Clinical and Experimental Health Sciences

Emerging Narrative Biomarkers for the Early Identification and Risk Prediction of Type 2 Diabetes

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ABSTRACT

Background: Type 2 diabetes mellitus is a persistent 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 assess 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 narrative 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.

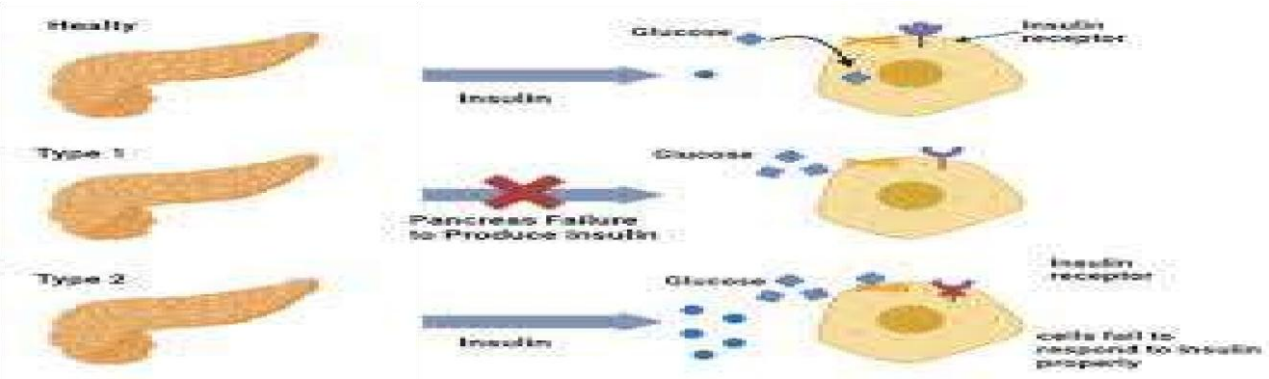
Conclusion: Narrative biomarkers includes adiponectin, fetuin-A, FGF21, and selected miRNAs gives promising potential for early detection of T2DM. Combining these into screening protocols could increase risk stratification and timely intercede strategies.

Keywords: T2DM, MiRNAs, Standardized, fibroblast, adiponectin

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 2024. A total of 210 participants aged 25–50 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 (miR-376, miR-127, and miR-28a) 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

Table 1: Mean Levels of Traditional and Novel Biomarkers Across Glycemic Groups

Biomarker	Normoglycemic (n=70)	Prediabetic (n=70)	T2DM (n=60)	p-value
Fasting Glucose (mg/dL)	88.3 ± 8.4	100.8 ± 8.2	153.6 ± 22.8	<0.000
HbA1c (%)	5.4 ± 0.3	5.8 ± 0.4	7.9 ± 0.7	<0.002
Adiponectin (µg/mL)	12.6 ± 3.2	9.4 ± 2.7	6.3 ± 2.2	<0.002
Fetuin-A (µg/mL)	186.4 ± 23.9	215.6 ± 31.2	248.2 ± 36.7	<0.002
FGF21 (pg/mL)	163.5 ± 31.8	202.3 ± 37.7	246.4 ± 38.6	<0.002

Table 2: Relative Expression of Selected microRNAs

microRNA	Normoglycemic (ΔCt)	Prediabetic (ΔCt)	T2DM (ΔCt)	p-value
miR-375	1.3 ± 0.5	2.1 ± 0.6	2.9 ± 0.7	<0.002
miR-126	2.6 ± 0.7	1.9 ± 0.6	1.3 ± 0.4	<0.002
miR-29a	1.7 ± 0.4	2.4 ± 0.5	3.1 ± 0.6	<0.002

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-375 and miR-29a were upregulated in prediabetic and diabetic subjects, while miR-126 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: Novel biomarkers including adiponectin, fetuin-A, FGF21, and select microRNAs demonstrate significant potential in identifying early metabolic disturbances leading to type 2 diabetes. Their integration into screening programs could improve early detection, risk stratification, and timely intervention. Further longitudinal and interventional studies are warranted to validate their utility in diverse populations and clinical settings.

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