Metabolism Open 26 (2025) 100372

Contents lists available at ScienceDirect

Metabolism Open

journal homepage: www.sciencedirect.com/journal/metabolism-open

Assessment of DNA glycation in the prediabetic State: Early indicator of glycemic stress

Tanish Baweja [a], Abhishek Dikshit [a], Shazia Bano [c], Sanjiv Kumar Bansal [b], Sana Alam [c,*]

[a] Hamdard Institute of Medical Sciences and Research, New Delhi, 110062, India
[b] Department of Biochemistry, SGT University, Gurugram, Haryana, 122505, India
[c] Department of Biochemistry, Hamdard Institute of Medical Sciences and Research, New Delhi, 110062, India

ARTICLE INFO

Keywords:
Diabetes mellitus
Prediabetes
Glycation
DNA
Fructose

ABSTRACT

Introduction: Glycation of nucleic acids secondary to hyperglycemia can lead to structural alterations and the formation of neoantigens. These molecular changes may elicit an early immune response. This study investigates the interaction between serum autoantibodies from prediabetic individuals and fructose-glycated human placental DNA, aiming to assess DNA glycation as a potential early indicator of glycemic stress.

Design: and Methods: To investigate structural modifications in DNA produced by glycation, purified placental DNA was incubated with fructose (25 mM) at 37 °C for 5, 10, and 15 days, followed by spectrophotometric analysis. Peripheral blood samples were collected from 50 normoglycemic (mean age: 39.70 ± 6.63 years; 26 males, 24 females) and 50 prediabetic (mean age: 40.84 ± 5.44 years; 23 males, 27 females) adult patients, matched for age, sex, body mass index, and socio-economic conditions. The presence of circulating antibodies against glycated DNA was evaluated using direct and competitive ELISA.

Results: Fructose-mediated glycation of DNA resulted in hyperchromicity and a new absorbance peak at 360 nm, indicating structural modification. Direct ELISA revealed significantly higher levels of anti-DNA autoantibodies in prediabetic sera (0.367 ± 0.225) compared to controls (0.239 ± 0.118; $p = 0.003$). Competitive ELISA showed that these antibodies had greater specificity for glycated DNA, with maximum inhibition by fructose-modified DNA at 37.86 ± 2.57 %, versus 23.01 ± 2.33 % for native DNA ($p < 0.01$).

Conclusion: The study concludes that DNA glycation occurs in prediabetic patients with intermediate hyperglycemia as a result of high blood glucose. This suggests that glycated DNA may serve as an early molecular indicator of glycemic stress, with potential applications in risk assessment and early detection strategies for individuals at risk of progressing to type 2 diabetes.

1. Introduction

Diabetes mellitus (DM), a metabolic disorder characterized by high blood sugar levels, has reached epidemic proportions globally, emerging as one of the most significant public health challenges. The alarming aspect of this crisis is the large proportion of individuals with undiagnosed diabetes and impaired glucose tolerance, who are at risk of developing severe complications without timely intervention. Addressing this burden is critical for effective disease management and prevention strategies.

The global prevalence of impaired glucose tolerance reached 541 million in 2021 and is expected to rise to 730 million by 2045. In India, Prevalence of impaired glucose tolerance (IGT) indicates a worrisome situation with 40 million people affected in 2021 predicted to reach 65 million by 2045 [1].

Prediabetes, apart from progressing into Diabetes Mellitus, may cause several complications on its own such as nephropathy (including and not restricted to microalbuminuria, chronic renal disease etc), neuropathies (heart rate variabilities) retinopathy and macrovascular disease [2].

At the heart of these complications lies chronic hyperglycemia, which triggers the non-enzymatic glycation of biomolecules, including DNA, resulting in the formation of advanced glycation end-products (AGEs). Glycation refers to the reaction between reducing sugars and proteins, lipids, or nucleic acids without enzymatic control, and this process accelerates under sustained hyperglycemia [3]. AGEs activate

* Corresponding author. Department of Biochemistry, Hamdard Institute of Medical Sciences and Research, New Delhi, 110062, India.
E-mail address: sana2k2@gmail.com (S. Alam).

https://doi.org/10.1016/j.metop.2025.100372
Received 24 March 2025; Received in revised form 19 May 2025; Accepted 29 May 2025
Available online 1 June 2025

proinflammatory pathways, resulting in oxidative stress and playing a pivotal role in the pathogenesis of diabetic complications. Notably, high levels of exogenous AGEs have been linked to the development of microvascular complications such as nephropathy and retinopathy [4]. Oxidative stress produced in this setting worsens hyperglycemia, creating a vicious cycle of cellular and molecular dysfunction.

Among the various AGEs, nucleotide-derived AGEs remain relatively understudied but are of particular interest due to their potential impact on genome stability and cell viability. The chemical changes in DNA resulting from glycation include strand breaks and the formation of adducts, which can contribute to long-term molecular damage. Given the unique characteristics of DNA, such as its stability, uniform distribution in cells, and relatively longer lifespan compared to proteins or RNAs, it becomes evident that measuring DNA-AGEs may offer a more persistent and reliable method for monitoring glycemic status in hyperglycemic individuals [10].

