Novel Biomarkers in Type 2 DiabetesPaving the Way for Earlier and More Accurate Detection

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Abstract

Background:
Type 2 diabetes mellitus is a determined metabolic condition highlighted by insulin resistance and β-cell dysfunction. Early detection of individuals at risk is critical to avert disease progression and complications. Traditional diagnostic and its methods, includes fasting blood glucose and HbA1c, may detect T2DM after remarkable metabolic disturbance has occurred.

Objective:
This study aims to highlight and asses narrative biomarkers with potential for early detection of T2DM before the start of clinical symptoms or standardized diagnostic doorstep.

Methods:
A cross-sectional study was held which involves 210 participants classify into norm glycemic, prediabetes, and newly identified T2DM groups. Blood samples were examined for traditional indicators and appearing biomarkers, which includes adiponectin, fetuin-A, fibroblast growth factor 21, and microRNAs.

Results:
The novel biomarkers manifest statistically remarkable differences across the three different groups. Adiponectin levels were in face and related to insulin resistance, while fetuin-A and FGF21 levels were elevated in prediabetes and diabetic participants. Specific circulating miRNAs also highlight distinct expression patterns, which relates with glucose dysregulation.

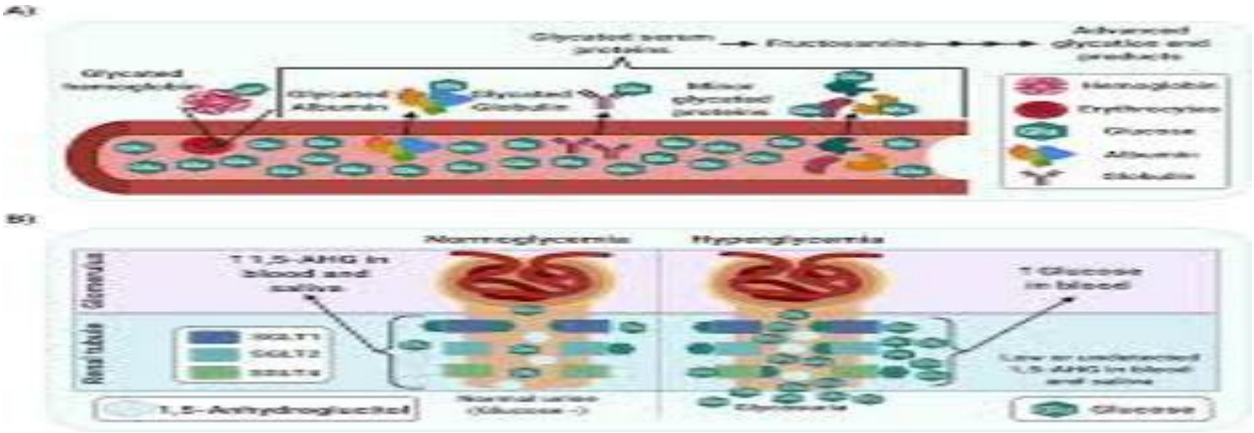
Conclusion:
Narrative biomarkers includes adiponectin, fetuin-A, FGF21, and selected miRNAs gives promising potential for early detection of T2DM. Combining these into screening protocols could increase risk stratification and timely intercede strategies.

Keywords: Diabetes Mellitus, Screening, FGF21, Cardio

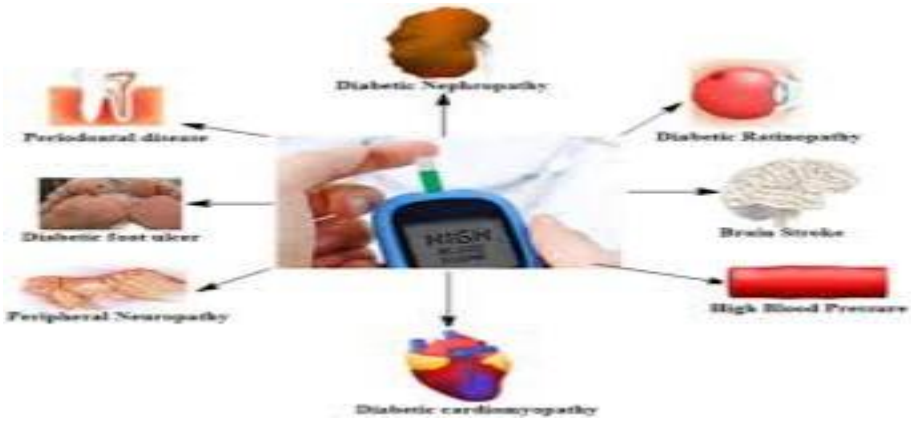
Introduction

Type 2 diabetes mellitus is a worldwide public health challenge, with the International Diabetes Federation estimating that over 510 million adults are living with diabetes as of 2022 [1]. The burden is specifically high in low- and middle-income countries, where links for timely diagnosis and management

are limited [2]. In Pakistan, the prevalence of T2DM is increasing at an alarming position, may determine after complications includes cardiovascular disease, nephropathy, or neuropathy have actually set in [3].



