Original article:

Association of Fructosamine and HbA1c in Newly Diagnosed Type 2 Diabetes Mellitus Patients

Saba Khan[1], Roshan Alam[2*], Mohammad Mustufa Khan[3]

[1]Assistant Professor, Department of Biochemistry, Integral Institute of Medical Sciences & Research, Integral University, Lucknow, Uttar Pradesh, India
[2]Professor & Head, Department of Biochemistry, Integral Institute of Medical Sciences & Research, Integral University, Lucknow, Uttar Pradesh, India
[3]Assistant Professor, Department of Life Sciences, Institute of Applied Medicines & Research, Ghaziabad, Uttar Pradesh, India
Corresponding Author: Dr. Roshan Alam, Professor & Head,Department of Biochemistry,Integral Institute of Medical Sciences & Research, Integral University, Lucknow, Uttar Pradesh, India

ABSTRACT

Introduction: Uncontrolled blood sugar is the main culprit for high levels of morbidity and mortality in diabetic patients worldwide. The blood glycated hemoglobin (HbA1c) and fructosamine provide a good picture of average plasma glucose for the previous 2-3 months and 2-3 weeks, respectively.

Aim: To associate the HbA1c and Fructosamine in newly diagnosed Type 2 diabetes mellitus (T2DM) patients to find an alternative marker and better predictor for the early development of diabetic complications.

Material and Methods: Total 70 subjects (35 T2DM and 35 age and gender-matched healthy controls) were enrolled from the rural and suburban population of North India. Biochemical investigations were performed by commercial kits using Chemistry Auto-analyzer. $P<0.05$ was considered statistically significant.

Result: The mean of fasting blood sugar (FBS), post-prandial blood sugar (PPBS), HbA1c and fructosamine have significantly increased in T2DM patients compared to healthy controls ($p<0.0001$). FBS, PPBS, HbA1c, and Fructosamine have a significant positive correlation in T2DM patients ($p<0.01$). Fructosamine has a significant positive correlation with FBS, PPBS and HbA1c ($p<0.01$, $p<0.01$, $p<0.01$, respectively). A linear regression was performed to find the predictor of Fructosamine. The model showed HbA1c as the only strong predictor ($p=0.002$). In addition, a linear regression was performed to find the predictor of HbA1c. The model showed FBS and Fructosamine as the strong predictors ($p=0.000$, $p=0.002$, respectively).

Conclusion: Fructosamine has a significant positive correlation with FBS, PPBS, and HbA1c in T2DM patients. HbA1c has been observed as a strong predictor of fructosamine. However, FBS and fructosamine have seen as strong predictors of HbA1c. Fructosamine may act as a potential biomarker for the diagnosis of diabetes and its complications in the Asian population.

Keywords: Glycated Hemoglobin, Fructosamine, Type 2 Diabetes Mellitus, Body Mass Index

INTRODUCTION

Diabetes is the 7th leading cause of death and with the combination of obesity and hypertension (HTN), this leads to cardiovascular diseases (CVDs) which are the first leading cause of death globally (WHO, 2016). The prevalence of diabetes mellitus (DM) and obesity are increasing parallel in worldwide (IDF, 2013). A recent study reported

that the number of adults with diabetes in the world increased from 108 million in 1980–422 million in 2014, due to population growth, aging, and the rise in overweight and obesity. Globally, the prevalence of diabetes has increased in both genders equally, in men from 43% in 1980 to 90% in 2014 and in women from 50% to 79% in women (Ezzati et al. 2016).

India is the second largest contributor to regional mortality, with one million deaths attributable to diabetes. In 2015, India had 69.2 million people with diabetes and 36.5 million impaired glucose tolerance (IGT) people (20–79 years) which are expected to rise to 123.5 million and 63.6 million by 2040, respectively. The prevalence of diabetes is high in urban than in rural India (14.2% vs. 8.3%) and prediabetes prevalence was found to be nearly same (urban 14.5%; rural 14.7%) (Anjana et al. 2011).

