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Investigating the Significance of Glycosylated Hemoglobin A1C (HbA1C) Test in the Diagnosis and Management of Diabetic Individuals.

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ABSTRACT

Background: Glycosylated hemoglobin (HbA1c) has been used as the "gold standard" for glycemic control and as a predictor of diabetes complications. HbA1c has become a solid biomarker for diagnosis and prediction of diabetes, because of the meaningful information offered by a single HbA1c test. It is also helpful in the treatment of pre-diabetes and other kinds of diabetes.

Objective: To reveal sensitivity of HbA1c in contrast to other diabetes diagnostic tests, to report the performance, effectiveness and validity of HbA1c test in the diagnosing and monitoring diabetes. To find out the awareness rate of significance of HbA1c test in diabetic monitoring.

Material & Methods: A cross-sectional research was conducted through a random sample approach, during the months of September and December of 2021. A sample size of 40 patients and health professionals including technologist and Doctor were taken. The data was gathered through a pre-validated research questionnaire among patients and health workers in major hospitals of Islamabad and Rawalpindi. Data was analyzed through Statistical Package for the Social Science (SPSS) software version 22. **Result:** The results found that 85% patients are agree with the significance of HbA1c test in diabetic monitoring while 15% patients are disagreeing with the significance of HbA1c test in diabetic monitoring. The results also reveal that 47% health professional feel that HbA1c test has better diagnostic accuracy than other diabetes diagnostic tests, 22% believe it is more dependable than other glucose tests, and 30% believe it is successful in diabetes mellitus prognosis. **Conclusion:** It was determined that in assessing and managing diabetes mellitus HbA1c test is considered one of the significant diagnostic test. It has the capacity to recall the previous three months' cumulative history of Glycosylated hemoglobin. The accuracy, sensitivity and reliability of HbA1c test is very high and clear in contrast to other blood glucose diagnostic tests. HbA1c test is more accurate than both a fasting glucose test and random glucose test. Moreover, HbA1c test does not need any fasting it perform any time.

Keywords: diabetes mellitus, diagnosis, disease management, blood test, HbA1c.

INTRODUCTION

Diabetes mellitus is classified into three major types; type 1 (insulin dependent), type 2, (insulin independent) and gestational diabetes mellitus (GDM). Type 1 diabetes occur more commonly in children and individual under the age of thirty years, however it can also effect older age peoples.

Insulin secretion is impaired in Type 1 diabetes due to idiopathic or autoimmune attack of insulin-secreting beta cells in the pancreas' islets of Langerhans [1]. Type 2 is the most frequent type of diabetes through worldwide which mainly affects peoples over the age of thirty years however several cases have been recently identified among obese youngsters. Type 2 diabetes mellitus has been also called as non-insulin-dependent diabetes mellitus (NIDDM) or late onset diabetes. Type 3 diabetes which as known as gestational diabetes (GDM) recognized when glucose intolerance is manifest first during pregnancy. Various studies show the involvement of disruption and abnormalities in the insulin signaling pathway, leading to decrease in glucose uptake and transport in adipocytes and skeleton muscle of the pregnant women [2]. According to the World Health Organization, diabetes affected 9% of the global population in 2014.

Pakistan is stand as the seventh-largest country in the world in terms of diabetes prevalence, with 10% of the population of Pakistan suffering from the condition. In this 10% of population 66 percent are suffering from severely abnormal HbA1c levels. According to the Pakistan National Diabetes Survey, 13.9 percent of Sindh's adult population (aged 25 and over) has type 2 diabetes. Diabetes Mellitus type 2 affects 8.6% of the Baluchi population. While in Khyber Pakhtunkhwa (KPK) type 2 Diabetes Mellitus affects 11.6 percent of adult women and 9.2 percent of adult males [3].

For the diagnosis diabetes and pre-diabetes, there are four types of blood tests accessible in laboratories: A) Blood glucose (plasma) test: This test may be used at any time of day to monitor blood glucose levels. A blood glucose level of 200 mg/dl or greater is required for diagnosis. B) Fasting plasma glucose test: This is the most common way to diagnose diabetes in men, non-pregnant women and children. C) Oral glucose tolerance test: This test is used when diabetes is suspected but the results of fasting plasma glucose test are normal. D) Hemoglobin A1c test: This test determines how much glucose is bound to hemoglobin. The quantity of glucose bound to hemoglobin increases as blood glucose levels rise. The American Diabetes Association advises an A1C level of fewer than 7%. Hemoglobin is an oxygen-transport iron-containing metallic protein found in vertebrates' red blood cells, as well as in some invertebrates' tissues [4].

