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Original research article

ASSOCIATION OF SERUM ADENOSINE DEAMINASE LEVELS WITH ACUTE KIDNEY INJURY IN DIABETIC PATIENTS

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Abstract: *Diabetes mellitus is a significant global health issue, and complications such as acute kidney injury (AKI) are prevalent in patients with type 2 diabetes. Serum adenosine deaminase (ADA) has been suggested as a potential biomarker for various metabolic conditions, including inflammation and kidney injury, but its association with diabetic kidney health remains understudied.* ***Objective:*** *To assess the association of serum adenosine deaminase (ADA) levels with acute kidney injury (AKI) in patients with type 2 diabetes.* ***Methods****: This observational comparative study was conducted at DHQ Teaching Hospital KDA, Kohat, from February 7, 2023, to August 7, 2023, following ethical approval. A total of 120 participants were enrolled, including 60 patients with type 2 diabetes and 60 non-diabetic controls. Laboratory investigations for both groups included serum ADA (U/L), HbA1c (%), and estimated glomerular filtration rate (eGFR) (mL/min/1.73 m²). Statistical comparisons between groups were made using appropriate tests, and correlations between serum ADA and other parameters were assessed.* ***Results:*** *The mean age of diabetic patients was 55.40 ± 8.29 years, and that of controls was 54.58 ± 21.64 years. The mean serum ADA level in diabetic patients was significantly higher at 43 ± 4.29 U/L compared to 16.32 ± 1.20 U/L in controls (p = 0.0001). Diabetic patients had a mean HbA1c of 8.30 ± 0.59%, significantly higher than that of controls (5.28 ± 0.59%) (p = 0.0001). The mean eGFR in diabetic patients was 82.61 ± 17.22 mL/min/1.73 m², lower than in controls (105.97 ± 12.07 mL/min/1.73 m²) (p = 0.0001). In diabetic patients, serum ADA levels were positively correlated with HbA1c (indicating poorer glycemic control) and negatively correlated with eGFR (suggesting declining kidney function).* ***Conclusion:*** *Elevated serum adenosine deaminase levels in type 2 diabetic patients are significantly associated with poor glycemic control and decreased kidney function. These findings indicate that serum ADA could serve as a potential biomarker for monitoring glycemic status and kidney health in diabetic patients at risk for acute kidney injury.*

Keywords: Diabetes, Acute kidney injury, serum adenosine deaminase, association.

Introduction

Diabetes mellitus (DM), or diabetes for short, is a complicated metabolic ailment defined by hyperglycemia, which is a medical condition that occurs when blood glucose levels remain consistently high (1-3). Hyperglycemia and its related dysfunctions in glucose, lipid, and protein metabolism impact various organs in the body, causing disruptions in their normal functioning. (4, 5) The pathophysiology of acute kidney injury (AKI) in diabetic patients involves both large blood vessel (macrovascular) and small blood vessel (microvascular) difficulties. Macrovascular causes, including atherosclerosis, hypertension, and dyslipidemia, lead to renal ischemia, which hampers the kidney's capacity to regulate fluid and electrolyte equilibrium (6, 7). Microvascular alterations, such as enlargement of the glomeruli, expansion of the mesangium, and impairment of podocyte function, worsen kidney injury by altering the filtration mechanisms and increasing inflammation and fibrosis (8, 9). In addition, diabetic nephropathy, a frequent consequence of diabetes, substantially increases the likelihood of AKI due to its gradual progression and the occurrence of glomerulosclerosis & tubulointerstitial fibrosis (10). Serum adenosine deaminase, an enzyme involved in the metabolism of purines, plays a vital role in regulating immune system responses including inflammatory processes (11). The dysregulation of adenosine deaminase activity in persons with diabetes has been associated with several clinical pathways that contribute to kidney damage, such as oxidative stress, endothelial dysfunction, or inflammatory cascades (12). Diabetic patients with AKI show higher levels of serum adenosine deaminase, indicating heightened immune activation and inflammation within the renal milieu (13).
Diabetic individuals with AKI have shown higher levels of serum adenosine deaminase, indicating heightened immune activation and tissue inflammation in the renal microenvironment. Due to the paucity of literature on this subject locally, the aim of this study is to find out the association of serum adenosine deaminase levels with acute kidney injury among diabetic patients at our health setup. Therefore, it is imperative to examine the association between serum adenosine deaminase levels and AKI in diabetic patients to further our comprehension of diabetic kidney disease and improve patient care in this vulnerable population.

