Survey of primary care physicians about their comprehension of HBA1C, and their understanding of the common medical conditions that can affect the accuracy of HBA1C

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Abstract

Haemoglobin is a red blood cell protein, and the free glucose in blood tends to bind to this protein. This process is known as “glycosylation”; the result of this binding is HBA1C, or glycated haemoglobin. HBA1C measures the amount of sugar bound to haemoglobin (1).

As the life span of a red blood cell is 2-3 months HBA1C is checked every 3 months for monitoring of diabetes(2).

Hba1c does not only give us a decisive and dependable measurement of chronic hyperglycaemia but is also a good indicator of long term complications in type 2 diabetes mellitus (3).

This would seem simple and straightforward, but in reality health care professionals need to be very vigilant and critical when interpreting values of HBA1C as HBA1C is affected by many other medical conditions and medications, and most of these medical conditions co-exist with Diabetes mellitus or develop as a result of diabetes itself.

In this research we did a cross sectional study among family physicians working in the Primary Health Care Corporation, Doha, Qatar to see the awareness and understanding of the different medical conditions that can affect the accuracy of HBA1C levels and to see if the physicians are aware of any alternative bio marker other than HBA1C,that is reliable in conditions in which HBA1C cannot be accurately used.

Key words: primary care physicians, HBA1C, Qatar

Introduction

This is a cross sectional study that was conducted among fifty family physicians working in Primary Health Care Corporation, Doha, Qatar as family physicians are very commonly involved in diagnosis, management and follow up of patients suffering from type 2 diabetes mellitus.

The main aim of this study was to find out the depth of understanding and comprehension of HBA1C by primary health care physicians.

(1) If physicians were confident to diagnose type 2 diabetes mellitus based on values of HBA1C,
(2) If physicians were aware of different medical conditions and medications that can affect the accuracy of HBA1C,
(3) If physicians are aware of an alternative bio marker to HBA1C.

The physicians involved were both male and female and all of them had post graduate diploma or degree from their respective countries, in primary care.

The results from the study are shown below in the table and graphs and are quite interesting.

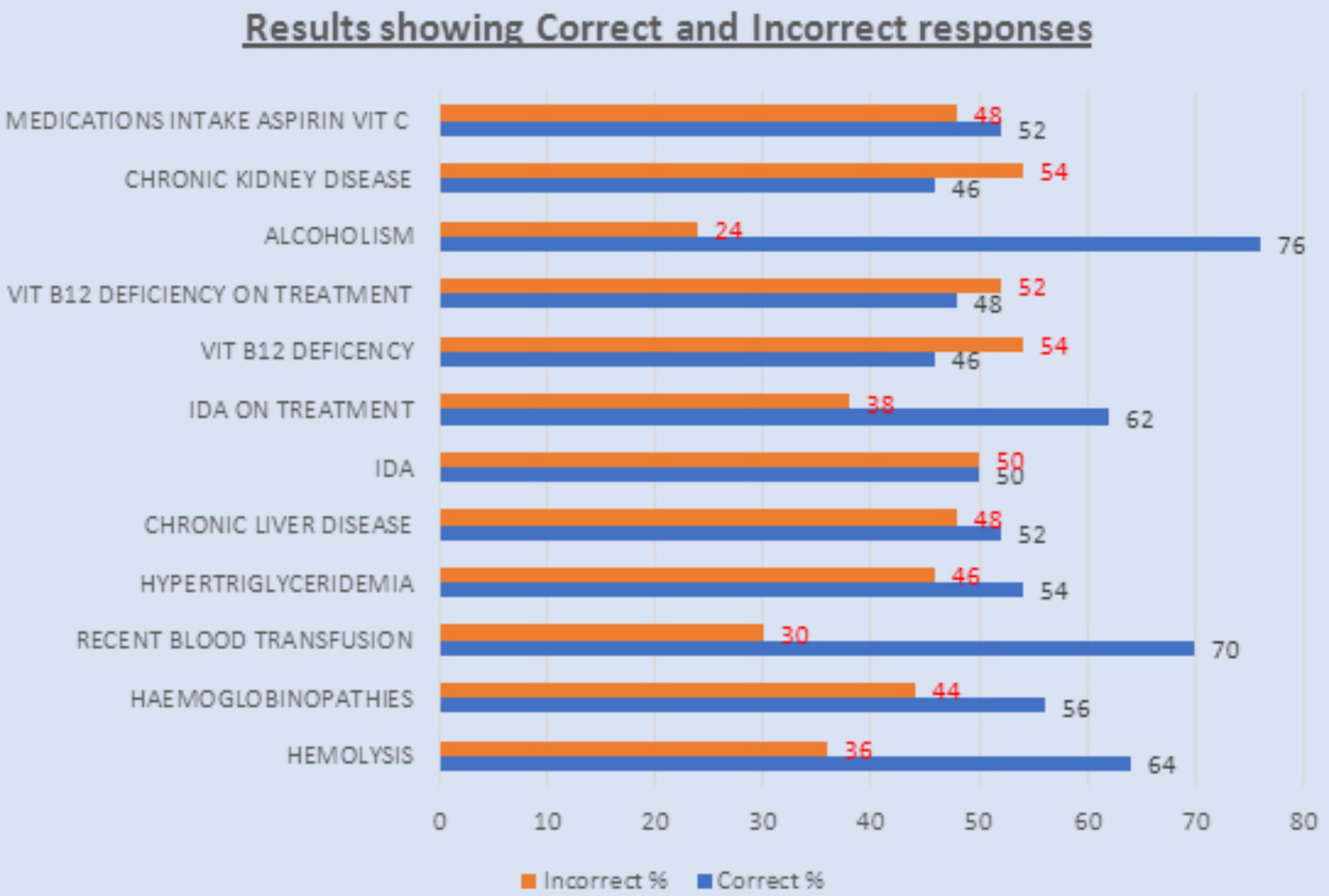
Figure 1: Answers to Basic Questions Showing Family Physicians Confidence in Dealing with Type 2 Diabetes Mellitus

