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EVALUATION OF FASTING GLUCOSE, FRUCTOSAMINE, HBA1C, AND VITAMIN D IN IMPAIRED GLUCOSE HOMEOSTASIS AND TYPE 2 DIABETES MELLITUS

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ABSTRACT

Introduction: Impaired glucose homeostasis and type 2 diabetes mellitus (T2DM) represent a growing public health burden. While fasting plasma glucose (FPG) and HbA1c are routinely used for diagnosis and monitoring, alternative markers such as fructosamine provide information on short-term glycaemic control. Vitamin D deficiency has also been implicated in glucose dysregulation and insulin resistance.

Aims: To evaluate fasting plasma glucose, fructosamine, HbA1c, and serum vitamin D levels in controls, pre-diabetic patients, and patients with type 2 diabetes mellitus.

Materials and methods: The present study was a Cross-sectional study. This Study was conducted in August 2022– October 2025 duration. Department of Index Medical college Hospital & Research centre, Indore, M. P. The study population included 100 participants in each group (control, pre-diabetic, and diabetic).

Result: In this study, age and gender distribution were comparable across groups ($p = 0.996$ and 0.911). Vitamin D_3 deficiency was highly prevalent but did not differ significantly among the groups (controls 77.0%, pre-diabetic 63.0%, diabetics 73.0%; $p = 0.394$). Fructosamine, fasting plasma glucose, and HbA1c levels increased significantly from controls (229.60 ± 12.98 µmol/L, 86.63 ± 9.71 mg/dL, 4.60 ± 0.33%) to pre-diabetic and diabetic participants ($p < 0.0001$). Serum vitamin D_3 levels showed a significant negative correlation with HbA1c in pre-diabetic ($r = −0.337$, $p = 0.034$) and diabetic patients ($r = −0.589$, $p = 0.001$), indicating an association between lower vitamin D_3 status and poorer glycaemic control.

Conclusion: Fructosamine is a useful adjunct marker for assessing intermediate-term glycaemic control, especially in pre-diabetes and T2DM. The high prevalence of vitamin D deficiency highlights the need for routine assessment and possible correction to improve glycaemic outcomes.

Keywords: Type 2 diabetes mellitus; Prediabetic; Fasting plasma glucose; Fructosamine; HbA1c; Vitamin D

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by persistent hyperglycaemia due to insulin resistance and impaired insulin secretion. It poses a major global health challenge, with steadily increasing prevalence and significant morbidity from microvascular complications such as retinopathy, nephropathy, and neuropathy, as well as macrovascular complications including cardiovascular disease and stroke [1]. Early identification of impaired glucose homeostasis, particularly at the prediabetic stage, is critical to prevent or delay progression to overt diabetes and its associated complications.

Fasting blood glucose (FBG) and glycated haemoglobin (HbA1c) are widely used for the diagnosis and monitoring of T2DM. While HbA1c reflects average glycemia over 2–3 months, it may not capture short-term fluctuations, particularly in conditions affecting red blood cell turnover. Fructosamine, representing glycation of serum proteins over the preceding 2–3 weeks, serves as an intermediate-term glycaemic marker, offering complementary information to HbA1c [2].

Vitamin D, a corticosteroid hormone, is increasingly recognized for its role in glucose metabolism. It modulates insulin secretion and sensitivity and contributes to pancreatic β-cell function. Several studies have reported an inverse relationship between serum 25-hydroxyvitamin D levels and glycaemic indices, suggesting that vitamin D deficiency may contribute to impaired glucose regulation and poor glycaemic control in T2DM [3,4]. Moreover, vitamin D status has been associated with both HbA1c and fructosamine levels, indicating its potential as an adjunctive biomarker in glycaemic assessment [5]. The present study aims to comparatively evaluate fasting blood glucose, fructosamine, HbA1c, and vitamin D levels in individuals with impaired glucose homeostasis and type 2 diabetes mellitus, to explore their interrelationships and assess their utility as biochemical markers for early detection, monitoring, and management of dysglycemia.

