



Significance of HbA_{1c} test application in clinical practice

Rufina Menezes¹, Rahul Jadhav², Rajesh Ingole³, Vishal Nangare⁴, Nilesh Chavan⁵.

¹Hi-tech pathology lab, Umbergothan Naka, Virar West-401301, Maharashtra, India.

²Zoology Research Laboratory, E.S.A. College of Science, Vasai Road – 401 202, Maharashtra, India.

³Sai – Darshan pathology lab, Virar west- 401303, Maharashtra, India.

⁴Dept. of Zoology, Siddharth College of Arts, Commerce and Science, Fort, Mumbai 400 001, Maharashtra, India.

⁵Dept. of Zoology, Gokhale Education Society's Arts, Commerce and Science College, Shreewardhan. Dist.- Raigad- 402110, Maharashtra, India.

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ABSTRACT

According to studies, HbA_{1c} fluctuation is a significant risk factor for diabetic complications in people with type 2 diabetes. HbA_{1c} has established its mark when it comes to detecting sugar control in Type 2 diabetics. The present study was carried out to establish the importance of regularly monitoring HbA_{1c} levels in Type 2 diabetic patients along with traditional Fasting blood sugar (FBS) and 2 hours Post prandial blood sugar (PPBS) levels. There is an impact of day to day variation in diet on fasting and postprandial blood glucose. Hence, it becomes necessary to monitor their HbA_{1c} levels to get an idea of their blood glucose control over the period of 3 months. A further study of post glucose blood sugar levels may provide an unbiased sugar levels as compared to traditional post prandial sugar levels to avoid the bias in the study.

Keywords: Diabetes, Blood sugar levels, application, HbA_{1c}.

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¹ Author : Rufina Menezes.

Email for correspondence: rufinamenezes@yahoo.co.in

INTRODUCTION:

Diabetes is a leading disease worldwide and is rapidly establishing its dominance in all age groups, various financial background as well as ethnicity. 422 million people worldwide present with diabetes, the majority of who belong to low and middle-income nations and Diabetes is directly responsible for 1.5 million fatalities annually, WHO, (2011). The number of diabetics in India in 2011 was 61.3 million which has now raised to 74.2 million in 2021, FDP, (2021). The expected undiagnosed cases in India are over 57% of adult diabetics which accounts to around 43.9 million people. When dealing with diabetics, it is very essential to look at different aspects of diagnostic methods Pradeepa *et al.*, (2021). While most of the doctors and patients stick to traditional Fasting blood sugar (FBS) and Post prandial blood sugar (PPBS) levels, some doctors prefer more advanced testing methods like fasting and post prandial insulin levels and quarterly HbA_{1c} levels along with traditional FBS and PPBS levels. Most of the patients of the study group preferred doing FBS and PPBS and self-adjusting their medicinal doses. However it has been observed that due to variations in the diet, the observed glucose levels tend to vary greatly. Hence it has become essential to monitor the HbA_{1c} levels of the patients to actually know how good they have been at maintaining their blood sugar levels in reality. The WHO and the American Diabetes Association (ADA) advocate using glycated haemoglobin (HbA_{1c}) as a diagnostic test in addition to fasting blood glucose (FBG), with a cut-off value of 6.5% for the diagnosis of diabetes mellitus (DM) and 6.1% for the diagnosis of pre-diabetes.

HbA_{1c} fluctuation is an important risk factor for diabetic complications in people with type2 diabetes, Prentice *et al.*,

(2016). The possibility that glucose fluctuation may increase the risk of both microvascular and macrovascular complications, has garnered more interest in the researchers. According to Karnchanasorn *et al.*, (2016), around 7 million people go undiagnosed diabetics whereas the few that are diagnosed have already suffered the consequences of diabetic complications by the time they have been diagnosed. Sherwani *et al.*, (2016) conclude that HbA_{1c} can be an adequate and easily manageable test that can be used for diagnosis of diabetes even in low and middle income populations. They further add that HbA_{1c} along with Fasting glucose test greatly increases the efficacy of the tests. The HbA_{1c} assay serves as the foundation for the suggested objectives for metabolic control of diabetes, ADA, (2007); European diabetes policy group, (1999); Nathan *et al.*, (2009).