The majority of people with diabetes (>90%) have T2DM. Unfortunately, more than 50% of people with T2DM still remained undiagnosed (Joshi et al. 2008).

"Asian Indian Phenotype" because of (greater abdominal adiposity, higher waist circumference, and lower body mass index [BMI]) makes Asian Indians more prone to diabetes and premature coronary artery diseases (CADs) (Mohan et al. 2007). Indians are known to have a relatively unfavorable risk profiles for T2DM and CVD (Khoo et al. 2011). A follow-up study of Chennai Urban Population-based Study (CUPS) cohort showed that the overall mortality rates were nearly three times higher (18.9 vs. 5.3 per 1000 person-years, P = 0.004) in people with diabetes compared to nondiabetic subjects (Mohan et al. 2006).

The American Diabetes Association (ADA) Standards of Medical Care in Diabetes added glycosylated hemoglobin (HbA1c) as an important criterion for the diagnosis of prediabetes and diabetes (5.7%–6.4% and ≥6.5%, respectively) (ADA, 2010). In T2DM, higher HbA1c indicating poorer control of blood glucose levels. The HbA1c level is proportional to average blood glucose concentration over the previous 4 weeks to 3 months (Vikøren et al. 2014).

However, Fructosamine, discovered about 30 years ago, is a marker of glucose control reflecting the average glycaemic level over the preceding 2–3 weeks (Nagasaka et al. 1988). It may be more appropriate for monitoring early response to treatments (Nagasaka et al. 1988). Its measurement is quick, technically simple, inexpensive, precise, fairly free of interferences, unaffected by red blood diseases and easily automated for use with micro-sample volumes (Baker et al. 1985, Hindle et al. 1986, Dafallah et al. 1994, Koga et al. 2011).

Serum fructosamine appears to be a good predictor of adverse outcome in patients with known diabetes and those with unrecognized diabetes or hyperglycemia. It can serve as an alternative to HbA1c in the setting of preoperative glycemic assessment (Shohat et al. 2017).

Fructosamine and GA have utility as alternate markers in those patients where the HbA1c assay is unreliable. Also, they can identify poor glucose control more rapidly than HbA1c, i.e., short-term hyperglycemia. A major promise will be their ability to predict those pre-diabetic patients who go on to clinical diabetes since this could lead to major lifestyle and pharmacological interventions to prevent the onset of diabetes and its complications. Finally, they may also have a role in pregnancy for the management of diabetes given that they can provide a measure of glycemia over 2 to 3 weeks rather than 8 to 12 weeks. Glycated albumin has been reported to be a better marker than HbA1c for the assessment of glucose control in people with

33

diabetes with chronic kidney disease and those on hemodialysis and peritoneal dialysis (Gounden et al. 2017).

Glycemic control during pregnancy and proper diagnosis of Gestational diabetic patients needed to prevent the complications. For this purpose, fructosamine assay can provide a good index of glycemic control, especially in diabetic pregnant patients. Fructosamine assay is reliable, technically simple, low cost, and consume low time for analysis. Hence, it can be considered an alternative choice for first-line monitoring of diabetic patients and the fructosamine determination is more consistent when compared to HbA1c. It determines the average glucose over the past 2-3 weeks and the assay is not affected by the food eaten during the day. Hence, it can be measured at any time during the day. It may be a very useful clinical adjunct and indicator for monitoring glycemic control in gestational diabetic patients (Ayyappan et al. 2015).

METHODS & MATERIALS

Subject Selection

This case-control study was approved by the institutional ethical committee of the University. Subjects with T2DM and healthy controls were enrolled from the outpatients attending the Diabetes Clinic, Integral Institute of Medical Sciences & Research, Integral University, Lucknow (India) based on the inclusion/exclusion criteria. Written informed consent was taken from each subject and all procedures performed in studies involving human participants were in accordance with the ethical standards of this university and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards (WMA, 2013).