MATERIALS AND METHODS

This is a cross-sectional study conducted at Department of Biochemistry, Index Medical college Hospital & Research centre, Indore, M. P. The duration of study is August 2022- October 2025. The total 300 (Control-100, Pre-diabetic-100 & Diabetic - 100) numbers of subjects will be included, having same sex & age group 18-59 yrs.

Inclusion Criteria:

1. All case was included with age, sex Match.
2. Apparently healthy volunteers as a control
3. Clinically diagnosed impaired glucose homeostasis FBG 100-125 mg/dl & HbA1c between 5.7% to 6.4% was include.
4. Diagnosed pattern of diabetes mellitus type 2 as per WHO & ADA was included.

Exclusion criteria:

- Type I of diabetes patients was excluded from the study.
- Exclusion criteria include patent below 18 years or known or suspected with pregnancy, liver diseases, kidney disease, smoker, alcoholic, acute & chronic respiratory disorder, cardiovascular disorder of medications like corticosteroids as dose vitamin D therapy.

Parameters:

FBS – Glucose oxidase peroxidase, serum fructosamine-measured by Hitachi 7180, $HbA1_C$–HPLC method and vitamin D -Chemiluminescence Immunoassay (CLIA) method. In all subjects FBS, Glycated albumin, HbA1c and vitamin D values were estimated and compare in controls, pre diabetes & type 2 diabetes.

Statistical Analysis: For statistical analysis, data were initially entered into a Microsoft Excel spreadsheet and then analysed using SPSS (version 30.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5.0). Numerical variables were summarized using means and standard

deviations, while Data were entered into Excel and analysed using SPSS and GraphPad Prism. Numerical variables were summarized using means and standard deviations, while categorical variables were described with counts and percentages. Two-sample t-tests were used to compare independent groups, while paired t-tests accounted for correlations in paired data. Chi-square tests (including Fisher's exact test for small sample sizes) were used for categorical data comparisons. P-values ≤ 0.05 were considered statistically significant.

RESULT

Table 1: Association of Serum Vitamin D3 Status with Groups (Control, Pre-Diabetic, Diabetic)

Serum Vitamin D_3 Status	Control (n = 100)	Diabetic (n = 100)	Pre-Diabetic (n = 100)	Total (n = 300)	Chi-Square	P-value
Deficiency (<40 ng/mL)	77 (77.0%)	73 (73.0%)	63 (63.0%)	213 (71.0%)	3.73	0.155
Sufficiency (40–60 ng/mL)	23 (23.0%)	27 (27.0%)	37 (37.0%)	87 (29.0%)		
Total	**100 (100%)**	**100 (100%)**	**100 (100%)**	**300 (100%)**		

Table 2: Comparison of Biochemical Parameters across Groups (Control, Pre-Diabetic, Diabetic)

