42 million if we skipped the tests when seeing the OO and OOO patterns of FPGs or choose to order the tests when seeing XXO, XO, OX and OOX patterns, instead.

Acknowledgments

The authors would like to thank two university hospitals for their cooperation of data collecting. This study was supported by the 90th Anniversary of Chulalongkorn University Fund (Ratchadaphiseksomphot Endowment Fund).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.04.030.

Authors' contributions

WI and JS participated in the conception and study design. WI responsible for the data collection, data analysis and drafted the manuscript. JS contributed to reading and revising the manuscript. All authors read and approved the final manuscript.

Conflicts of interest

The authors declare no conflicts of interest in this work.

Funding

This study was supported by the 90th Anniversary of Chulalongkorn University Fund (Ratchadaphiseksomphot Endowment Fund).

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