Questions	YES IN %	NO IN %
Are you a practicing family physician	100	0
Are you confident: to interpret hba1c results	100	0
to make diagnosis based on hba1c	100	0
manage type 2 diabetes mellitus	100	0
diagnosis and management of pre-diabetes	100	0

Figure 2: Shows the Different Conditions that can Affect the HBA1C and the Percentage of Correct and Incorrect Answers by the Family Physicians

Effect On Hba1c	Correct Answers in %	Incorrect Answers in %
Hemolysis	64	36
Haemoglobinopathies	56	44
Recent Blood Transfusion	70	30
Hypertriglyceridemia	54	46
Chronic Liver Disease	60	40
Iron Deficiency Anaemia	50	50
Treatment of IDA with Iron	62	38
Vit B12 Deficiency	46	54
Vit B12 Deficiency Treatment	48	52
Alcoholism	76	24
Chronic Kidney Disease	46	54
Intake Aspirin	52	48
Awareness Of Alternative Biomarker To Hba1c	20	80

Figure 3: Shows the Correct Answers in Blue and Incorrect Answers in Orange as Percentage



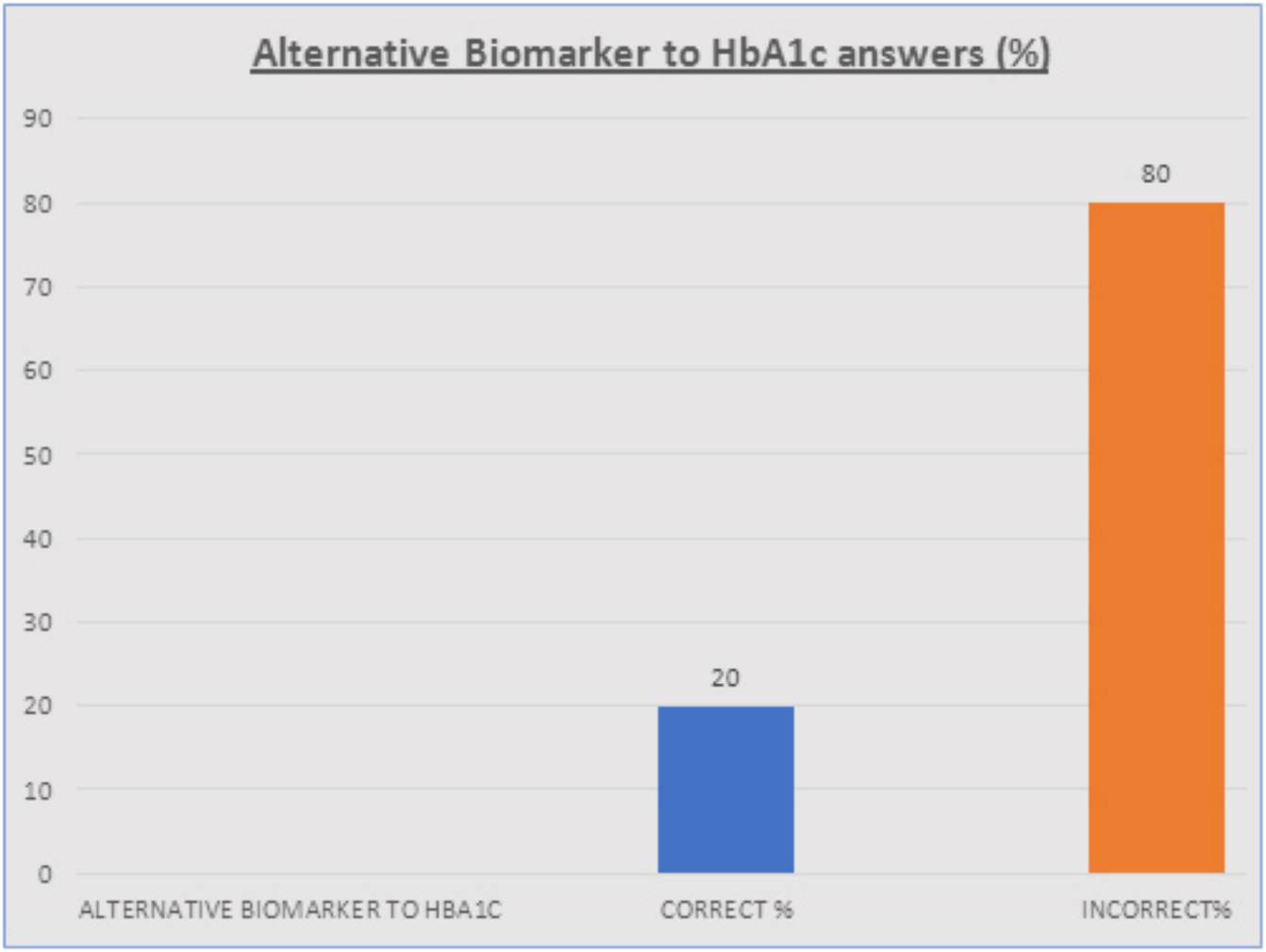
As obvious from data above all family physicians were confident that they can interpret HBA1C readings to diagnose and manage type 2 diabetes mellitus (FIGURE 1), but when asked in depth about different medical conditions that can interfere with validity and accuracy of HBA1C there were many incorrect answers (FIGURE 2).

As very obvious from data above there is a marked percentage of wrong answers, even against common conditions such as iron deficiency anaemia, vitamin b12 deficiency chronic kidney disease etc. (FIGURES 2, 3).

This clearly indicates that the physicians involved in the management of type 2 diabetes mellitus and interpretation of HBA1C results, are clearly not aware of how different medical conditions and commonly used medications can affect its accuracy and hence this can affect the entire management of