Methodology

This observational comparative study was conducted at DHQ Teaching Hospital KDA, Kohat from 07-02- 2023 to 07-08-2023 after obtaining ethical approval from the hospital. One hundred and twenty subjects aged 40 to 70 years of either gender were selected and allocated to two

groups using the non-probability consecutive technique. Sixty patients diagnosed with type 2 diabetes were labelled type 2 diabetics while sixty healthy patients were labelled controls. All the patients were subjected to laboratory examination for serum ADA (U/L), HbA1c (%) and eGFR (mL/min/1.73 m2). HbA1c ≤ 6.5% was defined as normal and Serum ADA ≤ 40 U/L was defined as normal. Serum ADA was assessed between both groups along with other laboratory parameters.

SPSS 24 was used for the assessment of variables. Independent Samples test and Pearson's coefficient of correlation were applied keeping the value of P significant at < 0.05.

Results

Sixty diabetes type 2 patients and sixty non-diabetic controls were selected for this study. The mean age of diabetics was 55.40±8.29 years while 54.58±21.64 years in controls. The mean BMI of diabetics was 25.97±0.80 kg/m2 while 21.64±0.76 kg/m2 in controls. The frequency of male patients in both groups was higher than female patients (Figure 1). In diabetics mean serum ADA was 43±4.29 U/L while 16.32±1.20 U/L in controls (P = 0.0001). Mean HbA1c in diabetics was 8.2975±0.594% while 5.28±0.59% in controls (P = 0.0001). The mean eGFR in diabetics was 82.61±17.22 while 105.97±12.07 (mL/min/1.73 m2) in controls (P = 0.0001) (Table 1). We observed that serum ADA was positively correlated with HbA1c, and negatively correlated with eGFR in diabetic patients (Table 2).