Total 70 samples (35 newly diagnosed T2DM and 35 ages and gender-matched healthy controls) aged between 20-70 years were enrolled for this study.

The study was conducted from January 2017 to June 2017. Screening and management of patients were done as per American Diabetes Association guidelines (ADA, 2015). Subjects have FBS $\geq$126mg/dl, or PPBS $\geq$200mg/dl (WHO, 2006), and HbA1c $\geq$ 6.5% were considered as cases (ADA, 2010). Subjects have FBS <110mg/dl, or PPBS <140mg/dl (WHO, 2006), and HbA1c 4.7-5.4% were also considered as controls (ADA, 2010). Subjects (both cases and controls) with ischemic heart disease, angina, myocardial infarction (MI), electrocardiogram abnormalities, those with another concurrent sickness like the chronic liver disease, hypothyroidism or those on drugs like diuretics, pregnant women and women using oral contraceptives were excluded from the study.

Study design

Age and gender-matched case and control subjects were enrolled for keen observation and avoiding various confounding factors. HbA1c and Fructosamine were estimated in all subjects and correlated between case and control groups.

Laboratory Investigation

Clinical parameters were analyzed in all subjects using the commercially available kit by Siemens Dimensional RxL Max Integrated Chemistry System (Siemens Healthcare Diagnostics, Inc**.,** Tarrytown, NY, USA). HbA1c was measured by using whole blood EDTA samples on Bio-Rad D10 high-performance liquid chromatography (HPLC) analyzer (Bio-Rad, Hemel Hempstead, UK). Quality control was carried out every day of testing following the manufacturer's instructions using Biorad Lyphocheck Haemoglobin A1c controls (Grant et al., 2017). Measurement of glycated albumin/fructosamine was done by the nitroblue tetrazolium (NBT) colorimetric method (Mashiba et al., 1992).

34

Statistical Analysis

Statistical analysis was applied to all data using IBM SPSS Statistics for Windows, Version 22.0. (Armonk, NY: IBM Corp). Mean ± SD (Standard Deviation) of all quantitative clinical parameters were calculated in T2DM and healthy controls. Pearson correlation was performed to find the correlation between various parameters. Multiple linear regression analysis was performed to find the independent predictor for the diagnosis of blood sugar level. P-values were calculated by student unpaired t-test. Statistically significant was considered as p <0.05.

RESULTS

In this study, the mean age of T2DM patients (47.69±10.82 years) and healthy controls (44.80±8.75 years) have been found. In T2DM patients, male-female ratio 1.06 is found and in healthy controls, this ratio is 1.19. Anthropometric parameters BMI were significantly increased in T2DM patients compared to healthy controls (p<0.0001). Mean of FBS, PPBS, HbA1c, and fructosamine was found significantly higher in T2DM patients compared to healthy controls (p<0.0001) (Table 1).

Table 1: Characteristics of T2DM and healthy control subjects

Parameters	T2DM (n=35)	Controls (n=35)	P-value
Age (years)	47.69±10.82	44.80±8.75	0.22
Gender (M/F)	18/17	19/16	1.00
BMI (kg/m2)	24.72±1.78	22.27±1.62	0.0001*
FBS (mg/dl)	208.74±59.52	92.57±6.71	0.0001*
PPBS (mg/dl)	268.14±82.85	126.31±7.02	0.0001*
HbA1c (%)	9.15±2.16	5.07±0.38	0.0001*
Fructosamine (Units/L)	2.58±0.32	1.69±0.15	0.0001*

Data was represented as Mean±SD (Standard Deviation).

*Statistical significant was considered as P<0.05.