type 2 diabetes mellitus in these patients. Keeping in mind that in patients with type 2 diabetes mellitus, conditions like chronic kidney disease and hypertriglyceridemia ,vitamin B12 deficiency, iron deficiency anaemia can co- exist and some conditions can be the effect of the treatment itself, such as vitamin b12 deficiency secondary to metformin treatment (4).

Obviously if certain conditions affect the accuracy and validity of HBA1C, then is there any alternative biomarker to HBA1C than can be used in most of these medical conditions? This was the second part of our survey and the answer is given in Figure 4.

Figure 4: Shows Answers to Alternate Biomarker to HBA1C as Percentage, 80 percent Incorrect, 20 percent Correct



This clearly shows that the majority of family physicians are not aware of an alternate test or biomarker to HBA1C, that could be used instead of HBA1C in situations or medical conditions that can affect the accuracy of HBA1C itself.

About 80% of physicians' answers to this was Fasting blood sugar or (OGTT), oral glucose tolerance test, which are both incorrect answers, only 20% suggested glycated albumin which is the correct answer.

Discussion

Although HBA1C is a standard test in diagnosis and management of type 2 diabetes mellitus, there are different medical conditions that can affect its levels, especially conditions that can effect survival or longevity of red blood cells.(2) (5)

Different studies have shown that iron deficiency anaemia is associated with falsely increased levels of HBA1C which can result in both misdiagnosis and management of type 2 diabetes mellitus (7). On the contrary taking iron and treating iron deficiency anaemia lowers HBA1C as iron deficiency improves both in pregnant and non-pregnant subjects v(8)(9).

