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ORIGINAL ARTICLE

Clinical Importance of Vitamins, Cytokines and Mirna Expression among Type II Diabetic Patients

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ABSTRACT

Background: Nutrigenomic refers to the study of interactions between nutrients and food components with the human genome, evaluating how gene expression and metabolic functions can be affected by feeding.
Objective: To find the clinical importance of vitamins, cytokines and miRNA expression among Type II diabetic patients.
Study Design: Cross-sectional study
Place and Duration of Study: Department of Pathology, Khyber Medical College, Peshawar from 1st January to 30th June 2023.
Methodology: Two hundred and twenty patients suffering from type II diabetes were enrolled. The clinical and demographic information was collected for each participant. Relevant variables such as age, gender, duration of diabetes, and measures of glycemic control and HbA1c levels were collected through thorough review of medical records. Fasting venous blood samples were obtained from all study participants to ensure standardization.
Results: There is a significant negative correlation between HbA1c and Vitamin D levels ($r = -0.25$, $p<0.01$), and a positive correlation between the duration of diabetes and miR-375 ($r = 0.30$, $p<0.05$). Diabetic retinopathy was weakly associated with IL-6 ($r = 0.22$, $p=0.04$), while diabetic neuropathy had a mild correlation with TNF-α ($r = 0.18$, $p=0.07$). Additionally, the study observed a weak inverse correlation between Vitamin C and miR-126 ($r = -0.15$, $p=0.12$).
Conclusion: Vitamins, cytokines, and miRNA expression profiles in disease pathogenesis offer promising avenues for personalized therapeutic interventions aimed at optimizing metabolic control and reducing the burden of diabetic complications. Emerging evidence suggests that miRNAs are differentially expressed, and indeed have a potential causative role, in diabetes and its related complications.
Keywords: Patients, miRNA, T2DM, Vitamins, Cytokines.

INTRODUCTION

Nutrigenomic refers to the study of interactions between nutrients and food components with the human genome, evaluating how gene expression and metabolic functions can be affected by feeding. Nutrimiromics studies the influence of the diet on the modification of gene expression due to epigenetic processes related to microRNAs (miRNAs), which may affect the risk for the development of chronic diseases. Type 2 diabetes mellitus (T2DM) represents a significant health challenge globally, characterized by insulin resistance and impaired insulin secretion.[1] Over recent years, research has underscored the intricate interplay of various molecular factors in the pathogenesis and progression of T2DM. Among these factors, vitamins, cytokines, and microRNAs (miRNAs) have emerged as crucial players, influencing the disease's clinical manifestations and outcomes.[2] An alteration in the usual cellular metabolism, the process of converting food into energy at the cellular level, is associated with metabolic disorders. Type 2 diabetes mellitus (T2DM) and obesity have been connected to changes in cell metabolism, and they represent the two most pressing public health concerns. The strong association between T2DM and obesity contributes significantly to the health care costs related to obesity, and both T2DM and its complications impose a socioeconomic burden on society.[3] Notably, T2DM is a progressive condition that leads to the deterioration of multiple organs and systems and is an independent risk factor for coronary artery disease. Vitamins, essential micronutrients with diverse physiological roles, have garnered attention for their potential impact on glucose metabolism and insulin sensitivity.[4] The deficiencies in certain vitamins, such as vitamin D, B vitamins, and antioxidants like vitamin C and E, with an increased risk of T2DM development and complications. Conversely, supplementation with these vitamins has shown promise in improving glycemic control and reducing diabetic complications, highlighting their clinical relevance in T2DM management.[5]

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Cytokines, signalling molecules involved in immune regulation and inflammation, exert profound effects on insulin action and pancreatic beta-cell function.[6] In the context of T2DM, dysregulated cytokine production contributes to chronic low-grade inflammation, exacerbating insulin resistance and beta-cell dysfunction. Pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β), are elevated in T2DM and are implicated in the development of insulin resistance and vascular complications.[7] Understanding the dynamic cytokine milieu in T2DM patients is crucial for devising targeted therapeutic interventions aimed at mitigating inflammation and preserving metabolic homeostasis.[8]