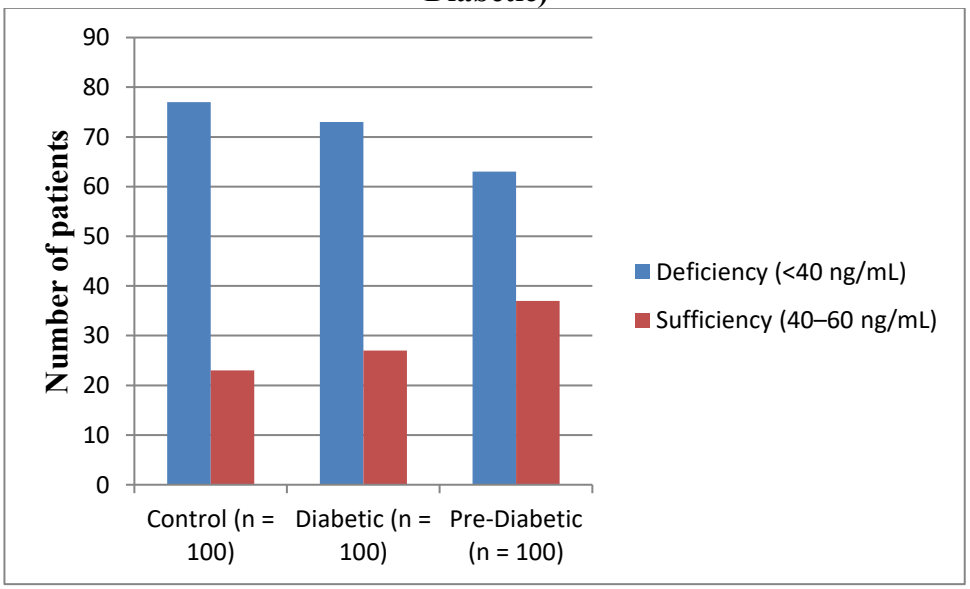
Parameter	Control (n = 100)	Pre-Diabetic (n = 100)	Diabetic (n = 100)	P-value
Fructosamine (µmol/L)	229.60 ± 12.98	287.67 ± 18.70	286.87 ± 14.90	<0.0001
Serum Vitamin D_3 (ng/mL)	26.80 ± 5.03	34.48 ± 9.97	32.57 ± 9.91	0.002
Fasting Plasma Glucose (mg/dL)	86.63 ± 9.71	120.25 ± 3.41	141.23 ± 12.18	<0.0001
HbA1c (%)	4.60 ± 0.33	5.56 ± 0.51	6.78 ± 0.35	<0.0001

Table 3: Correlation of Biochemical Parameters across Control, Pre-Diabetic, and Diabetic.

Group	Parameter Comparison	Pearson r	P-value	Remarks
Control (n = 100)	Fructosamine vs Vitamin D_3	−0.203	0.282	Negative correlation, Not significant
	Fructosamine vs Fasting Plasma Glucose	0.31	0.096	Positive correlation, Not significant
	Fructosamine vs HbA1c	0.642	<0.0001	Positive correlation, **Significant**
	Vitamin D_3 vs Fasting Plasma Glucose	−0.276	0.14	Negative correlation, Not significant
	Vitamin D_3 vs HbA1c	0.122	0.521	Positive correlation, Not significant
	Fasting Plasma Glucose vs HbA1c	0.325	0.08	Positive correlation, Not significant
Pre-Diabetic (n = 100)	Fructosamine vs Vitamin D_3	−0.404	0.01	Negative correlation, **Significant**
	Fructosamine vs Fasting Plasma Glucose	0.623	<0.0001	Positive correlation, **Significant**
	Fructosamine vs HbA1c	0.779	<0.0001	Positive correlation, **Significant**
	Vitamin D_3 vs Fasting Plasma Glucose	−0.276	0.085	Negative correlation, Not significant

	Vitamin D_3 vs HbA1c	−0.337	0.034	Negative correlation, **Significant**
	Fasting Plasma Glucose vs HbA1c	0.794	<0.0001	Positive correlation, **Significant**
Diabetic (n = 100)	Fructosamine vs Vitamin D_3	−0.589	0.001	Negative correlation, **Significant**
	Fructosamine vs Fasting Plasma Glucose	0.591	0.001	Positive correlation, **Significant**
	Fructosamine vs HbA1c	0.818	<0.0001	Positive correlation, **Significant**
	Vitamin D_3 vs Fasting Plasma Glucose	−0.334	0.077	Negative correlation, Not significant
	Vitamin D_3 vs HbA1c	−0.589	0.001	Negative correlation, **Significant**
	Fasting Plasma Glucose vs HbA1c	0.756	<0.0001	Positive correlation, **Significant**

Figure 1: Association of Serum Vitamin D3 Status with Groups (Control, Pre-Diabetic, Diabetic)