Similarly studies have shown that deficiency of vitamin B12 gives false increase in HBA1C and treatment of b12 deficiency decreases HBA1C levels (10)(11)(12).

Genetic disorders of haemoglobin can effect HBA1C readings depending on which haemoglobinopathy , as genetic disorders of haemoglobin are more common in African and Asian populations, Health care professionals should be vigilant as these genetic disorders of haemoglobin can give falsely high or low values of HBA1C; glycated albumin can instead be used for their glycaemic control (13)(14).

Depending on the stage of chronic kidney disease and shortened survival red blood cell time in advanced renal disease this can affect the accuracy of HBA1C(15).

Also, HBA1C is not a reliable test especially in advanced CKD and haemodialysis, so glycated albumin can be a way forward (16).

Cirrhosis due to resulting anaemia, and sequestration of red blood cells by enlarged spleen, can give falsely high HBA1C (17)(18).

So, if reliability and efficacy of HBA1C is affected in the above conditions, especially chronic kidney disease, some haemoglobinopathies and liver disease, is there an alternate biomarker? The answer is yes.

That is glycated albumin (19).

Figure 5

Box 1 Factors that influence HbA_{1c} and its measurement

- Erythropoiesis
  - Increased HbA_{1c}: iron, vitamin B_{12} deficiency, decreased erythropoiesis.
  - Decreased HbA_{1c}: administration of erythropoietin, iron, vitamin B_{12}, reticulocytosis, chronic liver disease.
- Altered haemoglobin
  - Genetic or chemical alterations in haemoglobin: haemoglobinopathies, methaemoglobin, may increase or decrease HbA_{1c}.
- Glycation
  - Increased HbA_{1c}: alcoholism, chronic renal failure, decreased intraerythrocytic pH.
  - Decreased HbA_{1c}: aspirin, vitamins C and E, certain haemoglobinopathies, increased intraerythrocytic pH.
  - Variable HbA_{1c}: genetic determinants.
- Erythrocyte destruction
  - Increased HbA_{1c} (increased erythrocyte life span): splenectomy.
  - Decreased HbA_{1c} (decreased erythrocyte life span): haemoglobinopathies, splenomegaly, rheumatoid arthritis or drugs such as antiretrovirals, ribavirin and dapsone.
- Assays
  - Increased HbA_{1c}: hyperbilirubinaemia, carbamylated haemoglobin, alcoholism, large doses of aspirin, chronic opiate use.
  - Decreased HbA_{1c}: hypertriglyceridemia.
  - Variable HbA_{1c}: haemoglobinopathies.

Glycated albumin is superior to HBA1C specially with rapid changes in glycaemia or rapid red cell turnover such as in haemolytic anaemias, chronic kidney disease haemodialysis.(21)

Glycated albumin is superior to HBA1C in evaluating glycaemic control in advanced chronic kidney disease (22) (19).

In a study in Japan it was demonstrated that during the end of pregnancy when there is increased demand for iron and this can affect the accuracy of HBA1C as the glycated albumin levels remained unaltered (19).

Interestingly poor control of glycemia or therapeutic inertia or no or little response to medications in type 2 diabetes mellitus can be a result of overlooking other factors or medical conditions that can affect the HBA1C (23).

This poor control of HBA1C will not only lead to more complications in patients but also will cause economic burden on the health care system in a country (23).

Electronic research of “Pubmed” database in USA from 2011 TO 2015 suggested that

“there are physician led barriers to achieve good glycaemic control “ and one of them is “the lack of diabetes focussed education as a contributing factor to achieve therapeutic targets” (24).

A survey of 209 primary care physicians in Australia in 2017 concluded that “Nearly half of the primary care physicians reported learning needs related to pharmacological management of T2DM. Many lacked confidence in providing effective insulin treatment.”(24).