Formation of nucleotide AGE is linked to increased frequency of mutation in DNA and has a possible role in cytotoxicity [11]. Studies have shown the presence of anti-DNA antibodies in the sera of Type 1 and Type 2 DM patients thereby confirming the glycation of DNA. Recently, positive correlation between anti-glycated-DNA autoantibodies and HbA1c has also been reported [6,7]. Fructose, which is one of the main components of our diet, is a faster glycating agent, and can glycate both proteins and nucleotides. It can glycate DNA at a much faster rate [8]. The elevated protein-bound fluorescence observed in diabetic tissues may result from the reaction of fructose with proteins, indicating a high degree of protein fructation [12].

While most existing research in prediabetes has focused on oxidative DNA damage [13], which indicates that molecular changes occur prior to the clinical onset of diabetes, the role of DNA glycation in this early phase has not been investigated. Chronic hyperglycemia not only generates oxidative stress but also directly promotes DNA glycation, which contributes to AGE formation. This study aims to explore this critical early window by evaluating DNA glycation in individuals with prediabetes, specifically through the detection of anti-glycated DNA autoantibodies in their sera. The presence of these autoantibodies could serve as an early indicator of glycemic stress and underlying molecular injury, potentially providing a novel biomarker for risk stratification.

2. Material and methods

2.1. Study design

Case control study.

2.2. Study population

The study population included both males and females fulfilling the criteria for prediabetes (aged 25–65 years) undergoing Oral glucose tolerance test (OGTT) at a Tertiary care centre in New Delhi.

2.3. Sample size

The required sample size for this study was determined based on the desired 95 % confidence interval, an estimated prevalence of 14 % [24], and a margin of error of 7 %. Using the standard formula for sample size calculation for population proportions:

$$\frac{z^2 P\,(1-P)}{d^2}$$

where Z = 1.96 for 95 % confidence interval, P = 0.14 for the estimated prevalence and d = 0.07 for the margin of error, the estimated sample size is approximately 100 participants with cases and controls selected in a 1:1 ratio.

Table 1
The baseline characteristics of cases and controls.

Parameters	Cases	Controls	P- values
Age	40.84 ± 5.44	39.70 ± 6.63	0.35
BMI	26.58 ± 3.33	25.68 ± 3.55	0.194
Fasting Glucose	113.22 ± 7.39	84.86 ± 8.87	<0.001
HbA1c	6.05 ± 0.19	5.21 ± 0.25	<0.001
Male	23 (46 %)	26 (52 %)	0.68
Females	27 (54 %)	24 (48 %)	

2.4. Inclusion criteria

Prediabetic patients having fasting plasma glucose (FPG) of 100 mg/dl (5.6 mmol/l) to 125 mg/dl (6.9 mmol/l) or 2-h plasma glucose of 140 mg/dl (7.8 mmol/l) to 199 mg/dl (11.0 mmol/l) after ingestion of 75 g of oral glucose load (OGTT) [9]. Sera from healthy individuals (n = 50) served as control. They were matched for age, sex, body mass index and socio-economic conditions.

2.5. Exclusion criteria

The subjects having fasting blood glucose≥126 mg/dL and 2-h plasma glucose after ingestion of 75 g of oral glucose load >200 mg/dL (i.e. Diabetes Mellitus) were excluded. The pregnant females or subjects having anaemia, kidney, liver and thyroid disease or coexisting autoimmune disorder were excluded.

2.6. Collection of blood samples

Informed consents from patients as well as healthy subjects were obtained before taking blood samples. The clinical history, examination and other details of the patients were taken. Ethical clearance certificate was obtained prior to conduction of the study. 5 ml blood was withdrawn and transferred to plain vials. The sera were separated. All the serum samples were heated at 56 °C for 30 min to inactivate complement proteins [25] and stored at −20 °C after proper labelling.

The baseline characteristics of both cases and controls have been illustrated in Table 1.

2.7. Methods

2.7.1. Glucose concentrations during the OGTT will be used as the diagnostic standard for identifying prediabetes [9]

a) Impaired fasting glucose (IFG): Fasting plasma glucose (FPG) of 100 mg/dl (5.6 mmol/l) to 125 mg/dl (6.9 mmol/l)
b) Impaired glucose tolerance (IGT): 2-h plasma glucose of 140 mg/dl (7.8 mmol/l) to 199 mg/dl (11.0 mmol/l) after ingestion of 75 g of oral glucose load

Plasma glucose was analysed in Beckman Coulter AU480 analyser.

2.7.2. Assessment of glycated haemoglobin

Glycated haemoglobin was estimated by Bio-Rad D-10 HPLC analyser. For detecting prediabetes by HbA1c, the recommended threshold of 5.7–6.4 % was used [9].