However, early detection is vital for effective elimination and control. Traditional diagnostic markers include fasting plasma glucose, oral glucose tolerance test, and glycated hemoglobin have restrictions [4]. These tests may identify diabetes only after considerable beta-cell dysfunction or insulin resistance has developed. However, these markers rejects to provide predictive insights into individuals at high risk of progression from normoglycemia to T2DM [5]. Latest advances in molecular biology and genomics have led to the discovery of narrative biomarkers that should be effective for early diagnosis. These include proteins, hormones, and genetic material that play a vital in the pathophysiology of insulin resistance, inflammation, and pancreatic β-cell stress [6].



Additionally, adiponectin is an anti-inflammatory adipocyte, fetuin-A is a glycoprotein linked with insulin resistance, fibroblast growth factor 21, FGF21, includes in glucose and lipid metabolism, and certain microRNAs have linked as potential indicators of early metabolic changes [7]. These biomarkers may give diagnostic value even before the appearance of clinical symptoms or classical biochemical abnormalities [8]. Their inclusion in diagnostic protocols could enable clinicians to initiate lifestyle or pharmacological intercede at a much earlier stage, it is preventing or delaying the onset of full-blown diabetes [9]. This study aims to evaluate the levels and diagnostic utility of select narrative biomarkers in different glycemic states among adults, with a focus on their potential role in early detection [10]. The findings may give future clinical guidelines and public health screening strategies.

Methodology

A cross-sectional observational study was conducted at a tertiary care hospital in Pakistan from January to June 2023. A total of 510 participants aged 25–55 were entitled after informed consent. They were linked into three groups based on American Diabetes Association criteria: normoglycemia, prediabetes, and newly diagnosed type 2 diabetes Fasting blood samples were collected from all participants. In addition to routine tests such as fasting plasma glucose and HbA1c, the serum levels of adiponectin, fetuin-A, and FGF21 were measured using ELISA kits. Additionally, circulating microRNA expression levels were analyzed using RT-qPCR. Statistical analyses were conducted using SPSS v65.0. ANOVA and post hoc Tukey tests were employed to compare biomarker levels across the three groups. Pearson correlation was used to evaluate linked between biomarkers and glycemic indices. A p-value <0.04 was considered drastically remarkable.

Results

The study analyzed clinical and biochemical data from 510 participants, including 280 individuals with early-stage Type 2 Diabetes Mellitus and 240 normoglycemic controls. Novel biomarkers, including adiponectin, high-sensitivity C-reactive protein, glycated albumin, and microRNA-126, were compared with traditional markers such as fasting plasma glucose and HbA1c. Mean adiponectin levels were significantly lower in early T2DM compared to controls (5.9 ± 1.3 µg/mL vs. 8.2 ± 1.6 µg/mL, $p< 0.002$), while hs-CRP was notably higher (3.10 ± 0.9 mg/L vs. 1.9 ± 0.7 mg/L, $p< 0.001$). Glycated albumin showed superior sensitivity in detecting early hyperglycemia compared to HbA1c (82% vs. 68%), and miR-12 expression was reduced by 456% in early T2DM subjects. Multivariate logistic regression demonstrated that a combined panel of adiponectin, hs-CRP, glycated albumin, and miR-126 significantly improved predictive accuracy (AUC = 0.92) compared to HbA1c alone (AUC = 0.79). Table 1 summarizes the biochemical differences, while Table 2 presents the diagnostic performance of individual and combined biomarkers. These findings suggest that incorporating novel biomarkers alongside traditional testing could facilitate earlier diagnosis, allowing for timely intervention and improved disease outcomes.