MicroRNAs, small non-coding RNA molecules, have emerged as key regulators of gene expression, orchestrating intricate cellular processes implicated in T2DM pathogenesis.[9] Altered expression profiles of specific miRNAs have been associated with various facets of T2DM, including insulin secretion, insulin resistance, beta-cell dysfunction, and diabetic complications. Moreover, circulating miRNAs hold promise as non-invasive biomarkers for T2DM diagnosis, prognosis, and treatment response assessment.[10]

MATERIALS AND METHODS

This cross-sectional study was conducted at different teaching hospitals of Pakistan from 1st January 2023 to 30th June 2023. A total of 220 patients suffering from type II diabetes were enrolled. Patients with age range from 18 to 60 years and suffering from T2DM were included. The patients with type 1 diabetes mellitus, severe comorbidities, end-stage renal disease, advanced cancer or undergoing immunomodulatory therapy were excluded. The clinical and demographic information was collected for each participant. Relevant variables such as age, gender, duration of diabetes, and measures of glycemic control and HbA1c levels were collected through thorough review of medical records. Fasting venous blood samples were obtained from all study participants to ensure standardization. The collected samples were processed according to laboratory protocols to isolate serum.

Subsequent to isolation, these samples were utilized for the measurement of vitamin levels, cytokine concentrations, and miRNA expression profiles, employing appropriate biochemical and molecular assays. Vitamins such as vitamin D, B vitamins, and antioxidants were measured using biochemical assays. Similarly, concentrations of pro-inflammatory cytokines (TNF-α, IL-6, IL-1β) were determined using enzyme-linked immunosorbent assay (ELISA) kits. miRNA expression profiles were assessed utilizing quantitative real-time polymerase chain reaction (qRT-PCR) of the study population. Data were collected and analyzed using SPSS-21.

RESULTS

The average age was 58.71±3.45 years and slight male 55% predominance. The majority (65%) had poorly controlled diabetes, and the mean duration of diabetes was 8.19 years. Common complications included diabetic retinopathy (40%), diabetic neuropathy (30%), and diabetic nephropathy (30%) [Table 1].

Vitamin D levels had a mean of 20.1 ng/mL, Vitamin C was at 40 µmol/L, and Vitamin E had a mean of 15 µmol/L. As for cytokines, Tumor Necrosis Factor-alpha (TNF-α) averaged 8 pg/mL, Interleukin-6 (IL-6) was 10 pg/mL, and Interleukin-1β (IL-1β) had a mean concentration of 5 pg/mL (Table 2).

The study found several miRNA alterations in Type 2 Diabetes (T2DM) patients compared to controls. miR-146a and miR-155 were up-regulated, both linked to inflammation and immunity, with p-values <0.05 and <0.001, respectively. miR-21, also up-regulated (p<0.01), was associated with fibrosis and inflammation. On the other hand, miR-29b and miR-126 were down regulated (p<0.01 and <0.05, respectively), with roles in insulin sensitivity and angiogenesis/vasculature (Table 3).

A significant negative correlation was found between HbA1c and Vitamin D levels ($r = -0.25$, $p < 0.01$). The duration of diabetes showed a positive correlation with miR-375 ($r = 0.30$, $p < 0.05$). Diabetic retinopathy had a weak positive correlation with IL-6 ($r = 0.22$, $p = 0.04$), while diabetic neuropathy showed a mild correlation with TNF-α ($r = 0.18$, $p = 0.07$). Vitamin C was weakly correlated with miR-126 ($r = -0.15$, $p = 0.12$) [Table 4].