The HbA1c test is important in the diagnosis and prognosis of diabetes patients, since it allows for a more complete knowledge of insulin and insulin resistance. HbA1c and insulin resistance have been demonstrated to have a direct relationship, with HbA1c being more strongly related with insulin sensitivity in healthy people with normal glucose tolerance [5]. The HbA1c test benefits in diagnosis diabetes include feasibility as a single blood-draw without fasting, measurement accuracy, minimal day-to-day variation, and pre-analytical consistency of the sample HbA1c can be used to specify people with diabetes or prediabetes as in number of ways. The normal value become less than 42 mmol/mol (below then 6.0%) [6].

An erythrocyte has a usual lifetime of 120 days. As the erythrocyte circulates in the presence of hyperglycemia, the N-terminal valine residues of the hemoglobin chain undergo non enzymatic glycation. The HbA1c generated as a result accounts for 60 to 80% of total Glycosylated hemoglobin. The number "1c" denotes the chromatographic order of hemoglobin detection. The glycation of hemoglobin happens throughout the erythrocyte's 120-day life cycle [7]. The glycation process has a strange pattern to it. The first 25% of glycation happens in the first 1 to 2 months of the erythrocyte's life cycle, which followed by another 25% the following month. The remaining HbA1c is generated during the erythrocyte's senescence, which occurs around 1-2 months before the test. As a result, senescent erythrocytes had higher HbA1c levels than reticulocytes. Furthermore, the idea that HbA1c indicates average glycaemia during the previous 6 to 8 weeks is based on this logic [7, 8].

Huisman and their fellows were the first to isolate HbA1c in 1958 [9]. Bookchin and Gallop were the first to define it as a glycoprotein in 1968 [10]. Rahber with their colleagues in 1969 reported the high level of HbA1c in diabetic patient [11]. In 1975 Bunn and their fellows revealed the mechanism which leading to the development of HbA1c [12]. Koeing was the first to suggest the use of HbA1c test as a biomarker for assessing the blood glucose level in diabetic individual in 1976 [13].

There are two methods of HbA1c analysis: charge difference -based technique and structural-difference based technique. The first group includes ion exchange chromatography and capillary electrophoresis. whereas the second group includes enzymatic assay, immunoassay, and affinity chromatography. Thus, techniques based on diverse principles, such as immunoturbidimetry, ion-exchange high-performance liquid chromatography (HPLC), enzymatic assay and boronate affinity chromatography, can be used consistently to determine HbA1c [14-16].

In 2009, The International Diabetes Federation, American Diabetes Association and the European Association for the study of Diabetes established an International Expert Committee, which decided that a HbA1c cut point $\geq 6.5\%$ can be used for diagnosis of diabetes mellitus. The World Health Organization recommended using HbA1c $> 6.5\%$ for diabetes diagnosis in 2011. In diabetic non pregnant people, the objective for HbA1c in diabetes monitoring remains at 7% [17]. The World Health Organization suggested the cut-off of HbA1c test (> 6.5 percent) ≥ 48 mmol/mol and was proposed for diagnosis in 2011 [18]. The American Diabetes Association (ADA) recently endorsed HbA1c with a cut point of > 6.5 percent as an alternative to fasting plasma glucose (FPG)-based guideline for diagnosing diabetes [19].

Materials and Methodology

In this research design descriptive cross sectional study was used to determine the significance of HbA1c in the diagnosis and management of diabetic individuals, Study population for this research included health professionals and patients visiting private hospitals of Rawalpindi and Islamabad. Both gender male and female, patients having diabetes, health care experts including physician, endocrinologist and diagnostic professional laboratory technologist were included in this research study. In contrast children and non-diabetic patients were excluded from the research study. Data was collected after approval from Ethics and Research committee of Bashir Institute of Health Sciences Islamabad and respective private hospitals from where data has been collected. Data of the current study was gathered through a pre-validated research questionnaire among patients and health workers. The study was conducted during September to December 2021. Sample size for this research was 40 patients and health professional. Non probability convenience sampling method was used for data collection. For data analysis, SPSS software version 22 was used.