BMI: Body Mass Index, FBS: Fasting Blood Sugar, PPBS: Post-Prandial Blood Sugar, HbA1c: Glycosylated Haemoglobin

Clinical parameters FBS, PPBS, HbA1c, and Fructosamine have the significant positive correlation in T2DM patients (p<0.01). Anthropometric parameters BMI has a significant positive correlation in T2DM patients (p<0.01). Fructosamine has significant positive correlation with BMI, FBS, PPBS and HbA1c (p<0.05, p<0.01, p<0.01, p<0.01, respectively) (Table 2).

35

Table 2: Correlation of clinical parameters in T2DM cases

Parameters→↓	Age	BMI	FBS	PPBS	HbA1c	Fructosamine
Age	1	0.038	0.103	0.222	0.107	0.061
BMI	-	1	0.434**	0.264	0.395*	0.428*
FBS	-	-	1	0.798**	0.964*	0.846**
PPBS	-	-	-	1	0.839**	0.763**
HbA1c	-	-	-	-	1	0.897**
Fructosamine	-	-	-	-	-	1

*Correlation is significant at the 0.05 level (2-tailed)

**Correlation is significant at the 0.01 level (2-tailed)

BMI: Body Mass Index, FBS: Fasting Blood Sugar, PPBS: Post-Prandial Blood Sugar, HbA1c: Glycosylated Haemoglobin

A linear regression was performed so as to find the predictor of Fructosamine. Model showed HbA1c as the only strong predictor (β=1.129, p=0.002, CI: 0.068 to 0.271) (Table 3).

Table 3: Linear regression analysis to show the dependence of Fructosamine on study parameters in T2DM cases

Coefficients

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95% Confidence Interval for B	
	B	Std. Error	Beta			Lower Bound	Upper Bound
(Constant)	.897	.393		2.284	.030*	.094	1.699
Age (years)	-.001	.002	-.044	-.539	.594	-.006	.004
BMI (kg/m^2)	.021	.016	.114	1.289	.207	-.012	.053
FBS (mg/dl)	-.002	.002	-.342	-1.120	.272	-.005	.002
PPBS (mg/dl	.000	.001	.068	.450	.656	-.001	.001
HbA1c (%)	.169	.050	1.129	3.405	.002*	.068	.271

Dependent Variable: Fructosamine (Units/L)

* *Statistical significant was considered as P<0.05.

BMI: Body Mass Index, FBS: Fasting Blood Sugar, PPBS: Post-Prandial Blood Sugar, HbA1c: Glycated Haemoglobin

In addition, a linear regression was performed to find the predictor of HbA1c. Model showed FBS and Fructosamine as the strong predictors {(β=0.668, p=0.000, CI: 0.018 to 0.030), (β=0.253, p=0.002, CI: 0.673 to 2.698), respectively} (Table 4).

Table 4: Linear regression analysis to show the dependence of HbA1c on study parameters in T2DM cases

Coefficients

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95% Confidence Interval for B	
	B	Std. Error	Beta			Lower Bound	Upper Bound
(Constant)	-.029	1.345		-.022	.983	-2.780	2.721
Age(Year)	-.001	.008	-.003	-.080	.937	-.016	.015
BMI Kg/m2	-.043	.051	-.035	-.830	.413	-.148	.062
FBS(mg/dl)	.024	.003	.668	8.360	.000*	.018	.030
PPBS(mg/dl	.003	.002	.123	1.822	.079	.000	.007
Fructosamine (Units/L)	1.685	.495	.253	3.405	.002*	.673	2.698

Dependent Variable: HbA1c (%)

* *Statistical significant was considered as P<0.05.

BMI: Body Mass Index, FBS: Fasting Blood Sugar, PPBS: Post-Prandial Blood Sugar, HbA1c: Glycated Haemoglobin

DISCUSSION

The clinical parameters of T2DM patients like FBS, PPBS, HbA1c, and fructosamine were found significantly increased as compared to healthy controls. The study has reported that blood sugar levels were significantly raised in T2DM patients as compared to healthy controls (Chawla et al., 2016). Poor glycemic controls in patients with diabetes are prone to early development of diabetic complications like microvascular and macrovascular complications (Mohan et al., 2007, Chawla et al., 2016).