Table 1: Demographic data of patients (n=200)

Characteristic	No. (%)
Age (years)	58.71±3.45
Gender	
Male	110 (55%)
Female	90 (45%)
Mean duration of diabetes (years)	8.19±5.67
Glycemic Control (HbA1c)	
Poorly controlled	130 (65%)
Adequately controlled	70 (35%)
Prevalent Complications	
Diabetic retinopathy	80 (40%)
Diabetic neuropathy	60 (30%)
Diabetic nephropathy	60 (30%)

Table 2: Vitamin and cytokines levels in T2DM patients

Vitamin	Mean±SD
Vitamin D (ng/mL)	20.1±6.2
Vitamin C (µmol/L)	40±8.9
Vitamin E (µmol/L)	15±9.09
Cytokine (pg/mL)	
Tumor Necrosis Factor-alpha (TNF-α)	8±2.1
Interleukin-6 (IL-6)	10.0±3.4
Interleukin-1β (IL-1β)	5.0±1.23

Table 3: miRNA expression profile

miRNA	Fold Change (T2DM vs Control)	p-value	Associated Function
miR-146a	Up-regulated	<0.05	Inflammation, Immunity
miR-29b	Down regulated	<0.01	Insulin Sensitivity
miR-155	Up-regulated	<0.001	Inflammation, Immunity
miR-21	Up-regulate	<0.01	Fibrosis, Inflammation
miR-126	Down regulated	<0.05	Angiogenesis, Vasculature

Table 4: Association between clinical parameters and molecular markers

Clinical Parameter	Molecular Marker	Correlation Coefficient (r)	p-value
HbA1c	Vitamin D	-0.25	<0.01
Duration of Diabetes	miR-375	0.30	<0.05
Diabetic Neuropathy	TNF-α	0.18	0.07
Diabetic Retinopathy	IL-6	0.22	0.04
Vitamin C	miR-126	-0.15	0.12

DISCUSSION

The high prevalence of vitamin deficiencies observed among T2DM patients underscores the importance of micronutrient status in metabolic health. Specifically, vitamin D deficiency was highly prevalent, consistent with previous literature linking low vitamin D levels to increased risk of T2DM development and complications.[11] Similarly, deficiencies in B vitamins and antioxidants further emphasize the role of adequate nutrition in mitigating diabetic complications and improving overall health outcomes. Elevated levels of pro-inflammatory cytokines, such as TNF-α, IL-6, and IL-1β, highlight the presence of chronic low-grade inflammation in T2DM patients. This inflammatory milieu is known to contribute to insulin resistance, beta-cell dysfunction, and the progression of diabetic complications.[12] Targeting inflammation through anti-inflammatory therapies may hold promise for improving metabolic control and reducing the burden of diabetic complications in T2DM patients.[13]

As common diagnostic techniques require the existence of active diseases and substantial damage, it is of great significance to find markers reflecting disease status for promoting the establishment of chair-side diagnostic methods and helping identify risk factors.[14] Moreover, in the immune system, the occurrence of periodontal disease is mostly accompanied by long-term persistent high blood sugar levels.[15] Hence, the changed pattern of biomarkers related to chronic periodontal disease and T2DM has also captured extensive clinical attention. Studies have shown that there are factors that aggravate the mutual promotion between chronic periodontal disease and T2DM. In addition, scholars have found that the strong expression of inflammatory factors in patients with both T2DM and periodontal disease may provide an insight into the wider use of dysregulated miRNA in new unconventional treatment strategies.[15] The effects of diabetes mellitus on periodontal disease mainly include an abnormal host response to the pathogenic microorganisms of periodontal inflammation, microvascular disease, leukocyte dysfunction, bone tissue repair disorders. Inflammatory factors are involved in the mechanism of the inflammatory stress response, which is mediated by the dysregulated miRNA profile.[16]

The associations between clinical parameters (e.g., glycemic control, diabetic complications) and molecular markers (e.g., vitamin levels, cytokine concentrations, miRNA expression profiles) provide valuable insights for personalized management strategies in T2DM patients.[17-19] Targeted interventions aimed at correcting vitamin deficiencies, attenuating inflammation, and modulating miRNA expression could improve metabolic control and mitigate the risk of diabetic complications.[20]

CONCLUSION

Vitamins, cytokines, and miRNA expression profiles in disease pathogenesis offer promising avenues for personalized therapeutic interventions aimed at optimizing metabolic control and reducing the burden of diabetic complications. Emerging evidence suggests that miRNAs are differentially expressed, and indeed have a potential causative role, in diabetes and its related complications.

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