

Correlation of serum adenosine deaminase, minerals and oxidative stress with chronic kidney disease in tertiary care hospital

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Abstract: *Background:* Chronic Kidney Disease (CKD) is a progressive, irreversible decline in renal function that disrupts mineral homeostasis. Recently growing evidence has shown that inflammation play an important role in the onset and progression of CKD. Serum MDA is considered as suitable biomarker of oxidative stress in CKD and shows an inverse relationship with renal function. *Objective:* To estimate serum ADA, MDA, Calcium, Phosphorous, Creatinine and Urea levels in control and study group. To correlate ADA, MDA, Calcium and phosphorous with Creatinine. *Materials & Methods:* This study includes 50 patients of chronic kidney disease and 50 healthy controls. The study was conducted in Government Medical College & General Hospital, Kadapa, Andhra Pradesh. All the biochemical parameters were analysed using standard procedures. Statistical tests used were Descriptives, Student t test & Pearson's Correlation. *Result:* The study showed that significant decreased Calcium, significant increased ADA, Malondialdehyde and Phosphorous levels in CKD patients compared with healthy controls. The significant negative correlation between serum creatinine and Calcium, significant positive correlation between creatinine and ADA, MDA, Phosphorous were observed. *Conclusion:* The present study demonstrated significant hypocalcaemia, hyperphosphatemia, and elevated serum ADA, MDA levels in CKD patients.

Keywords: Adenosine deaminase, Oxidative stress, Minerals, Chronic Kidney disease.

Introduction

Chronic Kidney Disease (CKD) is a progressive, irreversible disorder characterized by gradual loss of kidney function due to destruction of functional nephrons. It ultimately progresses to end-stage renal disease (ESRD), defined by an estimated glomerular filtration rate (eGFR) below 15 mL/min/1.73 m² or the need for renal replacement therapy.

CKD affects nearly 10% of the global population and is recognized as one of the fastest growing causes of mortality worldwide. In India, the burden of CKD continues to rise because of increasing prevalence of diabetes mellitus, hypertension, obesity, metabolic syndrome and ageing of the population. Apart from causing renal failure, CKD significantly increases cardiovascular morbidity, healthcare expenditure and reduction in quality of life [1-3]. The kidneys regulate water balance, electrolyte homeostasis,

acid-base balance, endocrine functions and elimination of metabolic waste products. Progressive nephron loss leads to accumulation of uremic toxins, metabolic acidosis, anemia, endocrine dysfunction, inflammation and oxidative stress. These biochemical disturbances become more severe with advancing disease and contribute to cardiovascular disease, which remains the leading cause of death among CKD patients [4].

Disturbances in calcium and phosphorus metabolism develop early during CKD, often before overt symptoms appear. Reduced phosphate excretion causes phosphate retention, stimulating fibroblast growth factor-23, suppressing calcitriol synthesis and reducing intestinal calcium absorption. Hypocalcemia subsequently stimulates parathyroid hormone secretion, producing secondary hyperparathyroidism. These

abnormalities collectively constitute chronic kidney disease–Mineral and Bone Disorder (CKD–MBD), characterized by abnormalities of calcium, phosphorus, PTH, vitamin D and bone turnover. CKD–MBD is associated with renal osteodystrophy, vascular calcification, arterial stiffness and an increased risk of cardiovascular mortality [5-7].

Oxidative stress is a hallmark of CKD and results from an imbalance between reactive oxygen species (ROS) generation and antioxidant defense mechanisms. Increased ROS production arises from chronic inflammation, mitochondrial dysfunction, activation of NADPH oxidase, uremic toxins and repeated exposure to dialysis membranes. Oxidative stress promotes lipid peroxidation, endothelial dysfunction, inflammation and accelerated atherosclerosis, thereby contributing to progression of renal injury and cardiovascular complications.

Numerous studies have demonstrated progressively increasing oxidative stress with declining renal function [8-11]. Malondialdehyde (MDA) is a three-carbon aldehyde formed during lipid peroxidation of polyunsaturated fatty acids and is considered one of the most reliable biomarkers of oxidative stress. Increased serum MDA reflects free radical-mediated membrane damage and has consistently been reported in CKD and ESRD patients. Elevated MDA levels correlate with worsening renal function and increased cardiovascular risk, making it a useful biochemical marker for assessing oxidative injury in CKD [12-13].