Anthropometric parameter BMI has significantly higher in T2DM patients (24.72±1.78) than healthy controls, but constantly low. It showed that T2DM patients have low BMI although mostly they are middle-aged patients. Various studies were reported that Asian Indians have constantly low BMI in diabetic patients and they are more prone for the risk of cardiovascular disease at lower BMI

(Mohan et al. 2007, Deepa et al., 2009). Results showed that BMI has a significant positive correlation in T2DM patients. Accordance with our study, previous studies have reported that prevalence of diabetes and its complications increase with increasing of BMI (Ganz et al., 2014, Gray et al., 2015). BMI is one of the known parameters for the measurement of obesity, mainly general obesity. Presently, obesity is one of the main culprits of non-communicable and lifestyle diseases especially for T2DM worldwide. Ganz et al. reported that the risk of developing T2D for individuals who were overweight or obese was about 1.5–5 times higher than for individuals with normal BMI (Ganz et al., 2014).

Clinical parameters FBS, PPBS, HbA1c, and Fructosamine have the significant positive correlation in T2DM patients. FBS and PPBS are the established clinical parameters for the diagnosis of diabetes (WHO, 2006). In our study, HbA1c has

37

shown strong positive correlation with FBS and PPBS in T2DM patients. Sherwani et al. (2016) have also found the strong positive correlation between HbA1c and FBS in diabetic patients and suggested that elevated HbA1c may act as an independent risk factor for coronary heart disease and stroke in subjects with or without diabetes.

Fructosamine has a significant positive correlation with HbA1c in T2DM cases. Similar to our findings, several studies have reported that HbA1c values have good correlation with serum fructosamine in diabetic patients (Pandya et al., 1987; Narbonne et al., 2001). Similarly, Chen et al. (2002) conducted a prospective study in T2DM patients and suggested that serum fructosamine assay can better reflect average blood glucose concentration over the previous 3 to 6 weeks and HbA1c is better reflective over the previous 8 to 10 weeks.

In our study, one side HbA1c has been observed as strong predictor fructosamine. Another side, FBS, and fructosamine have seen as strong predictors of HbA1c. However, these all are the diagnostic markers for the measurement of blood sugar levels in diabetic and non-diabetic individuals. Selvin et al. (2014) demonstrated that fructosamine and glycated albumin were independently associated with prevalent retinopathy and the risk of incident chronic kidney disease and diabetes. These associations persisted after adjustment for traditional risk factors and added information after further adjustment for HbA1c or fasting glucose. Selvin et al. (2014) suggested that fructosamine and glycated albumin have prognostic utility for the prediction of diabetes, chronic kidney disease, and retinopathy in the community. Their results suggested that these nontraditional markers of hyperglycemia might be useful in clinical practice (Selvin et al., 2014). However, Manjrekar et al.

reported that serum fructosamine (FA) predicts the development of diabetes in high-risk populations, but it has less sensitivity in depicting chronic hyperglycemia. They also suggested that Serum FA along with waist circumference (WC) could be useful predictors of the development of diabetes in 'high-risk' individuals (Manjrekar et al., 2012).

Although the exact pathogenesis of T2DM is unclear, it is generally accepted that T2DM is a multifactorial disorder resulting from genetic polymorphisms and several environmental factors (Ben-Salem et al., 2014). Strict glycemic control, regular monitoring, and management of blood sugar are essential in healthy as well as in T2DM patients to prevent the progression and early development of diabetes and its complications. For this purpose, close observation of glycemic fluctuation is required in T2DM patients. Fructosamine estimation seems most promising biomarker than HbA1c because Fructosamine gives 2-3 weeks status of blood sugar while HbA1c gives 2-3 months status of blood sugar and inconsistent with the lifespan of red blood cells (RBCs). Younger and low number of RBC gives low HbA1c level while older and high number of RBC gives high HbA1c level in individual person.