RESULTS

Age characteristic of the patients undergoing HbA1c test:

The age characteristics of patients which undergoing HbA1c test for diagnosis or prognosis of diabetes. This Study revealed that 5 (12.5%) patients with age between 20 to 30 years, 8 (20%) patient with age between 31 to 40 years, 11 (27.5%) patients with age between 41 to 50, 5 (12.5%) patients with age between 51 to 60, 6 (15%) patients with age between 61 to 70, 5 (12.5%) patients with age 71 years or more, most patients have their HbA1c levels tested, which demonstrates that this test is especially important in middle-aged patients, as shown in table 1.

Table.1 characteristics of patients undergoing HbA1c test (n=40)1: .

Characteristics	Specifications	Frequency	Percent
Age	20 to 30 years	5	12.5%
	31 to 40 years	8	20%
	41 to 50 years	11	27.5%
	51 to 60 years	5	12.5%
	61 to 70 years	6	15%
	71 and above	5	12.5%
	Total	40	100%

Gender characteristic of the patients undergoing HbA1c test:

The gender characteristics of the patients which undergoing hba1c test for diagnosis or prognosis of diabetes. Study show that 26 patients (65%) are male and 14 patients (35%) patients are female out of total 40 diabetic patients undergo this test as show in table 2.

Significance of HbA1c test in diabetic monitoring:

Study revealed that 34 (85%) patients are agreeing with the significance of HbA1c test in diabetic monitoring while 6 (15%) patients are disagreeing with the significance of HbA1c test in diabetic monitoring as show in table 3.

Table 2: Characteristics of patients undergoing HbA1c test (n=40).

Characteristics	Specifications	Frequency	Percent
Gender	Male	26	65
	Female	14	35
	Total	40	100

Table 3: HbA1c test importance in diabetic monitoring (n=40).

Characteristics	Specification	Frequency	Percent
HbA1c test importance in diabetic monitoring	Yes	34	85
	No	6	15
	Total	40	100

Recommendation of HbA1c test for diabetic patient:

The recommended frequency of conducting HbA1c test for diabetic patient. According to the study, 16 (40 percent) health experts believe that diabetic patients should get a HbA1c test every three months, according to 11 (27 percent) health expert suggest it should be done every 6 months, 7 (17 percent) suggest HbA1c test at least once in a year, while 6 (15 percent) believe that the frequency of HbA1c testing should be determined by the severity of the patient's diabetes as show in figure 1.

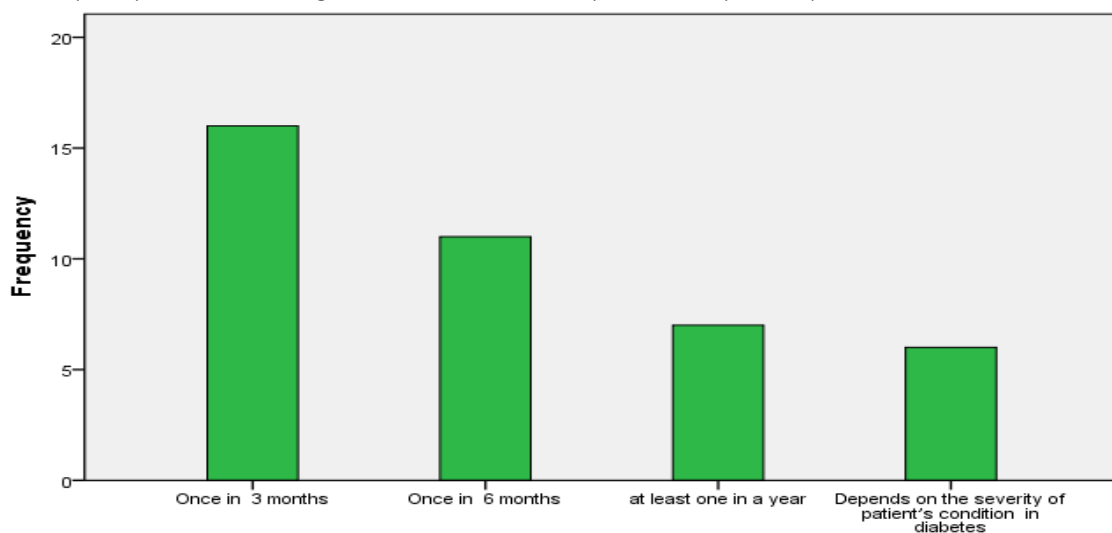


Figure 1: Recommendation of HbA1c test for diabetic patients

HbA1c test comparison with other diabetes diagnostic tests:

Demonstration and comparison of HbA1c test to other diabetes diagnostic tests based on key parameters just like diagnostic accuracy, reliability and effectiveness in glycemic management or diabetic management. Study reveal that 19 (47 percent) health experts believe it has superior diagnostic accuracy than other diabetes diagnostic tests, 9 (22 percent) believe it is more reliable than other glucose tests, and 12 (30 percent) believe it is effective in management of diabetes mellitus as show in figure 2.

