Original article

Significance of HbA1c in Diagnosing and Prognosing Diabetes Related Complications

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Abstract

Background:
Diabetes mellitus, characterized by chronic hyperglycemia, results in serious complications. The HbA1c assay plays a central role in the diagnosis and monitoring of diabetes.

Objective:
To evaluate the contribution of HbA1c in the diagnosis and prediction of diabetes complications.

Methods:
The cohort was conducted at Sir Salimullah Medical College, Dhaka, Bangladesh from July 1, 2017, to July 30, 2018, over 96 diabetic patients aged more than 18 years to determine the importance of the HbA1c for diagnosing and predicting diabetic complications such as retinopathy, nephropathy, neuropathy, and cardiovascular complications. HbA1c, fasting blood glucose (FBG), postprandial blood glucose (PPBG), lipid profile, and renal/liver tests were conducted every three months for one year. For determining correlation and relation, correlation and regression analysis were done.

Results:
Average HbA1c was 8.2±1.4%, indicating poor glycemic control. HbA1c correlated strongly with FBG (r=0.72) and PPBG (r=0.68). Complications included retinopathy (15.6%), nephropathy (20.8%), neuropathy (26%), and cardiovascular events (18.7%). Increased HbA1c was linked to an increased risk of complications (HR 1.45, 95% CI: 1.20-1.75, p<0.001). Age, diabetes duration, LDL cholesterol, and serum creatinine were also predictive.

Conclusion:
HbA1c plays a very significant role in the diagnosis and management of diabetes, with good correlations to glycemic control and complications, emphasizing its relevance to clinical practice.

Keywords: Diabetes, HbA1c, Diagnosis, Diabetic complications

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Introduction:

Diabetes mellitus, a chronic metabolic disorder characterized by hyperglycemia, has become a global epidemic with significant health implications. The global prevalence of diabetes is alarmingly high and continues to rise, particularly in developing countries where healthcare resources are often limited. Wild et al projected that the number of people with diabetes worldwide would increase from 171 million in 2000 to 366 million by 2030, highlighting the urgent need for effective diagnostic and management strategies to combat this growing health crisis.[1] Guariguata et al further reinforced this concern, providing updated estimates and projections that underscored the rapid escalation

of diabetes cases, especially in low and middle income countries.[2] The International Diabetes Federation (IDF) reported in 2019 that the prevalence of diabetes had reached 9.3% globally, affecting approximately 463 million adults, with projections indicating a rise to 700 million by 2045.[3] The growing incidence of diabetes in Bangladesh is a reflection of worldwide patterns, driven by urbanization, dietary changes, and physical inactivity. Studies by Animaw and Seyoum and Nanditha et al highlight the socio-economic and healthcare challenges of diabetes control in developing countries, in this case, South Asia.[4,5] Diabetes causes severe complications such as cardiovascular disease, neuropathy, nephropathy, and retinopathy, as described by Sherwani et al and Dagogo-Jack, which can drastically affect quality of life if not managed well.[6,7] Early detection and active management are crucial, according to Mudaliar and Henry.[8] Traditional diagnostic tests like OGTT and FPG are also limited, as Kim et al and Jesudason et al assert, in the sense that OGTT is cumbersome and FPG can fail to diagnose diabetes.[9-11] The HbA1c test, measuring average blood glucose levels over a 2–3 month period, has become a reliable tool for diabetes management. Sherwani et aland Misra and Garg emphasized its ease and stability, especially since it does not require fasting.[6,12] However, conditions like hemoglobinopathies and iron deficiency can affect HbA1c levels, leading to misdiagnosis, as per Herman and Cohen and Coban et al.[13,14] Regional variations in HbA1c values, as documented by Solomon et al, also render it challenging to interpret in multicultural populations, like Bangladesh.[15]

Methods:

This cohort was conducted in the Department of Physiology, Sir Salimullah Medical College, Dhaka, Bangladesh, between July 1, 2017, and July 30, 2018, to determine the importance of the HbA1c test for diagnosing and predicting diabetic complications. A total of 96 patients above the age of 18 years with an established diagnosis of type 1 or type 2 diabetes for one year or more were selected. Individuals with hemoglobinopathies, chronic kidney disease, or disorders of red blood cell turnover were excluded because these conditions would confound HbA1c measurement. After ethical approval, participants underwent extensive clinical assessments that included medical history, physical examination, and laboratory tests. Baseline HbA1c was measured using high-performance liquid chromatography (HPLC), and follow-up measurements were done every three months for a year. Other than HbA1c, fasting blood glucose (FBG), postprandial blood glucose (PPBG), lipid profile, and renal and liver function tests were also monitored. HbA1c and FBG/PPBG correlation was found out using correlation coefficients and regression analysis. The research also evaluated the relationship between the degree of HbA1c and the development of diabetes complications such as retinopathy, nephropathy, neuropathy, and cardiovascular complications. Multivariate Cox proportional hazard regression models were used to adjust for confounders and compare the risk of complications based on various HbA1c levels. SPSS version 26 was utilized in the analysis, and continuous variables are shown as mean±standard deviation (SD) and categorical variables as percent. ANOVA was used for continuous variables and chi-square tests were used for categorical variables to compare them. A p-value of <0.05 was regarded as significant.

Results:

The study population (n=96) was also demographically heterogeneous, with the highest percentage being in the age group of 36-45 years (22.9%), followed by 26-35 years (18.8%) and 56-65 years (17.7%). The gender distribution included 56.3% males. The average duration of diabetes was 10.5 ± 6.3 years, and 72.9% of them had type 2 diabetes. The baseline mean HbA1c was 8.2 ± 1.4%, which indicates poor glycemic control. Mean FBG and PPBG were 145.3 ± 35.6 mg/dL and 210.4 ± 50.7 mg/dL, respectively, demonstrating poor control of glucose. Lipid profile was suggestive of dyslipidemia with mean total cholesterol 190.7 ± 45.3 mg/dL, LDL 120.5 ± 30.6 mg/dL, HDL 40.3 ± 10.2 mg/dL, and triglycerides 160.8 ± 75.4 mg/dL. The average serum creatinine level was 1.2 ± 0.4 mg/dL, reflecting generally normal renal function, and the average ALT was 30.6 ± 10.3 U/L, reflecting normal liver function in most subjects.

Table-I: Baseline Characteristics of Study Population (n=96)

Basic Characteristics	
Age (Years) no. (%)	
18-25	12(12.5)
26-35	18(18.8)
36-45	22(22.9)
46-55	15(15.6)
56-65	17(17.7)
66-75	8(8.3)
76-85	4(4.2)
Sex no. (%)	
Male	54(56.3)
Female	42(43.7)
Type of Diabetes no. (%)	
Type 1	26(27.1)
Type 2	70(72.9)
Duration of Diabetes (years) Mean±SD	10.5± 6.3
HbA1c (%)Mean ± SD	8.2±1.4
Fasting Blood Glucose (mg/dL) Mean±SD	145.3±35.6
Postprandial Blood Glucose (mg/dL) Mean±SD	210.4±50.7
Total Cholesterol (mg/dL) Mean±SD	190.7±45.3
LDL Cholesterol (mg/dL) Mean±SD	120.5±30.6
HDL Cholesterol (mg/dL) Mean±SD	40.3 ±10.2
Triglycerides (mg/dL)	160.8±75.4
Serum Creatinine (mg/dL) Mean±SD	1.2±0.4
ALT (U/L) Mean ± SD	30.6±10.3

The study found significant correlations between HbA1c levels and other glycemic parameters. There was a strong positive correlation between HbA1c and fasting blood glucose (FBG) levels, with a correlation coefficient (r) of 0.72 and a p-value of <0.001, indicating that higher HbA1c levels were associated with higher FBG levels. Similarly, a substantial positive correlation was observed between HbA1c and postprandial blood glucose (PPBG) levels, with a correlation coefficient (r) of 0.68 and a p-value of <0.001 (Table-II).

Table-II: Correlation between HbA1c and Other Glycemic Parameters (n=96)

Glycemic Parameters	Correlation Coefficient (r)	p-value
Fasting Blood Glucose	0.72	<0.001
Postprandial Blood Glucose	0.68	<0.001

The incidence of diabetes-related complications among the study participants was notable. Retinopathy was observed in 15 participants (15.6%), reflecting significant damage to the retinal blood vessels due to prolonged hyperglycemia. Nephropathy was reported in 20 participants (20.8%), indicating kidney damage that could potentially lead to renal failure if not managed effectively. Neuropathy, the most common complication, was present in 25 participants (26.0%), suggesting widespread nerve damage associated with diabetes. Additionally, cardiovascular events were documented in 18 participants (18.7%), highlighting the increased risk of heart disease and related complications in the diabetic population (Table-III).