2.7.3. Modification of DNA by fructose

Human placental DNA was screened and made pure of proteins and single stranded regions [15]. Pilot experiments were done to know the optimum DNA and fructose concentrations and the time period to produce maximal changes in DNA structure from glycation. The structural alteration was further examined by UV–Visible spectrophotometry. Human placental DNA (10 μg/ml) and 25 mM fructose at 37 °C were incubated together for different time periods (5, 10 and 15 days) in phosphate buffer saline (pH 7.4) as described earlier. After incubation,

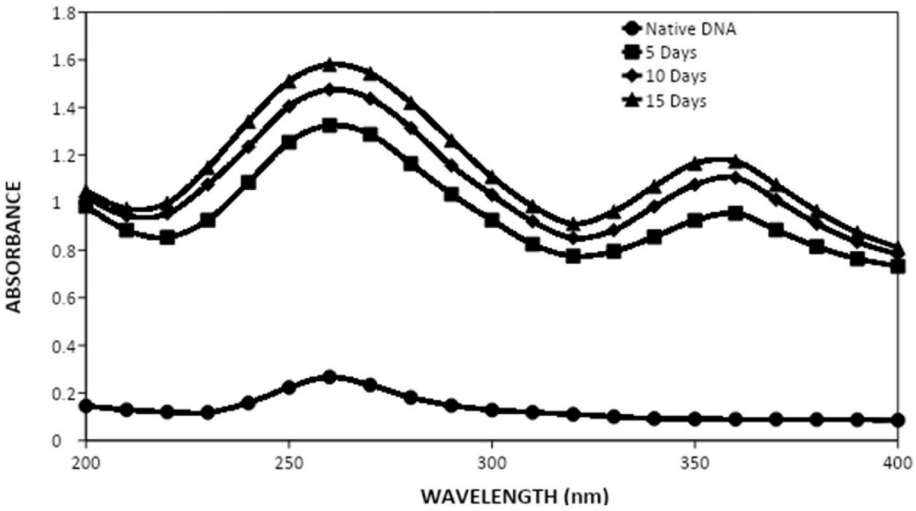

Fig. 1. Profile of native DNA incubated with 25 mM fructose for 5, 10, 15 days.

the samples were dialyzed to remove any unbound fructose [6].

2.7.3.1. Absorption spectroscopy. The absorbance profile of both native (control) and glycated DNA was seen on Ultraviolet–visible (UV/Vis) spectrophotometer in the wavelength range of 200–400 nm. Hyperchromicity was calculated as follows:

$$Hyperchromicity = \frac{Abs.\ of\ modified\ DNA - Abs.\ of\ control\ DNA}{Abs.\ of\ modified\ DNA}\ x\ 100$$

2.7.4. ELISA (enzyme linked immunosorbent assay)

A) Direct binding ELISA:

An enzyme-linked immunosorbent assay (ELISA) was performed using flat-bottomed polystyrene plates, as previously described [16]. Wells were coated with 100 μL of either native DNA (negative control) or fructose-glycated DNA (test), both at a concentration of 2.5 μg/mL in Tris-buffered saline (TBS). Plates were incubated for 2 h at room temperature and then overnight at 4 °C. Two blank wells were included on each plate. After incubation, the wells were emptied and washed three times with TBS containing Tween-20 (TBS-T) to remove unbound antigen. Remaining binding sites were blocked with 150 μL of 2 % non-fat dry milk in TBS (pH 7.4) for 4–6 h at room temperature, followed by a single wash. Sera from prediabetic individuals (n = 100) and apparently healthy controls (n = 100) were tested in the assay. Each serum sample was applied to wells coated with both native and glycated DNA to assess the binding of circulating antibodies to each antigen. Diluted sera (1:100 in TBS-T, 100 μL per well) were added and incubated for 2 h at 37 °C and overnight at 4 °C. Wells were then extensively washed with TBS-T, and anti-human IgG conjugated to alkaline phosphatase was added and incubated for 2 h at 37 °C. Following four washes with TBS-T and three with distilled water, para-nitrophenyl phosphate substrate was added. The color development was measured at 410 nm using a microplate reader. Results were expressed as the mean difference in absorbance between test and control wells (A_{test} – $A_{control}$). Sera that showed a high degree of antibody binding to the antigens were selected for further analysis to assess antibody specificity using competitive ELISA.

Table 2
Absorbance and hyperchromicity of human placental DNA incubated with 25 mM fructose.

INCUBATION TIME	ABSORBANCE AT 260 nm	% HYPERCHROMICITY
0	0.267	
5 Days	1.325	79.8 %
10 Days	1.475	81.9 %
15 Days	1.581	83.1 %

B) Competitive ELISA:

Competitive ELISA was performed to evaluate the antigenic specificity of serum antibodies [17]. ELISA plates were coated with 100 μl of native human DNA (2.5 μg/ml) for 2 h at room temperature, followed by overnight incubation at 4 °C. For the competition assay, varying concentrations of inhibitors (native and glycated human DNA; 0–20 μg/ml) were pre-incubated with a constant amount of serum from selected subjects for 2 h at room temperature and then overnight at 4 °C to allow immune complex formation. These immune complexes were subsequently added to the antigen-coated wells. All remaining steps, including washing, secondary antibody incubation, and substrate development, were identical to those described for the direct binding ELISA. Antibodies not bound to the soluble inhibitor could bind to the plate-bound antigen, while those already complexed with inhibitor antigen could not. The degree of inhibition (reduction in signal) reflected the specificity of serum antibodies for native versus glycated DNA. Greater inhibition by glycated DNA indicated higher antibody specificity for glycated DNA.

$$Percent\ Inhibition = \frac{Abs.of\ uninhibited - Abs.\ of\ inhibited}{Abs.of\ uninhibited}\ x\ 100$$

2.8. Statistical analysis

It was performed using SPSS 26. The data was presented as mean ± standard deviation (SD). Statistical significance of data was determined by Student's *t*-test and a *p* value of <0.05 was considered as significant.