Adenosine deaminase (ADA) is an important enzyme in purine metabolism that catalyzes the deamination of adenosine to inosine. ADA is widely distributed in lymphoid tissues and plays a central role in lymphocyte maturation, macrophage activation and cell-mediated immunity. Chronic inflammation and immune activation associated with CKD increase ADA activity, particularly in patients receiving maintenance hemodialysis. Elevated serum ADA has been proposed as a marker of inflammatory activity and may complement oxidative stress markers such as MDA in evaluating CKD severity [14].

Material and Methods

The study was conducted in the Department of Biochemistry with the collaboration of Department of General Medicine in Government medical college & General Hospital, Kadapa. 50 patients with CKD and 50 healthy controls were included in the study.

- *Group I:* Control group
 - a) This group consists of healthy subjects.
 - b) Age group between 20-70years from both sex
- *Group-II:* Study group

Inclusion criteria:

- a) Chronic Kidney Disease
- b) CKD patients not undergoing haemodialysis
- c) Subjects with age group of 20-70years from both sex

Exclusion criteria: Subjects with other chronic inflammatory diseases, patients on haemodialysis, acute infections, Diabetes Mellitus, tuberculosis and liver diseases were excluded from the study.

Sample collection storage and processing: For each case and control group, about 5 ml of blood will be obtained by venipuncture. Blood sample was collected in plain tubes. Blood will be allowed to clot at room temperature for about 30 minutes and then centrifuged at 3000 rpm for 15 minutes. The separated serum was stored until further analysis.

Statistical Analysis: Data will be collected and entered in MS excel worksheets and results will be analysed with appropriate statistical tools like ‘t’ test and Pearson’s correlation using SPSS software.

Results were expressed as mean $\pm$ standard deviation. The significance of difference in means between controls and study group was done by unpaired ‘t’ test.

Determination of Biochemical parameters: The parameters Urea, creatinine and calcium were analyzed by fully Automated Chemistry Analyzer; Beckman Coulter AU480. Creatinine was analyzed by Jaffe’s method,

Urea was analyzed by Glutamate Dehydrogenase (GLDH) method, Calcium was analyzed by O – Cresolphthelein Complexone (OCPC) method. Phosphorous was analyzed by Molybdate UV method.

ADA was analyzed by purine nucleoside phosphorylase-xanthine oxidase (PNP-XOD) kinetic method. Malondialdehyde (MDA) was estimated by thiobarbituric acid reactive substances (TBARS) method.

Results

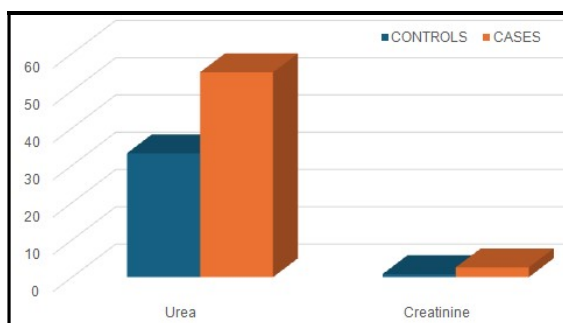
Data analysis was done using SPSS programme. p value was used to compare the groups. p value < 0.05 was considered significant. Table-1 shows that MDA, ADA and Phosphorous levels were significantly higher in the CKD compared with control group (p<0.05). The mean Calcium levels were significantly lower in the CKD compared with control group (p<0.05) (fig-1).

Table-1: Comparison of study variables in subjects with CKD and controls				
Sl. No.	Parameters	CKD (n-50) Mean ± SD	Controls (n-50) Mean ± SD	'p' value
1.	FBS (mg/dl)	96.43±7.25	94.74±8.98	<0.026
2.	Urea (mg/dl)	54.96 ±6.71	33.24±3.0796	<0.0001
3.	Creatinine (mg/dl)	2.63±0.4915	0.84±0.1524	<0.0001
4.	Calcium (mg/dl)	7.55±0.3548	9.87±0.5998	<0.0001
5.	Phosphorous (mg/dl)	7.10±0.3899	3.743±0.3442	<0.0001
6.	ADA (U/L)	52.08±4.5353	31.61±2.7521	<0.001
7.	MDA (µmol/L)	6.96±0.2628	4.23±0.3625	<0.0001
ADA-Adenosine deaminase, MDA- Malondialdehyde				

Fig-1: Comparison of ADA, MDA, Calcium & Phosphorous between Control and Study group.