Table-III: Incidence of DiabetesRelated Complications (n=96)

Complication	no. (%)
Retinopathy	15 (15.6)
Nephropathy	20 (20.8)
Neuropathy	25 (26.0)
Cardiovascular Events	18 (18.7)

Multivariate Cox model detected several predictors for diabetes complications. Elevated HbA1c increased the hazard with a hazard ratio (HR) of 1.45 (95% CI: 1.20-1.75, p < 0.001). Age (HR 1.10, 95% CI: 1.02-1.18, p = 0.01) and duration of diabetes (HR 1.08, 95% CI: 1.01-1.15,

Table-IV: Multivariate Cox Proportional Hazards Model for Risk of Complications(n=96)

Parameters	Hazard Ratio (HR)	95% Confidence Interval (CI)	p-value
HbA1c	1.45	1.20-1.75	<0.001
Age	1.10	1.02-1.18	0.01
Duration of Diabetes	1.08	1.01-1.15	0.02
LDL Cholesterol	1.12	1.05-1.20	0.001
Serum Creatinine	1.30	1.10-1.55	0.005

p = 0.02) were the other significant predictors. LDL cholesterol was also predictive (HR 1.12, 95% CI: 1.05-1.20, p = 0.001), and serum creatinine (HR 1.30, 95% CI: 1.10-1.55, p = 0.005) (Table-IV).

Discussion:

This study evaluated the significance of HbA1c in diagnosing and prognosing diabetes related complications. The baseline average HbA1c was 8.2±1.4%, which represents poor glycemic control, according to Wild et al's observation of poor glycemic control globally among patients with diabetes, especially in developing countries.[1] The study further identified a higher incidence of diabetes among males (56.3%), similar to findings in previous studies.[16,17] The correlation analysis demonstrated a strong positive correlation between HbA1c and fasting blood glucose (FBG) levels (r=0.72, p<0.001), as well as postprandial blood glucose (PPBG) levels (r = 0.68, p < 0.001). This is supported by the study conducted by Shimizu et al, which found similar significant correlations, emphasizing the reliability of HbA1c as an indicator of chronic glycemic control.[18] In addition, lipid profile analysis showed elevated levels of total cholesterol, LDL cholesterol, and triglycerides, coupled with low HDL cholesterol levels. These dyslipidemia patterns were observed in other studies, such as those by Tesfaye et al. and Agrawal et al., which linked lipid abnormalities to increased cardiovascular risk in diabetic patients.[19,20] Our study also identified significant associations between elevated HbA1c levels and the risk of various diabetes-related complications. The incidence of retinopathy (15.6%), nephropathy (20.8%), neuropathy (26.0%), and cardiovascular events (18.7%) among the participants underscores the severe impact of poor glycemic control. The hazard ratios for these complications, including HbA1c (HR 1.45), age (HR 1.10), duration of diabetes (HR 1.08), LDL cholesterol (HR 1.12), and serum creatinine (HR 1.30), highlight the multifactorial nature of diabetes complications. Studies by Virk et al and Lai et al further support these findings, demonstrating that HbA1c variability significantly increases the risk of microvascular complications.[21,22] In conclusion, our study confirms the significance of HbA1c in diabetes complications diagnosis and prediction. Complications were predicted by age and diabetes duration, in agreement with a study by Tannus et al in type 1 patients.[23] The interaction of HbA1c with neuropathy and CAN was also evident, in concordance with studies by Monti et al and Chen et al.[24,25] Although the prevalence of retinopathy and nephropathy was lower in our population compared to Agrawal et al's Northwest Indian study,[20] our findings supportsd the strong correlation of HbA1c with microvascular complications, as reported by McCarter et al.[26] The results reinstate the significant role of HbA1c in diabetes management, with the need for intensive glycemic control to prevent complications. Future research needs to cover the incorporation of HbA1c variability and additional biomarkers into personalized care plans.

Limitations:

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

Conclusion:

Finally, this research underlines the necessity of HbA1c testing for diagnosing and anticipating diabetes complications. High correlations of HbA1c with blood glucose values validate its efficacy in the tracking of glycemic control. Elevated HbA1c levels are associated with increased risks of complications such as retinopathy, nephropathy, neuropathy, and cardiovascular events. The results highlight the predictive role of factors such as age, duration of diabetes, LDL cholesterol, and serum creatinine in complications, validating the extensive application of HbA1c in diabetes care.

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