3. Observation and results

Demographic and Clinical Features of the Study Population.

The clinical and demographic characteristics of study population are elucidated in Table 1.

3.1. Absorption spectroscopy of native and fructose-modified-DNA

Human placental DNA (10 μg/ml) and 25 mM fructose were incubated together at 37 °C for 5, 10 and 15 days in phosphate buffer saline (pH 7.4). When spectrophotometric analysis was done post incubation,

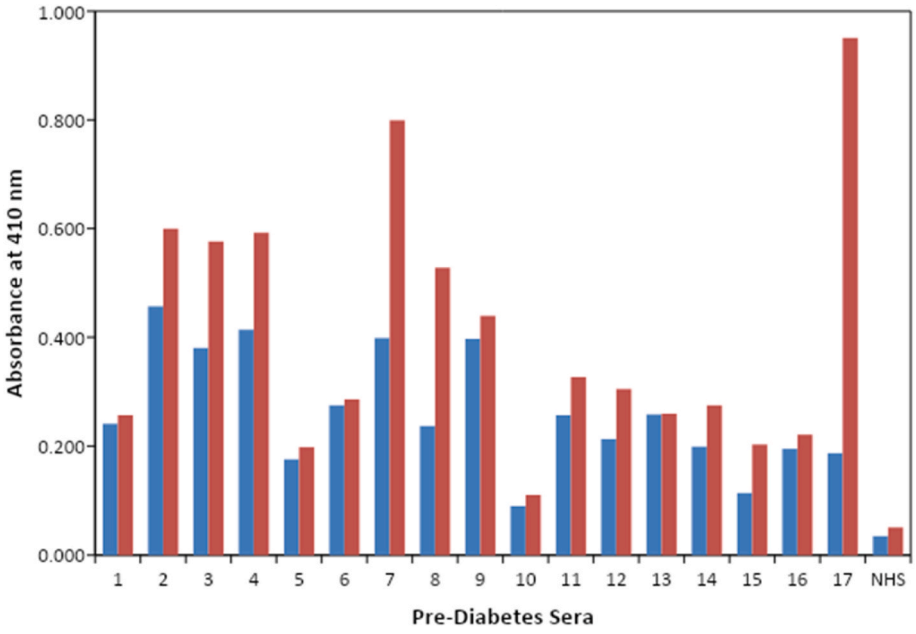

Fig. 2. Direct binding ELISA of prediabetic sera (1-17) with native DNA (■) and glycated-DNA (■). Pooled normal human sera (NHS) served as control. Microtitre plate was coated with respective antigens.

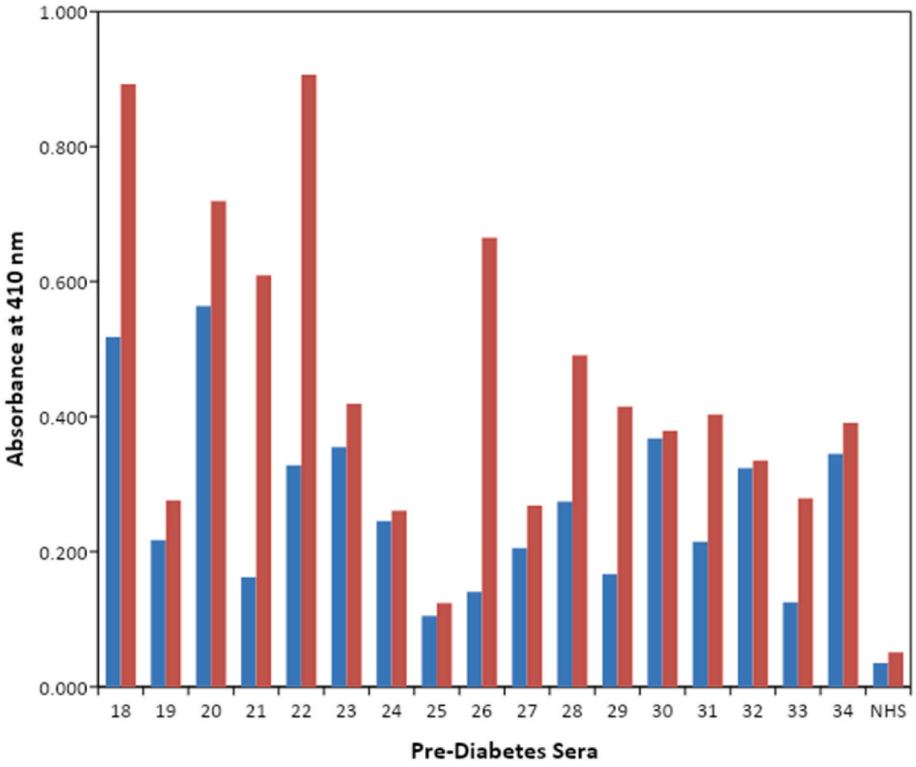

Fig. 3. Direct binding ELISA of prediabetic sera (18–34) with native DNA (■) and glycated-DNA (■). Pooled normal human sera (NHS) served as control. Microtitre plate was coated with respective antigens.