In this study, among control participants, 77 (77.0%) had serum vitamin D_3 deficiency and 23 (23.0%) had sufficiency. Among diabetic participants, 73 (73.0%) exhibited vitamin D_3 deficiency, while 27 (27.0%) had sufficient levels. In the pre-diabetic group, 63 (63.0%) had vitamin D_3 deficiency and 37 (37.0%) had sufficiency. The association between serum vitamin D_3 status and glycaemic group was not statistically significant ($p = 0.155$) **(Table 1).**

Comparison of biochemical parameters across the three study groups revealed statistically significant differences. Mean fructosamine levels were lowest in the control group (229.60 ± 12.98 µmol/L) and were significantly higher in both pre-diabetic (287.67 ± 18.70 µmol/L) and diabetic participants (286.87 ± 14.90 µmol/L) ($p < 0.0001$). Mean serum vitamin D_3 levels also differed significantly among the groups, with controls showing the lowest levels (26.80 ± 5.03 ng/mL), followed by diabetic (32.57 ± 9.91 ng/mL) and pre-diabetic participants (34.48 ± 9.97 ng/mL) ($p = 0.002$). Fasting plasma glucose levels demonstrated a progressive increase from controls (86.63 ± 9.71 mg/dL) to pre-diabetic (120.25 ± 3.41 mg/dL) and diabetic participants (141.23 ± 12.18 mg/dL), with the differences being statistically significant ($p < 0.0001$). Similarly, mean HbA1c levels increased significantly across the groups, from 4.60 ± 0.33% in controls to 5.56 ± 0.51% in pre-diabetic participants and 6.78 ± 0.35% in diabetics ($p < 0.0001$) **(Table 2).**

In the control group, fructosamine demonstrated a strong positive correlation with HbA1c ($r = 0.642$, $p < 0.0001$), indicating concordance between short-term and long-term glycaemic markers even among normoglycemic individuals. Correlations between fructosamine and vitamin D_3 ($r = -0.203$, $p = 0.282$) as well as fructosamine and fasting plasma glucose ($r = 0.310$, $p = 0.096$) were weak and not statistically significant. Vitamin D_3 showed weak, non-significant correlations with both fasting plasma glucose ($r = -0.276$, $p = 0.140$) and HbA1c ($r = 0.122$, $p = 0.521$). The correlation between fasting plasma glucose and HbA1c was also weak and not significant ($r = 0.325$, $p = 0.080$).

In the pre-diabetic group, fructosamine showed significant positive correlations with fasting plasma glucose ($r = 0.623$, $p < 0.0001$) and HbA1c ($r = 0.779$, $p < 0.0001$), reflecting early dysglycemia changes. A significant negative correlation was observed between fructosamine and vitamin D_3 levels ($r = -0.404$, $p = 0.010$). Vitamin D_3 also demonstrated a moderate negative correlation with HbA1c ($r = -0.337$, $p = 0.034$), while its association with fasting plasma glucose was weak and not statistically significant ($r = -0.276$, $p = 0.085$). Fasting plasma glucose showed a strong positive correlation with HbA1c ($r = 0.794$, $p < 0.0001$).

In the diabetic group, fructosamine exhibited strong positive correlations with HbA1c ($r = 0.818$, $p < 0.0001$) and fasting plasma glucose ($r = 0.591$, $p = 0.001$), confirming its role as a reliable intermediate-term glycaemic marker. Vitamin D_3 showed a strong negative correlation with both fructosamine ($r = -0.589$, $p = 0.001$) and HbA1c ($r = -0.589$, $p = 0.001$), suggesting an association between lower vitamin D_3 levels and poorer glycaemic control. The correlation between vitamin D_3 and fasting plasma glucose was weak and not statistically significant ($r = -0.334$, $p = 0.077$). A strong positive correlation persisted between fasting plasma glucose and HbA1c ($r = 0.756$, $p < 0.0001$). **(Table 3)**

DISCUSSION

In this study, the age and gender distribution among control, pre-diabetic, and diabetic patients was comparable, with most participants belonging to the 30–50-year age group and a slight male predominance across all groups. The association of age and gender with glycaemic status was not statistically significant, indicating that the study groups were well matched demographically and minimizing potential confounding effects. Similar observations have been reported by Rhee et al. [6] and Gerber et al. [7], who found no significant influence of age or gender on intermediate- and long-term glycaemic markers, including fructosamine and HbA1c.