Falsely elevated HbA1c in relation to a mean blood glucose concentrations can be achieved when RBC turnover is decreased, resulting in a disproportionate number of older RBC. This problem can occur in patients with iron, vitamin B12, or folate deficiency anemia. Inversely, increased RBC turnover leads to a greater proportion of younger RBC and falsely lower HbA1c values, such as in conditions with acute and chronic blood loss, hemolysis or pregnancy, anemia and patients treated for iron, vitamin B12, or folate deficiency, and treated with erythropoietin (Polgreen et al., 2003; Brown et al., 2008). HbA1c

38

values may be falsely high or low in those with end-stage renal disease (Ly et al., 2004).

In addition, HbA1c levels are no accurate in reflecting short-term glycemic changes. While glycemic control changes rapidly, HbA1c changes gradually. As a result, measuring HbA1c to evaluate responses to glucose-lowering treatment in DM patients may be useful after twelve weeks (Koga et al., 2011). In patients with fulminant type 1 DM (in which hyperglycemia rapidly occurs), HbA1c may not be a reliable indicator due to its normal or only slightly elevated levels (Imagawa et al., 2000).

In addition, a study suggested that fructosamine levels are strongly associated with serum glucose and HbA1c and may be used as a complementary marker of glucose metabolism. High levels of fructosamine are associated with an increased incidence of MI and death even after adjustment for major CVD risk factors (Malmström, 2017). A community-dwelling adult Youjiang, China population-based study reported that dyslipidemia significantly contributed to increasing serum fructosamine concentrations in males and it suggested that elevated serum fructosamine may indicate an increased risk of CVD in this adult population, mainly in males (Peng et al., 2017).

CONCLUSION

Fructosamine has a significant positive correlation with BMI, FBS, PPBS, and HbA1c in T2DM patients. HbA1c has been observed as a strong predictor of fructosamine. However, FBS and fructosamine have seen as strong predictors of HbA1c. Results showed that fructosamine may act as a potential biomarker for the diagnosis of diabetes and its complications in the Asian population.

REFERENCES

1. WHO: World Health Organization. World Health Day: WHO Calls for Global Action to Halt Rise in and Improve Care for People with Diabetes. World Health Organization; 2016. Available from: http://www.who.int/mediacentre/news/releases/2016/world‑health‑day/en/. [Last accessed on 2016 Apr 06].

2. IDF: International Diabetes Federation. IDF Diabetes Atlas. 6th ed. Brussels, Belgium: International Diabetes Federation; 2013.

3. Ezzati M, NCD Risk Factor Collaboration (NCD‑RisC) Members. Worldwide trends in diabetes since 1980: A pooled analysis of 751 population‑based studies with 4·4 million participants. Lancet 2016;387:1513–30.

4. Anjana RM, Pradeepa R, Deepa M, Datta M, Sudha V, Unnikrishnan R, et al. Prevalence of diabetes and prediabetes (impaired fasting glucose and/or impaired glucose tolerance) in urban and rural India: Phase I results of the Indian council of medical research ‑ India diabetes (ICMR‑INDIAB) study. Diabetologia 2011;54:3022‑7.

39

5. Joshi SR, Das AK, Vijay VJ, Mohan V. Challenges in diabetes care in India: Sheer numbers, lack of awareness and inadequate control. J Assoc Physicians India 2008;56:443‑50.

6. Mohan V, Sandeep S, Deepa M, Gokulakrishnan K, Datta M, Deepa R. A diabetes risk score helps identify metabolic syndrome and cardiovascular risk in Indians ‑ the Chennai Urban Rural Epidemiology Study (CURES‑38). Diabetes Obes Metab 2007;9:337‑43.