MATERIALS AND METHODS:

The study was a prospective study where a total of 743 patients were involved for three months duration. 10-12 hours fasting blood sample was collected in 2 ml fluoride and 3 ml EDTA vacutainer respectively and 2 ml of blood sample was collected 2 hours post prandial in a fluoride vacutainer. Blood glucose was estimated using GOD/POD method on Delta semiautomatic biochemistry analyser and HbA_{1c} was estimated by HPLC (high performance liquid chromatography) method using Tosoh G8 Glycohemoglobin Analyzer.

RESULTS:

A total of 743 patients were included in a study of which 412 were females and 331 were males. It was observed that there was a significant difference between the estimated actual glucose mean and the actual mean of the blood sugar levels.

Figure 1 : Number of respondents: Male to female ratio

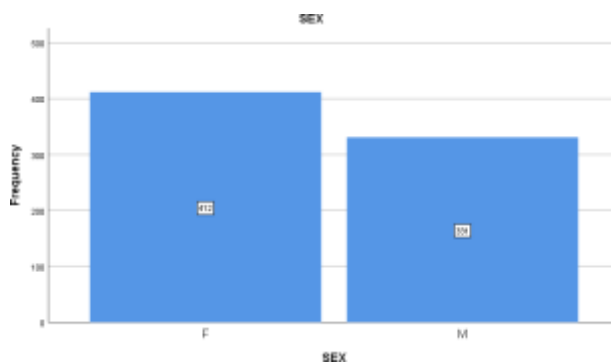
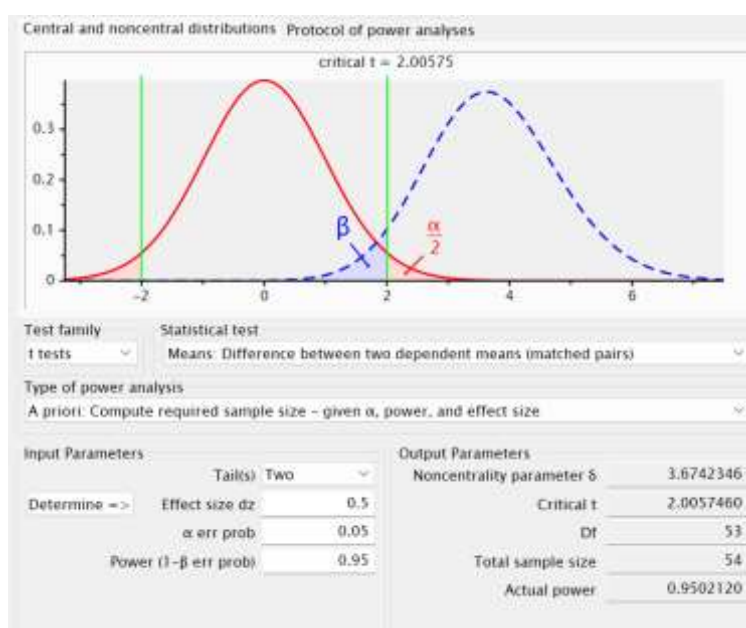


Figure 2 : Paired sample graph showing Beta distribution



Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	eAG	188.2738	742	46.07173	1.69135
	Actual avg.	161.3521	742	55.87413	2.05120

As per Faul *et al.* (2007) minimum required sample size to apply paired sample t test = 54

Paired Samples Test

		Paired Differences							
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference		t	df	Sig. (2-tailed)
					Lower	Upper			
Pair 1	eAG - Actual avg.	26.92166	54.14520	1.98773	23.01940	30.82391	13.544	741	.000

Paired t test is applied to examine significance difference in eAG and actual avg. It is seen that t statistics = 13.54 and p value = 0.000 which is less than LOS 5% indicating significant difference in eAG and actual avg.