Duration of diabetes undergoing HbA1c test:

16 (40%) patients which have more than 5 years of diabetes history are mostly experience with HbA1c test, 10 (25%) patients with less than 3 years of diabetes duration, 9 (22%) with 3 years of diabetic duration and 5 (12%) patients with 5 years' duration of diabetes experience this (hba1c) test. This also demonstrates the effectiveness of the HbA1c test in the diagnosis and long-term management of diabetes mellitus as show in figure 3.

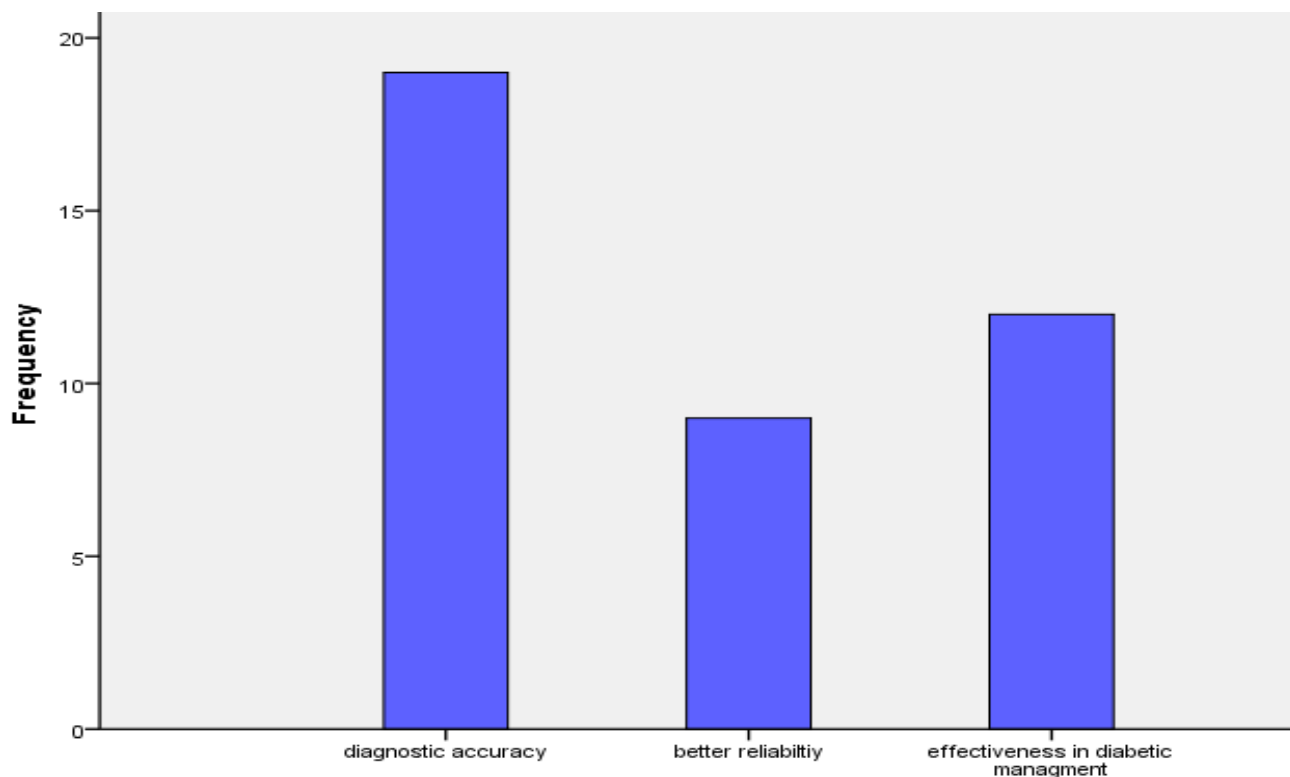


Figure 2:HbA1c test comparison with other diabetes diagnostic tests (n=40).