7. Khoo CM, Sairazi S, Taslim S, Gardner D, Wu Y, Lee J, et al. Ethnicity modifies the relationships of insulin resistance, inflammation, and adiponectin with obesity in a multiethnic Asian population. Diabetes Care 2011;34:1120‑6.

8. Mohan V, Shanthirani CS, Deepa M, Deepa R, Unnikrishnan RI, Datta M. Mortality rates due to diabetes in a selected urban South Indian population – The Chennai urban population study [CUPS‑16]. J Assoc Physicians India 2006;54:113‑7.

9. ADA: American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2010;33 Suppl 1:S62‑9.

10. Vikøren TB, Berg JP, Berg TJ. Sources of error when using haemoglobin A1c. TidsskrNorLaegeforen 2014;134:417‑21.

11. Nagasaka Y, Fujii S, Yaga K, et al. Clinical application of measuring serum fructosamine as an index of glycemic control in diabetic patients. Bull Yamaguchi Med Sch 1988;35:59–62.

12. Baker J, Reid I, Holdaway I. Serum fructosamine in patients with diabetes mellitus. N Z Med J 1985;98:532–5.

13. Hindle EJ, Rostron GM, Clark SA, et al. Serum fructosamine and glycated haemoglobin measurements in diabetic control. Arch Dis Child 1986;61:113–17.

14. Dafallah AA, Eskandarani H, Rehaimi A, et al. Fructosamine in HbS and G6PD-deficient Saudi Arabs in the Eastern Province of Saudi Arabia. Br J Biomed Sci 1994;51:332–5.

15. Koga M, Hashimoto K, Murai J, et al. Usefulness of glycated albumin as an indicator of glycemic control status in patients with hemolytic anemia. Clin Chim Acta 2011;412:253–7.

16. Shohat N, Tarabichi M, Tischler EH, Jabbour S, Parvizi J. Serum Fructosamine: A Simple and Inexpensive Test for Assessing Preoperative Glycemic Control. Journal of Bone & Joint Surgery 2017;99(22):1900–1907.

17. Gounden V, Jialal II. Fructosamine. Treasure Island (FL): StatPearls Publishing; 2017 Jun [Last Update: December 3, 2017]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470185/

18. Ayyappan S, Philips S, Kumar CK, Vaithiyanandane V, Sasikala C. Serum fructosamine a better indicator than glycated hemoglobin for monitoring gestational diabetes mellitus. J Pharm Bioallied Sci. 2015;7(Suppl 1): S32–S34.

19. WMA: World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA, 2013;310(20):2191-4.

20. ADA: American Diabetes Association. Standards of medical care in diabetes-2015. Diabetes Care, 2015; 38 Suppl 1: S1-S10.

21. ADA: Executive summary: Standards of medical care in diabetes. Diabetes Care, 2010; 33(Suppl 1):S4‑10.

22. WHO: World Health Organization. Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia, Report of a WHO/IDF Consultation. WHO Press, World Health Organization, 2006 Geneva (Switzerland).

23. Mashiba S, Uchida K, Okuda S, Tomita S. Measurement of glycated albumin by the nitroblue tetrazolium colorimetric method. ClinChimActa, 1992;212:3–15.

24. Grant DA, Dunseath GJ, Churm R, Luzio SD. Comparison of a point-care analyser for the determination of HbA1c with HPLC method. Practical Laboratory Medicine. 2017;8:26-29.

25. Chawla A, Chawla R, Jaggi S. Microvascular and macrovascular complications in diabetes mellitus: Distinct or continuum?. Indian J EndocrinolMetab 2016; 20(4): 546-551.

26. Mohan V, Sandeep S, Deepa R, Shah B & Varghese C. Epidemiology of type 2 diabetes: Indian scenario. Indian J Med Res 2007; 125:217-230.

27. Deepa M, Farooq S, Deepa R, Manjula D, Mohan V. Prevalence and significance of generalized and central body obesity in an urban Asian Indian population in Chennai, India (CURES: 47). European Journal of Clinical Nutrition 2009; 63(2):259–267.