the characteristic peak for native DNA at 260 nm was observed but glycation induced structural changes were also observed – hyperchromicity at 260 nm progressively increased with incubation period (Fig. 1). The percent hyperchromicity in glycated DNA was 79.80, 81.90 and 83.10 percent respectively (Table 2). Furthermore, a new peak appeared at 360 nm in the sample with glycated DNA. However, almost complete glycation was achieved by day 15 as further incubation did not produce much change in absorbance.

$$Hyperchromicity = \frac{Abs.\ of\ modified\ DNA - Abs.\ of\ control\ DNA}{Abs.\ of\ modified\ DNA}\ x\ 100$$

3.2. Results from enzyme immunoassays involving patient sera

a. Direct binding ELISA

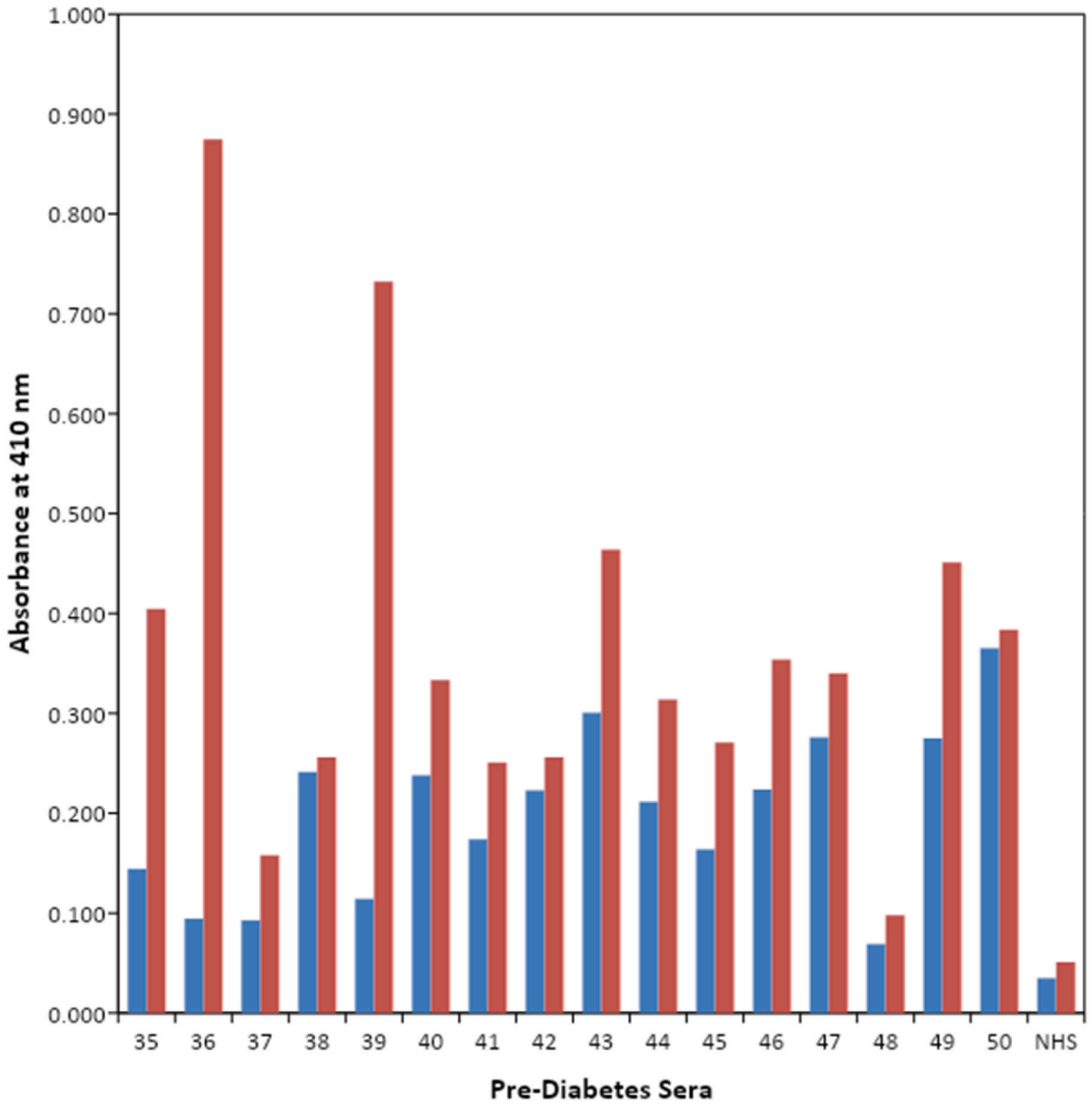

Fig. 4. Direct binding ELISA of prediabetic sera (35–50) with native DNA (■) and glycated-DNA (■). Pooled normal human sera (NHS) served as control. The microtitre plate was coated with respective antigens.