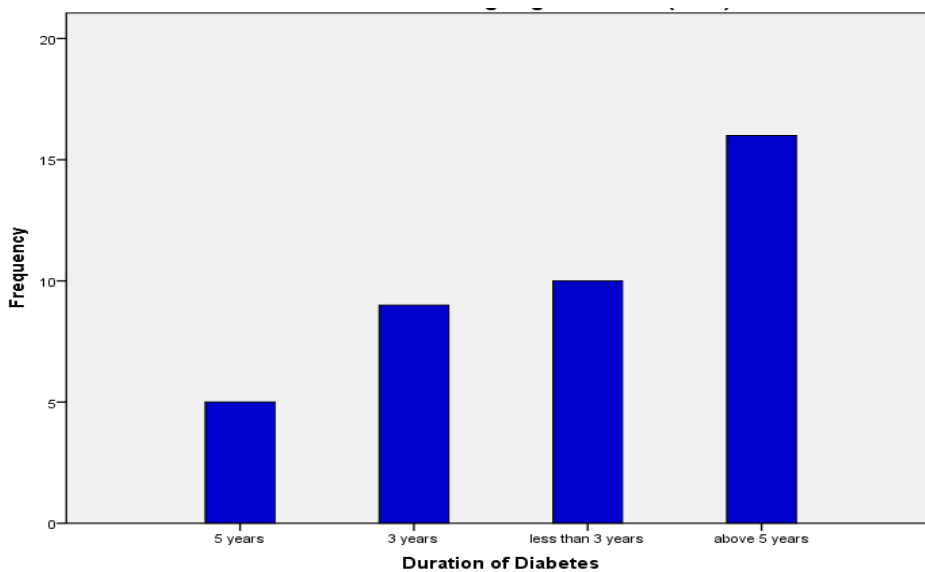


Figure 3: Duration of diabetes undergoing HbA1c test

Does HbA1c test is helpful in diabetes monitoring:

34 (85%) patients are agreeing with the significance of HbA1c test in diabetic monitoring while 6 (15%) patients are not satisfied with importance of HbA1c test in diabetic monitoring which is show in Figure 4.

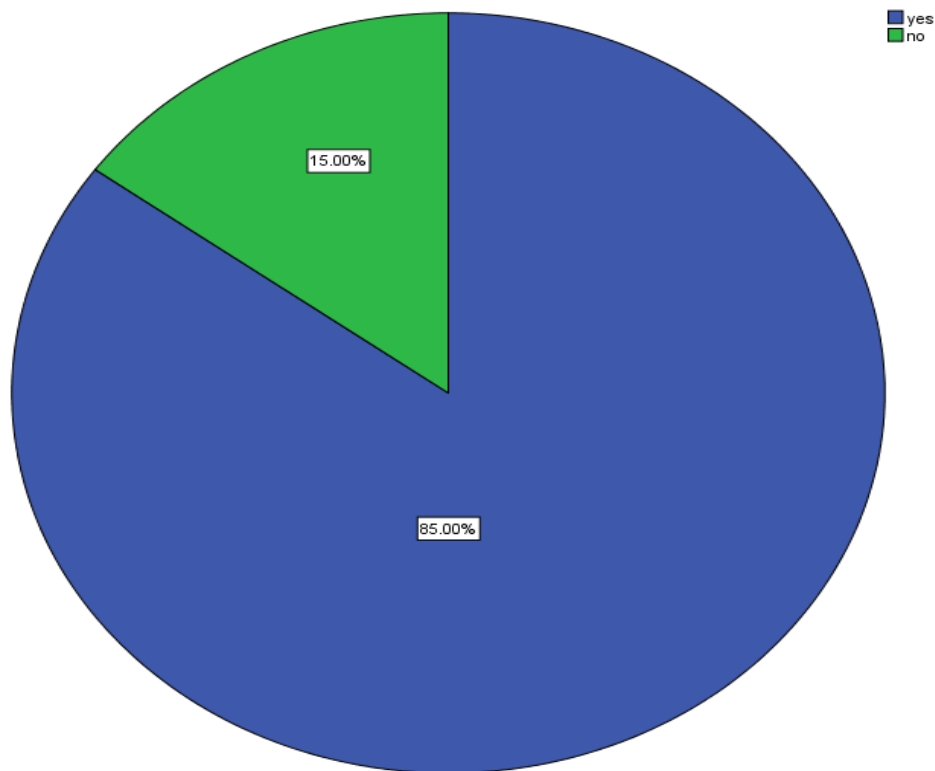


Figure 4: HbA1c test is helpful in diabetes monitoring

DISCUSSION

This study revealed that 85% patients are satisfied with the significance of HbA1c test in diabetic monitoring while 15% patients are disagreeing with the significance of HbA1c test in diabetic monitoring. The patients which are not agree with the significance of HbA1c is due to lack of education and awareness. A similar finding was achieved by Glasgow and Osteen, HbA1c was initially established as an essential test in the management of diabetes patients in 1976, however studies have indicated that diabetic individuals have been slow to adopt HbA1c. According to studies, around 25% of patients are aware of the importance of HbA1c in Diabetes and how to control it. In this study, 22 percent of patients were found to be aware of the significance of HbA1c in diabetes [20].