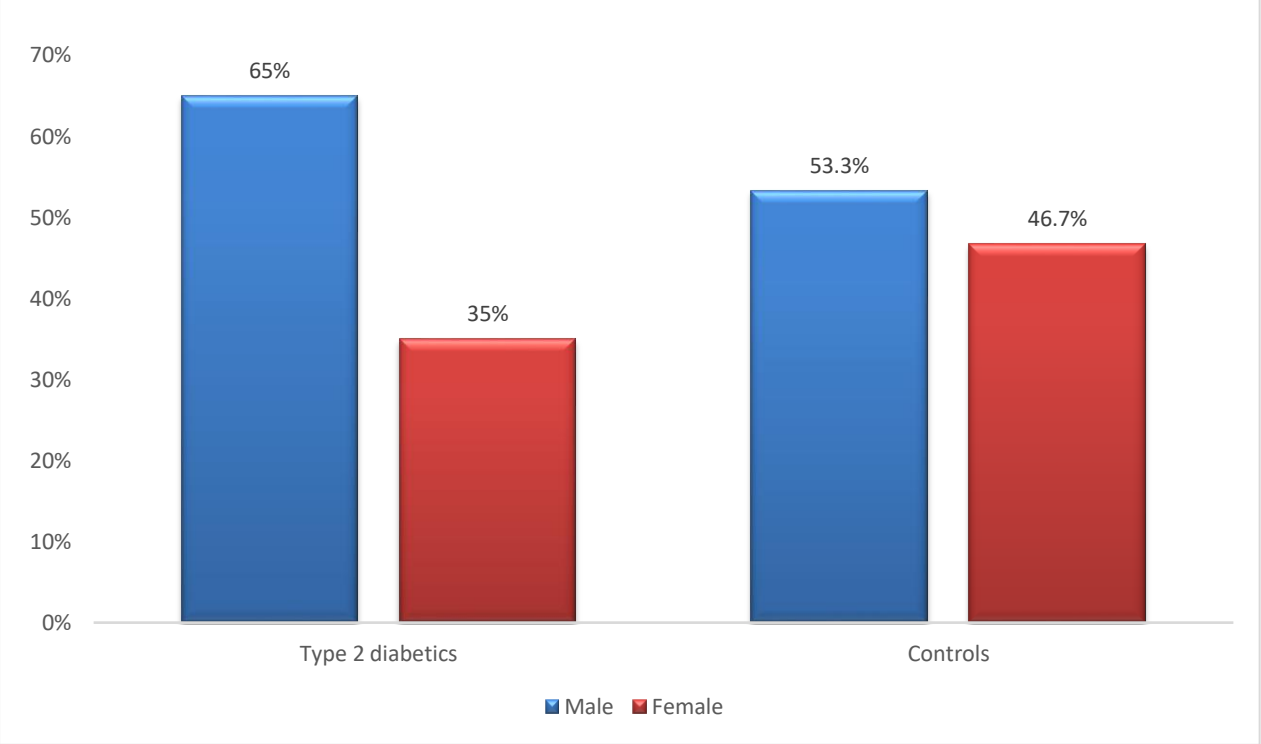

Figure 1 Gender distribution

Table 1 Comparison of various parameters between diabetics and controls

Parameters	Groups	N	Mean	Std. Deviation	P value
Serum ADA (U/L))	Type 2 Diabetics	60	43.00	4.290	0.0001
	Controls	60	16.32	1.200	
HbA1c (%)	Type 2 Diabetics	60	8.2975	.59402	0.0001
	Controls	60	5.2872	.59618	
eGFR (mL/min/1.73 m^2)	Type 2 Diabetics	60	82.6100	17.22742	0.0001
	Controls	60	105.9732	12.07058	

Table 2 Correlation of serum ADA with HbA1c, FPG and PPG

Serum ADA (U/L))	HbA1c (%)	eGFR
Pearson Correlation	.309	-.332
Sig. (2-tailed)	.016	.010
N	60	60

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Discussion

The association between high serum ADA levels and an increased risk of developing diabetic kidney disease can be explained by several different plausible processes. The progression of diabetic kidney disease is mostly influenced by inflammation, and macrophages are the cells that are responsible for initiating inflammation. The amount of macrophage infiltration in the cells of the kidney was found to have a close relationship with the reduction in renal filtration function, according to a study. (13)

By taking part in the breakdown of the blood-retinal barrier (BRB) via macrophage-derived cytokines, ADA contributes to the advancement of diabetic retinopathy (DR) in experimental diabetic retinopathy (DR). However, inhibiting ADA can help retain the function of the BRB (30). Therefore, a rise in serum ADA type 2 diabetics can hasten the start and progression of AKI by increasing macrophage infiltration in the kidney and the release of cytokines that are derived from macrophages (14). Furthermore, adenosine, which is the base of ADA, has been demonstrated in several studies to possess protective properties of the kidneys and the cardiovascular system. Adenosine can control the amounts of renin that are released, as well as the glomerular filtration rate and renal vascular tension in the kidney. (15)

Comparing the levels of ADA (U/L) in diabetes participants (43.00± 4.290) to those in the control group (16.32 ± 1.20), the current study found that diabetic subjects had significantly higher levels of ADA. The increased plasma ADA activity may be the result of aberrant T-lymphocyte response or expansion; this may indicate that the mechanism in question involves the release of the substance into the circulation. (16) As a result, we propose that the increased ADA activity observed in diabetic individuals might be the result of altered insulin-related T-lymphocyte function or an increase in immunological dysfunction. Previously, a study established that poor cell-mediated immunity has been linked with aberrant lymphocyte proliferation. (17)

According to the findings of this study, the ADA is elevated in people who have diabetes mellitus. It is suggested by the findings of the current study that serum ADA levels can also be utilized as a biomarker in the process of determining glycemic control in diabetes patients. This is because the study demonstrates that there is a strong positive link between serum ADA levels and Hba1c. Studies have demonstrated that there is a clear correlation between the activity and expression of ADA and the level and severity of inflammation. (18, 19)

We found a negative correlation between raised levels of ADA with decreased eGFR values in diabetic patients, which indicates AKI, similar observations have been reported by a study which showed that the elevated levels of ADA in diabetics type 2 were negatively correlated with eGFR, which is an important biomarker for AKI. (13)

Conclusion

We conclude that raised serum ADA is positively correlated with raised HbA1c and negatively correlated with eGFR, it plays an important role as a biomarker for the prediction of glycemic control in type 2 diabetic patients as well as acute kidney injury.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate.
Approved by the department concerned. (IRB-TCHC-230/22)

Consent for publication
Approved

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Not applicable

Conflict of interest

The authors declared an absence of conflict of interest.

Authors Contribution

MUHAMMAD USMAN
Revisiting Critically, Data Analysis & Final Approval of version
FAHIM SHAH
Revisiting Critically, Drafting, Concept & Design of Study

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