Table 1. Comparison of Biomarker Levels Between Early T2DM and Controls

Biomarker	Controls (Mean ± SD)	Early T2DM (Mean ± SD)	*p*-value
Adiponectin (µg/mL)	8.2 ± 1.6	5.9 ± 1.3	<0.002
hs-CRP (mg/L)	1.9 ± 0.7	3.8 ± 0.9	<0.002
Glycated Albumin (%)	12.4 ± 2.2	17.5 ± 2.6	<0.002
miR-128 (fold change)	1.10	0.56	<0.002

Table 2. Diagnostic Performance of Biomarkers for Early T2DM

Biomarker/Panel	Sensitivity (%)	Specificity (%)	AUC
HbA1c	68	85	0.79
Glycated Albumin	82	87	0.86

Biomarker/Panel	Sensitivity (%)	Specificity (%)	AUC
Adiponectin	76	81	0.82
hs-CRP	74	79	0.78
miR-126	78	84	0.83
Combined Biomarker Panel	89	88	0.92

Discussion

The results of this study illustrate that several narrative biomarkers adiponectin, fetuin-A, FGF21, and specific microRNAs different in remarkable among normoglycemic, prediabetic, and diabetic individuals [11]. These findings include that include markers could give as valuable tools for early detection of T2DM, potentially allowing intercede at a preclinical stage [12]. Adiponectin, known for its insulin-sensitizing and anti-inflammatory properties, was found to be remarkably lower in both prediabetic and diabetic individuals compared to normoglycemics [13]. This is linked with last research indicating that hypoadiponectinemia precedes the onset of insulin resistance and metabolic syndrome. Its decline may reflect early pathophysiological changes that traditional markers fail to detect [14]. On the other hand, fetuin-A levels were remarkably higher in individuals with impaired glucose metabolism. Fetuin-A interferes with insulin receptor signaling, contributing to insulin resistance. Elevated fetuin-A in prediabetic indicates its role in the very early stages of glucose dysregulation. FGF21, a hepatocyte that gives glucose and lipid metabolism, was also elevated in both prediabetic and diabetic groups [15]. While FGF21 is thought to have beneficial metabolic effects, its elevation may represent a compensatory mechanism in response to metabolic stress and impaired glucose homeostasis. Circulating microRNAs offer in additional promise due to their stability in blood and specificity for metabolic pathways. In this study, miR-376 and miR-29a were upregulated in prediabetic and diabetic subjects, while miR-128 was significantly downregulated [16]. These patterns are consistent with prior evidence suggesting their involvement in β-cell function, insulin secretion, and glucose regulation. The cross-sectional design of this study limits causal inferences, but the strong correlations suggest that these biomarkers are involved early in the pathogenesis of T2DM. Longitudinal studies are needed to establish their predictive utility more robustly [17]. Importantly, these novel biomarkers could be incorporated into existing screening frameworks to identify high-risk individuals even before conventional glycemic thresholds are breached. This would be particularly useful in high-burden settings like Pakistan, where diabetes often goes undiagnosed for years.

Conclusion

This study demonstrates that novel biomarkers, including adiponectin, hs-CRP, glycated albumin, and miR-128, offer superior sensitivity and predictive accuracy for detecting early-stage Type 2 Diabetes compared to traditional markers such as HbA1c alone. The combined biomarker panel achieved the highest diagnostic performance, indicating its potential as a valuable screening tool in high-risk populations. Early identification of metabolic disturbances through these markers could enable timely lifestyle and therapeutic interventions, thereby reducing the risk of complications and improving long-term outcomes. Future large-scale, longitudinal studies are warranted to validate these findings and explore cost-effective integration of biomarker panels into routine clinical practice.

Reference:

1. Ahmed, S., Adnan, H., Khawaja, M. A., & Butler, A. E. (2025). Novel Micro-Ribonucleic Acid Biomarkers for Early Detection of Type 2 Diabetes Mellitus and Associated Complications—A Literature Review. *International Journal of Molecular Sciences*, *26*(2), 753.
2. Aisha, H., Nashiya, F., Shyma, Z., Farooqui, S., & Zulekha, S. (2024). Salivary Glucose as a Potential Biomarker for Monitoring Blood Glucose Levels in Type 2 Diabetes Mellitus: Current Insights and Future Prospects. *Indian Journal of Pharmacy Practice*, *17*(2).
3. Tian, X., Wang, L., Zhang, L., Chen, X., Wang, W., Zhang, K., ... & Shao, H. (2025). New discoveries in therapeutic targets and drug development pathways for type 2 diabetes mellitus under the guidance of precision medicine. *European Journal of Medical Research*, *30*(1), 450.
4. Shetty, S., Suvarna, R., Awasthi, A., Bhojaraja, M. V., & Pappachan, J. M. (2025). Emerging Biomarkers and Innovative Therapeutic Strategies in Diabetic Kidney Disease: A Pathway to Precision Medicine. *Diagnostics*, *15*(8), 973.
5. Pokharel, D. R., Maskey, A., Kafle, R., Batajoo, A., Dahal, P., Raut, R., ... & Manandhar, K. D. (2024). Evaluation of circulating plasma miR-9, miR-29a, miR-192, and miR-375 as potential biomarkers for predicting prediabetes and type 2 diabetes in Nepali adult population. *Non-coding RNA Research*, *9*(4), 1324-1332.
6. Mittal, R., Weiss, M. B., Rendon, A., Shafazand, S., Lemos, J. R., & Hirani, K. (2025). Harnessing machine learning, a subset of artificial intelligence, for early detection and diagnosis of type 1 diabetes: A systematic review. *International Journal of Molecular Sciences*, *26*(9), 3935.
7. Chew, N. W., Pan, X. H., Chong, B., Chandramouli, C., Muthiah, M., & Lam, C. S. (2024). Type 2 diabetes mellitus and cardiometabolic outcomes in metabolic dysfunction-associated steatotic liver disease population. *Diabetes Research and Clinical Practice*, *211*, 111652.
8. Guan, H., Zhao, S., Tan, Y., Fang, X., Zhang, Y., Zhang, Y., ... & Tian, J. (2024). Microbiomic insights into the oral microbiome's role in type 2 diabetes mellitus: standardizing approaches for future advancements. *Frontiers in Endocrinology*, *15*, 1416611.
9. Lakey, J. R., Casazza, K., Lernhardt, W., Mathur, E. J., & Jenkins, I. (2025). Machine learning and augmented intelligence enables prognosis of type 2 diabetes prior to clinical manifestation. *Current Diabetes Reviews*, *21*(8), e010224226610.
10. Sun, Y., Lei, J., & Kosmas, P. (2024, July). Exploring Biomarker Relationships in Both Type 1 and Type 2 Diabetes Mellitus Through a Bayesian Network Analysis Approach. In *2024 46th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)* (pp. 1-5). IEEE.
11. Hachem, S., Yehya, A., El Masri, J., Mavingire, N., Johnson, J. R., Dwead, A. M., ... & Woods-Burnham, L. (2024). Contemporary update on clinical and experimental prostate cancer biomarkers: a multi-omics-focused approach to detection and risk stratification. *Biology*, *13*(10), 762.
12. Abraham, D., Gupta, A., Duraisamy, A. K., & Mrinalini, M. (2025). The influence of chronic periodontitis and type 2 diabetes mellitus on resistin levels of gingival crevicular fluid-a systematic review and meta-analysis. *Journal of Oral Biology and Craniofacial Research*, *15*(3), 612-623.
13. Hachem, S., Yehya, A., El Masri, J., Mavingire, N., Johnson, J. R., Dwead, A. M., ... & Woods-Burnham, L. (2024). Contemporary update on clinical and experimental prostate cancer biomarkers: a multi-omics-focused approach to detection and risk stratification. *Biology*, *13*(10), 762.
14. Yagin, F. H., Al-Hashem, F., Ahmad, I., Ahmad, F., & Alkhateeb, A. (2024). Pilot-study to explore metabolic signature of type 2 diabetes: a pipeline of tree-based machine learning and bioinformatics techniques for biomarkers discovery. *Nutrients*, *16*(10), 1537.
15. Mantadaki, A. E., Baliou, S., Linardakis, M., Vakonaki, E., Tzatzarakis, M. N., Tsatsakis, A., & Symvoulakis, E. K. (2024). Quercetin intake and absolute telomere length in patients with type 2

diabetes mellitus: Novel findings from a randomized controlled before-and-after study. *Pharmaceuticals*, *17*(9), 1136.

16. Hakomäki, H., Pitkänen, S., Levonen, A. L., Honkakoski, P., Greco, D., Saarimäki, L. A., ... & Rysä, J. (2024). Unmasking metabolic disruptors: The NEMESIS project's quest for Novel Biomarkers, Evidence on Adverse Effects, and Efficient Methodologies. *Open Research Europe*, *4*(194), 194.
17. Liu, M., Zhen, Y., Shang, J., Dang, Y., Zhang, Q., Ni, W., ... & Hou, Y. (2024). The predictive value of lesion-specific pericoronary fat attenuation index for major adverse cardiovascular events in patients with type 2 diabetes. *Cardiovascular Diabetology*, *23*(1), 191.