In this study it was shown that 27 percent patients aged 41 to 50 years mostly have tested their HbA1c levels, demonstrating that HbA1c test is extremely significant in middle-aged patients for determining glycemic status or to diagnosing diabetes. Mahrukh et al. in Lahore, Pakistan, carried out research that matched the findings of the current study [6].

Occurrence of diabetes is not generally dependent on gender but still more male underwent HbA1c test for diagnosis. Our Study revealed that 65% males and 35% female underwent HbA1c test. It means that the male to female ratio is higher.

In accordance with the present study's findings a work was done by A Fawwad, R Hakeem. According to the national diabetes census, males have a greater prevalence of diabetes than females, whereas females have a higher prevalence of impaired glucose tolerance (IGT) than males [21]. This research study showed that 85% patients are agree with the significance of HbA1c test in diabetes monitoring while 15% patients are disagreeing.

According to the study, 40 percent health experts believe that diabetic patients should get a HbA1c test every three months, according to 27 percent health expert suggest it should be done every 6 months, 17 percent suggest HbA1c test at least once in a year, while 15 percent believe that the frequency of HbA1c testing should be determined by the severity of the patient's diabetes. Most of the health professional suggested that HbA1c test must be performed once in three months. In conformity to the findings of our current study the American Diabetes Association (ADA) stated that in individuals with unstable diabetes, the National Institute for Health and Clinical Excellence (NICE) recommends HbA1c testing should be done every 2–6 months, with a value taken less than 3 months being considered as a signal of direction of change rather than a new steady state in UK.

Intervals of 6–1 months are indicated for those with stable diabetes on unchanged therapy. The American Diabetes Association (ADA) offers similar advice [22].

This Study shows that 47 percent health experts believe that HbA1c has superior diagnostic accuracy than other diabetes diagnostic tests, 22 percent believe it is more reliable than other glucose tests, and 30 percent believe it is effective in management of diabetes mellitus. The European Association for the Study of Diabetes also suggested that the HbA1c test be used to diagnose diabetes, with a 6.5 percent (48 mmol/mol) critical value, which was endorsed by the American Diabetes Association in 2010 [23].

According to this study, 22% of people feel it is more trustworthy than other glucose tests, This finding was also demonstrated in a research study by Shuolin Wu et al, who found that HbA1c or HbA1c combined with Fasting plasma glucose test is a best alternative for testing impaired glycol metabolism than Oral Glucose Tolerance Test [24].

CONCLUSION

HbA1c has become one of the most reliable tests in the diagnosis, assessment, and treatment of diabetes. It has the capacity to recall the previous three months' cumulative history of glycosylated hemoglobin. HbA1c is an accurate and simple-to-use test that provide fast results, despite the fact that HbA1c has been approved for diabetes diagnosis, in most nations throughout the world, many testing procedures and threshold levels are currently being debated. However, combining fasting glucose test (FGT) and HbA1c improves the diagnosis accuracy. HbA1c test is more accurate than both a fasting glucose test and random glucose test. Therefore, endocrinologists can use this test to diagnose and manage diabetes by providing medicines and treatments. This test is commonly performed for all forms of diabetes, although it is especially beneficial for type II diabetes. The importance of the HbA1c test is well acknowledged in educated families but not familiar in general population. It is necessary to highlight its awareness and advantages in the community.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

All the authors equally contributed in planning and collecting data, drafting manuscript and analyzing data to be qualified for authorships

FUNDING SOURCE

N/A All authors equally contributed in data collection, planning, drafting and finalizing this manuscript.

RECOMMENDATION

This study reveals the significance of HbA1c in the diagnosis and prognosis of diabetic patients. Based on the findings of our study, we recommend endocrinologists and laboratory technologists to educate the people and to create awareness about the significance of HbA1c in diagnosis and prognosis of diabetes because effectiveness and accuracy of HbA1c is proven.

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