Mean eAG =188.27 and mean actual avg. =161.35

Paired Samples Statistics

SEX			Mean	N	Std. Deviation	Std. Error Mean
F	Pair 1	eAG	189.5162	411	45.16886	2.22802
		Actual avg.	160.8719	411	52.47712	2.58851
M	Pair 1	eAG	186.7311	331	47.19191	2.59390
		Actual avg.	161.9484	331	59.90021	3.29241

Paired Samples Test

SEX			Paired Differences					t	df	Sig. (2-tailed)
			Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
						Lower	Upper			
F	Pair 1	eAG - Actual avg.	28.64430	52.65874	2.59746	23.53829	33.75031	11.028	410	.000
M	Pair 1	eAG - Actual avg.	24.78266	55.94236	3.07487	18.73384	30.83148	8.060	330	.000

Paired t test is applied to examine significance difference in eAG and actual avg of Males. It is seen that t statistics = 8.060 and p value = 0.000 which is less than LOS 5% indicating significant difference in eAG and actual avg.

Mean eAG =186.73 and mean actual avg. =161.94

Paired t test is applied to examine significance difference in eAG and actual avg. of Females. It is seen that t statistics = 11.028 and p value = 0.000 which is less than LOS 5% indicating significant difference in eAG and actual avg.

Mean eAG =189.51 and mean actual avg. =160.87

DISCUSSION:

A significance difference with a p value of 0.00 was seen between calculated eAG value and actual average of sugar levels among the participants. Glycation is the non-enzymatic binding of un-protonated free amino groups of proteins to free aldehyde groups of carbohydrates (such as glucose). Several soluble and insoluble proteins, as well as the structure and function of isolated components of the basement membrane, are affected by glycation. Due to the gradual and cumulative nature of these changes, there is a significant lag between the time of diagnosis and the onset and development of diabetes, Brownlee (2000); McCance *et al.*, (1993); Thorpe (1996); Vlassara *et al.*, (1968). In a study based on multi-ethnic Asian population residing in Singapore, Lim *et al.*, (2018) concluded HbA_{1c} (instead of FBG or OGTT) as a diabetes screening tool and showed that it is a suitable substitute for FBG. However, a study published by Little and Robert (2009), states that presence of Hb variants adversely alters the HbA_{1c} value. Further, it is now time to test the hypothesis linking the presence of a hemoglobinopathy with heretofore-unexplained elevations of HbA_{1c} concentrations out of proportion to continuously measured glucose and other metrics of mean glycemia in patients with type 2 diabetes, Klonoff, (2020). According to the World Health Organization, about 5.2% of the world population and over 7% of pregnant women carry a significant variant, and 1.1% of couples worldwide are at risk for having children with a hemoglobin disorder.

CONCLUSION:

With the explosion of diabetic cases worldwide HbA_{1c} can be considered as a cost effective way of diagnosing diabetes. We agree with Sherwani *et al.*, (2016) in concluding that HbA_{1c} test may continue to be used as a diagnostic and predictive

tool as the diabetes epidemic spreads around the world, improving patient care and producing positive clinical outcomes. However, it may be difficult to predict accurate HbA_{1c} levels in patient with various hemoglobinopathies. According to NGSP (National Glycohemoglobin Standardisation program), genetic variants like HbS trait (sickle cell hemoglobin), HbC trait, high levels of fetal hemoglobin (HbF) and chemically modified hemoglobin derivatives have the tendency to affect the precision of measuring HbA_{1c} levels. Introduction of Serum Insulin as a test may also provide a better understanding of the onset of diabetes and its progression. Insulin level can provide insight of either underproduction of insulin or insulin resistance.

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