Figs. 2–4 illustrate the results of the direct binding ELISA performed on individual serum samples. Sera from normal controls showed negligible binding to the coated antigens. In contrast, prediabetic sera demonstrated a notably higher reactivity, indicating the presence of anti-glycated DNA autoantibodies. Quantitative analysis revealed that the mean level of anti-DNA autoantibodies was significantly elevated in prediabetic individuals (0.367 ± 0.225) compared to healthy controls (0.239 ± 0.118;$p = 0.003$). Furthermore, nine prediabetic serum samples (labelled with '*') exhibited significantly higher binding to fructose-modified DNA than to native DNA ($p < 0.05$), and these were selected for subsequent analyses. Detailed data are presented in Table 3.

b. Competitive ELISA

Fructose-modified DNA inhibited the binding of autoantibodies in prediabetic sera more effectively than native DNA, with inhibition ranging from 34.5 % to 41.9 %, compared to 19.8 %–26.2 % for native DNA. The mean percent inhibition by native DNA was 23.01 ± 2.33 %, whereas fructose-modified DNA showed a significantly higher mean inhibition of 37.86 ± 2.57 % (Table 4). A Student's *t*-test confirmed this difference to be statistically significant ($p < 0.01$). These results indicate that fructose-modified DNA is a stronger inhibitor and suggest that the serum autoantibodies in prediabetic individuals exhibited greater specificity for glycated DNA. Fig. 5 illustrates the results of competitive ELISA for sera 17.

4. Discussion

In diabetes, chronic hyperglycemia leads to a glycation reaction between reducing sugars and proteins and nucleic acids non-enzymatically. The products so formed undergo a series of further rearrangements to form stable advanced glycation end products (AGEs) which are irreversible [3,4]. AGEs may result in chronic complication of diabetes by altering the structure and functions of proteins and extracellular matrix heterogeneously. Studies have shown that similar to proteins, DNA is also affected by glycation [5]. Furthermore, studies have suggested that fructose, which is a ketohexose sugar, is a much more potent initiator of the glycation reaction as compared to glucose

Table 3
Direct binding ELISA of prediabetic sera with native DNA and fructose-modified-DNA **(Absorbance at 410 nm).**

Prediabetes Sera	Direct Binding with	
	Native DNA	Fructose-modified-DNA
1	0.241	0.257
2	0.457	0.600
3	0.380	0.577
4	0.414	0.592
5	0.176	0.198
6	0.275	0.286
7*	0.398	0.799
8*	0.237	0.528
9	0.397	0.440
10	0.090	0.110
11	0.257	0.327
12	0.213	0.305
13	0.258	0.260
14	0.199	0.275
15	0.114	0.203
16	0.195	0.221
17*	0.187	0.951
18*	0.518	0.892
19	0.217	0.276
20	0.564	0.719
21*	0.162	0.609
22*	0.328	0.906
23	0.355	0.419
24	0.245	0.261
25	0.105	0.124
26*	0.141	0.665
27	0.205	0.268
28	0.274	0.491
29	0.167	0.415
30	0.368	0.379
31	0.215	0.403
32	0.324	0.335
33	0.125	0.279
34	0.345	0.391
35	0.144	0.405
36*	0.095	0.875
37	0.093	0.158
38	0.241	0.256
39*	0.114	0.732
40	0.238	0.333
41	0.174	0.251
42	0.223	0.256
43	0.301	0.464
44	0.211	0.314
45	0.164	0.271
46	0.224	0.354
47	0.276	0.340
48	0.069	0.098
49	0.275	0.451
50	0.365	0.384
Mean ± S.D.	**0.239 ± 0.118**	**1.367 ± 0.225**

Table 4
Summary of inhibition ELISA of selected prediabetes sera.

Prediabetes Sera	Maximum percent inhibition at 20 μg/ml	
	Native DNA	Fructose-modified-DNA
7	20.6	35.1
8	22.5	37.8
17	**26.2**	**41.9**
18	25.4	39.6
21	24.2	38.5
22	21.9	36.7
26	19.8	34.5
36	25.3	40.8
39	21.2	35.8
Mean ± S.D.	**23.01 ± 2.33 (%)**	**37.86 ± 2.57 (%)**

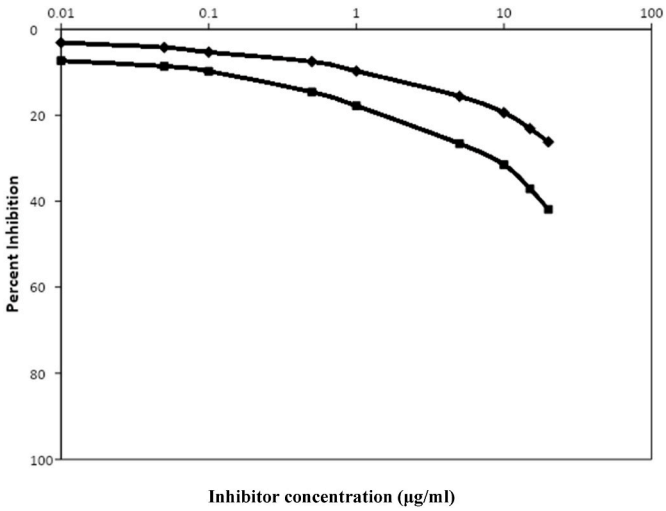

Fig. 5. Inhibition of prediabetes sera (17) binding by native DNA (—♦—) and fructose-modified-DNA (—■—). Microtitre wells were coated with native DNA (2.5 μg/ml).

[14].