Vitamin D deficiency was highly prevalent across all groups in the present study, affecting 77.0% of controls, 63.0% of pre-diabetic patients, and 73.0% of diabetic patients; however, this difference was not statistically significant. This finding underscores the widespread burden of hypovitaminosis D irrespective of glycaemic status. Comparable results have been reported by Di Pino et al. [13], who highlighted a high prevalence of vitamin D deficiency among individuals at risk of metabolic disorders, suggesting that suboptimal vitamin D status may coexist with impaired glucose metabolism rather than being solely a consequence of diabetes.

Fructosamine levels differed significantly among the study groups, with lower levels observed in controls and markedly higher levels in both pre-diabetic and diabetic patients, reflecting progressive deterioration of short-term glycaemic control. This supports the role of fructosamine as a sensitive intermediate-term glycaemic marker, particularly in early dysglycemia. Similar advantages of fructosamine and glycated albumin over HbA1c have been emphasized by Danese et al. [8] and Sumner et al. [15], especially in clinical situations where HbA1c may have limitations.

Mean serum vitamin D levels also showed a statistically significant difference among the groups, with relatively higher levels observed in pre-diabetic and diabetic patients compared to controls. This paradoxical finding may be attributable to increased medical surveillance, dietary counselling, or vitamin D supplementation among diagnosed patients. Nevertheless, the significant negative correlation between vitamin D levels and HbA1c in pre-diabetic and diabetic patients suggests that lower vitamin D status is associated with poorer glycaemic control. Similar associations between

vitamin D deficiency, insulin resistance, and impaired glucose regulation have been described by Sherwani et al. [14] and Di Pino et al. [13].

Fasting plasma glucose and HbA1c demonstrated a clear stepwise increase from controls to pre-diabetic and diabetic patients, with highly significant intergroup differences. This trend validates the diagnostic classification of the study population and aligns with established criteria for impaired glucose homeostasis. Comparable findings have been reported by Rosettenstein et al. [12] and Sherwani et al. [14].

Correlation analysis revealed a strong positive association between fructosamine and HbA1c across all groups, particularly among pre-diabetic and diabetic patients, confirming fructosamine as a reliable intermediate-term marker of glycaemic control. Additionally, the significant negative correlation between vitamin D and HbA1c in dysglycemia patients suggests a potential modulatory role of vitamin D in glucose metabolism. Similar relationships between micronutrient status and glycaemic variability have been reported by Suh and Kim [9] and Sumner et al. [15].

Overall, the present study highlights the clinical utility of fructosamine as an adjunctive glycaemic marker and emphasizes the widespread prevalence of vitamin D deficiency among both normoglycemic and dysglycemia individuals. Early identification of impaired glucose metabolism using complementary biomarkers, along with correction of vitamin D deficiency, may contribute to improved metabolic outcomes, particularly in patients with pre-diabetes and early diabetes.

CONCLUSION

In conclusion, this study demonstrates that fructosamine, fasting plasma glucose, and HbA1c levels progressively increase from controls to pre-diabetic and diabetic individuals, reflecting worsening glucose homeostasis. Although serum vitamin D_3 levels did not differ significantly among the groups, a negative association with glycaemic parameters was observed in pre-diabetic and diabetic patients, suggesting that lower vitamin D_3 status may contribute to impaired glucose regulation. These findings support the combined assessment of fructosamine and HbA1c, along with evaluation of vitamin D_3 status, for the early detection and improved management of dysglycemia.

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