

Percentage of Hemoglobin A1C (HbA1c) as an Indicator of Pre-Diabetic Condition in Impaired Glucose Level Patients

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Abstract: *Background:* The high prevalence of diabetes mellitus has emerged as a worldwide public health problem in the past 20 years. Type 2 diabetes is the most common form of diabetes, estimated to account for 85–90% of diabetes. Hemoglobin A(1c) (HbA1c) has been widely used as a clinically important assessment tool for outcome analyses related to glycemic control. The HbA1c test has been shown to predict the risk for the development of many of the chronic complications in diabetes. *Objectives:* The study was undertaken to find out if HbA1c levels can be used as indicator of the pre-diabetic condition in patients with impaired blood sugar levels around Kathmandu valley and to find out the percentage of HbA1c in those patients. Also a correlation analysis with impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) levels was carried out. *Methods:* The study was conducted in the Department of Biochemistry, Kathmandu University School of Medical Sciences. A total of 102 patients with impaired blood glucose levels participated in the study. Estimation of HbA1c was performed by using a commercial NycoCard Kit, a rapid *in vitro* test for the measurement of glycated hemoglobin in human blood. *Results:* The mean % of HbA1c was found to be 6.44902 amongst the 102 patients and no correlation was found to be observed between HbA1c with IFG and IGT values. *Conclusion:* In conclusion HbA1c % proved to be a valuable indicator of the pre-diabetic condition and could contribute to understanding the role of the various risk factors of dietary, social and physical nature in the development of diabetes.

Keywords: Diabetes Mellitus, HbA1C, Impaired Fasting Glucose (IFG)

1. Introduction

Type 2 diabetes mellitus is one of the most common chronic metabolic disorders characterized by hyperglycemia. It occurs due to defects in insulin secretion, insulin action or both and accounts for at least 90% of all cases of diabetes [15]. It is highly prevalent in the elderly and associated with various co-morbidities such as obesity, hypertension, hyperlipidemia, and cardiovascular disease, which ultimately lead to a condition called “Metabolic Syndrome” [16]. The International Diabetes Federation (IDF) estimates the global prevalence of type 2 diabetes at

6.6% (285 million cases) in 2010 and expects to reach to 7.8 % (438 million cases) by 2030. In addition to frank and symptomatic diabetes, there are two different Pre-diabetes conditions which are known as impaired fasting glucose (IFG) and impaired glucose tolerance (IGT). These are overlapping and essentially asymptomatic conditions characterized by impaired glycemia and are important known risk factors for type 2 diabetes [11].

Impaired glucose tolerance is defined as two-hour glucose levels of 140 to 199 mg/dl (7.8 to 11.0 mmol/l) on the 75 gram oral glucose tolerance test, and impaired fasting glucose is defined as glucose levels of 100 to 125

mg/dl (5.6 to 6.9 mmol/l) in fasting patients.

GHb, also referred to as glycohemoglobin, glycosylated hemoglobin (HbA1c) is a term used to describe a series of stable minor hemoglobin components formed slowly and nonenzymatically from hemoglobin and glucose. Since erythrocytes are freely permeable to glucose, the level of GHb in a blood sample provides a glycemic history of the previous 120 days, the average erythrocyte life span. Compared with fasting glucose, glycated hemoglobin has several advantages as a diagnostic test one of it being a higher repeatability. [18]. A number of clinical studies have demonstrated that HbA1c is a reliable index of diabetic control. The HbA1c test has been shown to predict the risk for the development of many of the chronic complications in diabetes analogous to using cholesterol determinations to predict the risk for development of cardiovascular disease.

A glycated hemoglobin HbA1c level $\geq 6.5\%$ (48 mmol/l) is now acceptable for diagnosing diabetes [6,10]. Measurement of HbA1c level can be used as a diagnostic test for diabetes if analysis is performed in a facility producing acceptable performance in external quality assurance; assays are standardized to criteria aligned to international reference values, and if no conditions which preclude its accuracy are present [10].

In addition, as the measuring process for glycated hemoglobin has become more accurate and standardized, the American Diabetes Association (ADA) in 2010 adopted glycated hemoglobin level over 6.5% as a new diagnostic criteria for diabetes and for high risk groups from 5.7% to 6.4% [3].

Hence this study was undertaken to identify if HbA1c levels can be used as an indicator of diabetic risk and to determine the percentage of HbA1c in patients with impaired blood sugar levels.

2. Methods

The current study was a cross sectional study with a sample size comprising of 102 patients with impaired blood glucose levels collected from the Biochemistry lab, Dhulikhel Hospital, an independent, not for profit, non government hospital located in the Dhulikhel, 30km from the national capital, Kathmandu.

A structured Pro-forma was used for the data collection. Parameters like HbA1c, IGF and PP were noted down.