28. Ganz ML, Wintfeld N, Li Q, Alas V, Langer J, Hammer M.The association of body mass index with the riskof type 2 diabetes: a case–control study nested inan electronic health records system in the UnitedStates. Diabetology& Metabolic Syndrome, 2014; 6:50.

29. Gray N,Picone G, Sloan F, Yashkin A. The Relationship between BMI and Onset of Diabetes Mellitus and its Complications. South Med J, 2015; 108(1):29–36.

30. Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients. Biomarker Insights, 2016; 11:95–104.

31. Pandya HC, Livingstone S, Colgan ME, Percy-Robb IW, Frier BM. Serum fructosamine as an index of glycaemia: Comparison with glycated haemoglobin in diabetic and non-diabetic individuals. Practical Diabetes International 1987;4(3):126-128.

32. Narbonne H, Renacco E, Pradel V, Portugal H, Vialettes B. Can fructosamine be a surrogate for HbA(1c) in evaluating the achievement of therapeutic goals in diabetes? Diabetes Metab, 2001;27(5 Pt 1):598-603.

33. Chen HS, Chen RL, Chang ZY, Li HD. A comparison of fructosamine and HbA1c for home self-monitoring blood glucose levels in type 2 diabetes. Zhonghua Yi Xue Za Zhi (Taipei), 2002; 65(4):151-5.

34. Selvin E, Rawlings AM, Grams M, Klein R, Richey A, Sharrett, Steffes M, Coresh J.Prognostic utility of fructosamine and glycated albumin for incident diabetes and microvascular complications. Lancet Diabetes Endocrinol, 2014; 2(4): 279–288.

35. Manjrekar PA, Hegde A, Shrilaxmi, d'Souza F, Kaveeshwar V, Jose A, Tasneem S, Shenoy R. Fructosamine in Non-diabetic First Degree Relatives of Type 2 Diabetes Patients: Risk Assessor. Journal of Clinical and Diagnostic Research, 2012; 6(5):770-773.

36. Ben-Salem A, Ajina M, Suissi M, Daher HS, Almawi WY, Mahjoub T. Polymorphisms of transcription factor-7-like 2 (TCF7L2) gene in Tunisian women with polycystic ovary syndrome (PCOS). Gene, 2014; 533:554-7.

37. Polgreen PM, Putz D, Stapleton JT. Inaccurate glycosylated hemoglobin A1C measurements in human immunodeficiency virus-positive patients with diabetes mellitus. Clin Infect Dis, 2003; 37:e53-6.

38. Brown JN, Kemp DW, Brice KR. Class effect of erythropoietin therapy on hemoglobin A(1c) in a patient with diabetes mellitus and chronic kidney disease not undergoing hemodialysis. Pharmacotherapy 2009;29:468-72.

39. Ly J, Marticorena R, Donnelly S. Red blood cell survival in chronic renal failure. Am J Kidney Dis, 2004;44:715-9.

40. Koga M, Murai J, Saito H, Kasayama S. Prediction of near-future glycated hemoglobin levels using glycated albumin levels before and after treatment for diabetes. J Diabetes Investig, 2011;2:304-9.

41. Imagawa A, Hanafusa T, Miyagawa J, Matsuzawa Y. A novel subtype of type 1 diabetes mellitus characterized by a rapid onset and an absence of diabetes-related antibodies. Osaka IDDM Study Group. N Engl J Med, 2000;342:301-7.

42. Malmström H. Epidemiological studies of fructosamine in relation to diabetes, cardiovascular disease and mortality. Thesis for Doctoral Degree (Ph.D.) from Institute of Environmental Medicine Karolinska Institutet, Stockholm, Sweden 2017. ISBN 978-91-7676-634-7.

43. Peng YF, Wei YS. The relationships between serum fructosamine concentrations and lipid profiles in community-dwelling adults. Scientific Reports 7: 6886.