Our study findings suggested that fructose-modified DNA exhibited significant damage, as indicated by hyperchromicity in the UV/Vis spectra at 260 nm in spectrophotometric physicochemical technique, which may be attributed to strand breaks, the destruction of nitrogenous bases, and the formation of DNA advanced glycation end products (AGEs). This hyperchromicity is likely due to damage to the sugar-phosphate backbone of the nucleic acid, potentially leading to the exposure of chromophoric bases as the double helix of DNA unfolds. The appearance of a peak at 360 nm could be related to the generation of DNA-bound AGEs, and this peak's intensity increased with longer incubation times, suggesting the accumulation of AGEs. Our results align with earlier studies on DNA glycation [5,18]. Furthermore, it's noted that structural alterations, such as strand breaks, can occur in DNA after exposure to various glycating agents, and these changes are particularly pronounced in conditions like diabetes mellitus (DM) where AGEs accumulate at high concentrations [19,20].

To confirm the occurrence of DNA glycation in prediabetes, we explored the binding characteristics of serum auto-antibodies to native DNA and glycated-DNA. Serum samples from prediabetic patients were analysed through direct and competitive ELISA. Direct ELISA revealed a stronger binding of serum autoantibodies to glycated DNA compared to native DNA, while competitive ELISA confirmed the higher specificity of these antibodies to glycated DNA. This suggests that circulating DNA-AGEs may act as antigenic targets resulting in generation of anti-glycated DNA-antibodies.

Previous studies on patients with Type 1 and Type 2 Diabetes Mellitus also revealed the presence of antibodies against glycated DNA, consistent with our findings [6]. As discussed above, DNA glycation results in formation of AGEs, which contribute to biochemical dysfunction. The persistence of these altered structures over time could trigger an immune response. Also, it has been suggested that these antibodies may form AGE-immune complexes which could play a significant role in development of atherosclerosis and contribute to microvascular disease progression. The role of these antibodies as potential biomarkers for the disease and its progression has been previously suggested [21,22].

Previous studies have also shown that hyperglycemia stimulates the production of reactive oxygen species (ROS) and excess levels of ROS damage the DNA. Thus, oxidative stress is a process that can be an important mediator of the damage to cell structures and may contribute in the etiopathogenesis and progression to diabetes [23]. Our study findings suggest that DNA damage occurs prior to the onset of type 2

diabetes, during the prediabetic stage. This extensive damage induced by glycation may alter the DNA structure to the point of creating immunogenic advanced glycation end products (AGEs). These modified DNA structures cause generation of neo-antigenic epitopes that serve as more potent antigens.

The presence of anti-glycated DNA antibodies in prediabetic individuals signifies an early immune response to glycation-induced molecular changes. Unlike traditional markers such as HbA1c, which reflect sustained hyperglycemia and only indirectly suggest tissue damage, anti-glycated DNA antibodies provide direct evidence of molecular injury and immune activation, highlighting their potential as valuable biomarkers. Incorporating these antibodies into screening protocols could enable earlier and more precise risk assessment in prediabetes, complementing existing tools like HbA1c. Their detection may help identify at-risk individuals before the onset of overt diabetes, enabling targeted interventions, such as lifestyle or pharmacological modifications, to delay or prevent progression to type 2 diabetes. Further research into their mechanistic role and integration into diagnostic panels could significantly enhance the management of prediabetic patients.

However, several key limitations should be noted in this study. Cross-reactivity of antibodies could lead to non-specific binding, potentially affecting the accuracy of antibody detection. Although the sample size was matched for age, gender, socio-economic status, and BMI, a larger, more diverse cohort would enhance generalizability. The time, temperature, and 25 mM fructose concentration used may not fully reflect physiological conditions. Additionally, the duration of prediabetes was not established, which could influence DNA glycation and autoantibody production, adding variability to the results.

5. Conclusion

This study provides novel evidence that DNA glycation and the generation of anti-glycated DNA autoantibodies occur early in the course of glycemic dysregulation, even before the onset of overt diabetes. The presence of these autoantibodies may serve as a promising biomarker for early glycemic stress, offering potential utility in risk stratification and the development of personalized preventive strategies. To fully establish their clinical value, future research should include longitudinal studies in larger and more diverse populations to determine their predictive significance for diabetes progression, as well as intervention trials to assess the impact of lifestyle or pharmacological modifications on these biomarkers.

CRediT authorship contribution statement

Tanish Baweja: Writing – original draft, Methodology, Investigation, Data curation, Conceptualization. **Abhishek Dikshit:** Writing – original draft, Formal analysis, Conceptualization. **Shazia Bano:** Investigation, Formal analysis, Data curation. **Sanjiv Kumar Bansal:** Writing – review & editing, Resources, Methodology. **Sana Alam:** Writing – review & editing, Supervision, Resources, Conceptualization.

Funding

None.

Conflict of interest

The authors declare that there are no conflicts of interest.