Estimation of HbA1c was performed by using a commercial NycoCard Kit which was used in the following manner:

NycoCard HbA1c is a boronate affinity assay. When blood is added to the reagent, the erythrocytes immediately lyse. All hemoglobin precipitates. The boronic acid conjugate binds to the cis-diol configuration of glycated hemoglobin. An aliquot of the reaction mixture is added to the test device, and all the precipitated hemoglobin, conjugate-bound and unbound remains on top of the filter. The precipitate is evaluated by measuring the blue (glycated hemoglobin) and the red (total hemoglobin)

colour intensity with the NycoCard READER II, the ratio between them being proportional to the percentage of HbA1c in the sample.

The test result was read within 5 minutes using the NycoCard READER II. The NycoCard READER II instruction manual was followed in analysis.

3. Data Processing and Analysis

Data gathered were checked for completeness and accuracy. Necessary coding was used to simplify the collected data which were then further processed.

The data analysis was carried out using SPSS (version 11.5 software (SPSS Inc., 233 South Wacker Drive, 11th Floor, Chicago, IL 60606-6307) to find the percentage of HbA1c in patients with impaired blood sugar levels.

4. Results

Table 1 and Figure 1 show the statistical analysis in the above patients: The mean % of HbA1c was 6.449020, median with % of HbA1c was 6.6, mode with % HbA1c was 6.7 and SD with % of HbA1c was 0.924.

Table 1. Statistical measurement of HbA1c

statistics	HbA1c
Mean	6.449020
Median	6.600000
Mode	6.7000
Std. deviation	0.9239117
Minimum	4.9000
Maximum	10.5000

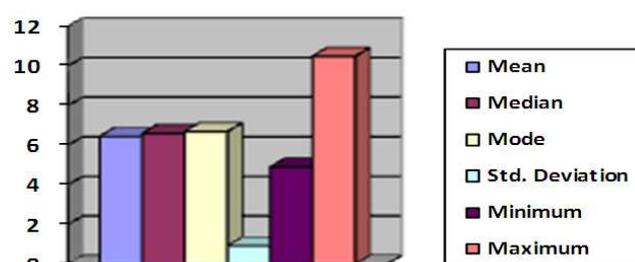


Figure 1. Bar diagram of statistical measurement of HbA1c

Correlation of HbA1c with IFG and IGT

The p values were not significant when correlation analysis were performed for HbA1c with IFG and IGT values. Since our values are very low at-0.02, 0.09 etc. there was no significant p value.

5. Discussion

In the present study, % of HbA1c was found to be

6.44902 amongst the 102 patients of Dhulikhel Hospital.

A study in a Developing Southern Chinese Population by Zhang et al. (2012) found a fasting plasma glucose (FPG) of ≥ 7.0 mmol/l, a 2-h PG of ≥ 11.1 mmol/l, and a HbA1c level of $\geq 6.5\%$. Diabetes was confirmed if the participants were diagnosed with diabetes if any two out of the three tests (the FPG, the 2-h PG and the HbA1c) were above the diagnostic thresholds. Pre-diabetes was defined if the participants had any following conditions: 1. a FPG between 5.6 to 6.9 mmol/l (Impaired Fasting Glucose [IFG]) 2. a 2-h PG between 7.8 to 11.0 mmol/l (Impaired Glucose Tolerance [IGT]), or 3. an HbA1c level between 5.7 to 6.4% [4].

HbA1c is used to monitor diabetes and to establish the degree of metabolic control. Deviation from individualized HbA1c targets prompts physicians to modify treatment strategies with lifestyle intervention and/or drug titration or changes. The use of HbA1c for diagnosing diabetes has the advantage that, in subjects with HbA1c $\geq 6.5\%$ (i.e., diabetes), baseline HbA1c is already measured and deviation from target is immediately available (no HbA1c measurement as a second step after FPG assessment). In subjects with HbA1c of 6.00–6.49% (i.e. high risk of diabetes), an effective prevention strategy can be immediately undertaken with the awareness that a single HbA1c is definitely more reliable than a single FPG to stratify the risk of the disease. Yet, in subjects with HbA1c of 5.50–5.99% plus other diabetes risk factors (e.g. central obesity, atherogenic dyslipidemia, hypertension, and/or metabolic syndrome), counseling can be immediately offered because diabetes risk is substantial, and single HbA1c assessment is definitely more reliable than single FPG to capture chronically high-normal glucose levels. Pertinent to this issue is the firm belief that the implementation of the standardization of HbA1c assay would proceed more rapidly worldwide if HbA1c were to also be used for diagnosing diabetes. HbA1c assessment is thus crucial for diabetes monitoring and prevention [22].

6. Conclusion

Our study firmly suggests that HbA1c % can be used as an indicator of the pre-diabetic condition. But further epidemiological and clinical studies in this region with large sample size are needed to better understand and confirm the role of HbA1c in determination of pre diabetic complications.

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