Figure 6: Shows the values of glycated albumin in diagnosis of type 2 diabetes mellitus (20). An Alternative Test to Guide the Diagnosis of Diabetes Mellitus

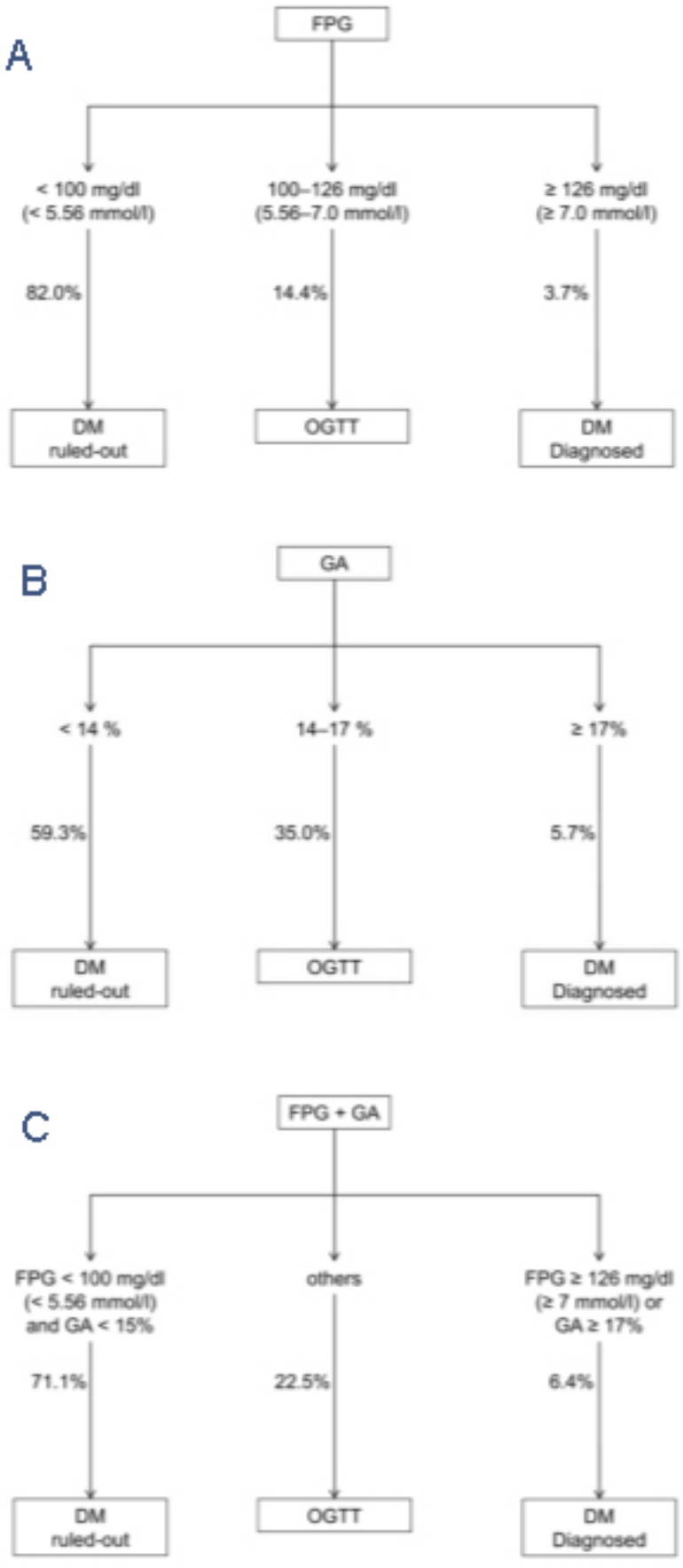


Figure 6: Screening strategies to find diabetes by OGTT.

Proportions of population in specific diagnostic category were shown:

(A) By impaired fasting glucose (IFG) criteria, that is, fasting plasma glucose (FPG) <100 mg/dl 5.56 mmol/L to exclude and FPG ≥ 126mg/dL (7.0 mmol/L) to diagnose diabetes.
The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), false positive rate, (FPR) and false negative rate (FNR) for this strategy were 78.8%, 100%, 100%, 98.1%, 0% and 21.2%

Conclusion

Not achieving therapeutic targets with HBA1C and poor glycaemic control is unfortunately a reality in today's health care in spite of many therapeutic interventions to treat and control type 2 diabetes mellitus.

The reason behind this is multifactorial, but one reason that we have tried to explore in this paper is that primary care physicians need to be more aware and vigilant, in interpreting values of HBA1C. It is not only a number in context to chronic glycemia , this number is affected in its accuracy by many other common medical conditions the majority of which co-exist in patients with diabetes mellitus and some are developed as complications of the disease itself.

Furthermore, it is important in todays advanced healthcare system to be aware of alternative biomarkers that are available instead of HBA1C in a small but definite group of patients, where HBA1C values cannot be depended upon.

This also suggests that more focused training is required in primary care physicians in regard to type 2 diabetes mellitus to prevent therapeutic inertia and to improve glycaemic control.

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