References

[1] Magliano DJ, Boyko EJ, IDF Diabetes Atlas 10th edition scientific committee. IDF diabetes atlas. tenth ed. Brussels: International Diabetes Federation; 2021. PMID: 35914061.
[2] Brannick B, Wynn A, Dagogo-Jack S. Prediabetes as a toxic environment for the initiation of microvascular and macrovascular complications. Experimental Biology and Medicine (Maywood, NJ) 2016;241(12):1323–31.
[3] Singh VP, Bali A, Singh N, Jaggi AS. Advanced glycation end products and diabetic complications. KOREAN J PHYSIOL PHARMACOL: official journal of the Korean Physiological Society and the Korean Society of Pharmacology 2014;18(1):1.
[4] Ahmad S, Dixit K, Shahab U, Alam K, Ali A. Genotoxicity and immunogenicity of DNA advanced glycation end products formed by methylglyoxal and lysine in presence of Cu2+. Biochemical and biophysical research communications 2011; 407(3):568–74.
[5] Ashraf JM, Arif B, Dixit K, Alam K. Physicochemical analysis of structural changes in DNA modified with glucose. Int J Biol Macromol 2012;51(4):604–11.
[6] Mustafa I, Ahmad S, Dixit K, Ahmad J, Ali A. Glycated human DNA is a preferred antigen for anti-DNA antibodies in diabetic patients. Diabetes Res Clin Pract 2012; 95(1):98–104.
[7] Ahmad J, Gupta A, Alam K, Farooqui KJ. Detection of autoantibodies against glycosylated DNA in diabetic subjects: its possible correlation with HbA1C. Dis Markers 2011;30(5):235–43.
[8] Takeuchi M, Iwaki M, Takino JI, Shirai H, Kawakami M, Bucala R, Yamagishi SI. Immunological detection of fructose-derived advanced glycation end-products. Lab Invest 2010;90(7):1117–27.
[9] American Diabetes Association Professional Practice Committee; 2. Diagnosis and classification of diabetes: *Standards of Care in diabetes—2024*. Diabetes Care 2024; 47(Supplement_1):S20–42.
[10] Jaramillo R, Shuck SC, Chan YS, Liu X, Bates SE, Lim PP, Tamae D, Lacoste S, O'Connor TR, Termini J. DNA advanced glycation end products (DNA-AGEs) are elevated in urine and tissue in an animal model of type 2 diabetes. Chem Res Toxicol 2017;30(2):689–98.
[11] Tamae D, Lim P, Wuenschell GE, Termini J. Mutagenesis and repair induced by the DNA advanced glycation end product N2-1-(carboxyethyl)-2'-deoxyguanosine in human cells. Biochemistry 2011;50(12):2321–9.
[12] Suarez G, Rajaram RA, Oronsky AL, Gawinowicz MA. Nonenzymatic glycation of bovine serum albumin by fructose (fructation): comparison with the Maillard reaction initiated by glucose. J Biol Chem 1989;264(7):3674–9.
[13] Al-Aubaidy HA, Jelinek HF. Oxidative DNA damage and obesity in type 2 diabetes mellitus. Eur J Endocrinol 2011;164(6):899–904.
[14] McPherson JD, Shilton BH, Walton DJ. Role of fructose in glycation and cross-linking of proteins. Biochemistry 1988;27(6):1901–7.
[15] Ali R, Dersimonian H, Stollar BD. Binding of monoclonal anti-native DNA autoantibodies to DNA of varying size and conformation. Mol Immunol 1985;22 (12):1415–22.
[16] Ali R, Alam K. Evaluation of antibodies against oxygen free radical-modified DNA by ELISA. Methods Mol Biol 2002;186:171–81.
[17] Dixit K, Ali R. Antigen binding characteristics of antibodies induced against nitric oxide modified plasmid DNA. Biochimica et Biophysica Acta (BBA)-General Subjects 2001;1528(1):1–8.
[18] Pethig R, Szent-Györgyi A. Electronic properties of the casein-methylglyoxal complex. Proc Natl Acad Sci 1977;74(1):226–8.
[19] Habib S, Ali A, Ali R. Preferential recognition of peroxynitrite modified human DNA by circulating autoantibodies in cancer patients. Cell Immunol 2009;254(2): 117–23.
[20] Yamasaki H, Pulkrabek P, Grunberger D, Weinstein IB. Differential excision from DNA of the C-8 and N2 guanosine adducts of N-acetyl-2-aminofluorene by single strand-specific endonucleases. Cancer Res 1977;37(10):3756–60.
[21] Rabbani N, Thornalley PJ. Dicarbonyls linked to damage in the powerhouse: glycation of mitochondrial proteins and oxidative stress. Biochem Soc Trans 2008; 36(Pt 5):1045–50.
[22] Turk Z, Ljubic S, Turk N, Benko B. Detection of autoantibodies against advanced glycation endproducts and AGE-immune complexes in serum of patients with diabetes mellitus. Clin Chim Acta 2001;303(1–2):105–15.
[23] Valko M, Leibfritz D, Moncol J, Cronin MT, Mazur M, Telser J. Free radicals and antioxidants in normal physiological functions and human disease. Int J Biochem Cell Biol 2007;39(1):44–84.
[24] Ramachandran A, Snehalatha C, Kapur A, Vijay V, Mohan V, Das AK, Rao PV, Yajnik CS, Prasanna Kumar KM, Nair JD, Diabetes Epidemiology Study Group in India (DESI). High prevalence of diabetes and impaired glucose tolerance in India: national Urban Diabetes Survey. Diabetologia (Berl) 2001;44(9):1094–101. https://doi.org/10.1007/s001250100627. PMID: 11596662.
[25] Koets P. The effect of heat inactivation on precipitation of serum proteins by means of sodium chromate in sera of normal and cancerous subjects. PubMed 1952;12(2): 100–3.