Fig-2: Comparison of Urea & Creatinine between Control and Study group.



Pearson's correlation analysis revealed significant negative correlations between serum creatinine and Calcium (r = - 0.194, p = 0.017). The significant positive correlation was observed between serum creatinine and Phosphorus (r = + 0.211, p = 0.019), ADA (r = + 0.138, p = 0.025) and MDA (r = + 0.306, p = 0.001). These results are detailed in Table-2 (Fig-2).

Table-2: Correlation between serum creatinine and phosphorous, ADA, MDA, Calcium			
Parameters	Pearson's r	p-value	Interpretation
Creatinine vs Phosphorus	+ 0.211	0.019	statistically significant
Creatinine vs ADA	+ 0.138	0.025	statistically significant
Creatinine vs MDA	+ 0.306	0.001	statistically significant
Creatinine vs Calcium	- 0.194	0.017	statistically significant
ADA-Adenosine deaminase, MDA- Malondialdehyde			

Discussion

Chronic kidney disease (CKD) is a progressive disorder characterized by irreversible loss of nephron function, leading to impaired excretion of metabolic waste products and disturbances in mineral metabolism, oxidative stress, and chronic inflammation. As renal function declines, abnormalities in calcium-phosphorus homeostasis become more pronounced and are accompanied by increased production of reactive oxygen species and inflammatory mediators. These alterations contribute significantly to cardiovascular morbidity and mortality, which remain the leading causes of death in CKD patients [15].

The present study demonstrated significantly higher serum urea, creatinine, phosphorus, ADA, and MDA levels, along with significantly lower serum calcium levels in CKD patients compared with healthy controls.

The significant elevation of serum urea and creatinine observed in the present study reflects reduced glomerular filtration rate and impaired renal excretory function, which are characteristic biochemical features of CKD. Similar observations have been reported by Webster et al., who described progressive accumulation of nitrogenous waste products with declining renal function [15].

A significant reduction in serum calcium with a concomitant increase in serum phosphorus was observed among CKD patients. Reduced renal phosphate excretion results in phosphate retention, while impaired activation of vitamin D decreases intestinal calcium absorption, leading to hypocalcaemia and secondary hyperparathyroidism. These abnormalities collectively constitute chronic kidney disease–Mineral and Bone Disorder (CKD-MBD). The findings of the present study are consistent with the KDIGO CKD-MBD Guideline, which recommends regular monitoring of calcium and phosphorus because disturbances begin early in CKD and worsen with disease progression [16].

Serum MDA levels were also significantly higher in CKD patients than in controls, indicating enhanced lipid peroxidation and oxidative stress. Increased oxidative stress in CKD results from excessive production of reactive oxygen species

together with reduced antioxidant defence mechanisms. Elevated MDA levels have consistently been reported in CKD patients and are associated with progressive deterioration of renal function. These findings are in agreement with Dounousi et al., who demonstrated progressively increasing oxidative stress with advancing stages of CKD [7].

Serum ADA levels were significantly elevated in CKD patients compared with healthy controls. ADA is a key enzyme involved in purine metabolism and cellular immunity. Increased ADA activity reflects persistent activation of lymphocytes and macrophages caused by chronic inflammation associated with uraemia. Similar findings were reported by Melissinos et al., who demonstrated significantly increased ADA activity in patients with chronic renal failure and suggested that elevated ADA reflects immune activation in CKD [11].

Overall, the biochemical alterations observed in the present study indicate that CKD is associated with impaired renal function, disturbed mineral metabolism, chronic inflammation, and increased oxidative stress, all of which contribute to disease progression and increased cardiovascular risk.

Creatinine versus Phosphorus: The present study demonstrated a significant positive correlation between serum creatinine and phosphorus ($r = +0.211$, $p = 0.019$). As renal function deteriorates, phosphate excretion decreases, resulting in progressive phosphate retention. Consequently, serum phosphorus levels increase with rising serum creatinine concentrations. Similar findings have been reported in the KDIGO CKD-MBD Guideline which identifies hyperphosphatemia as an important consequence of declining kidney function and a major contributor to CKD-MBD [16].

Creatinine versus ADA: A significant positive correlation was observed between serum creatinine and ADA ($r = +0.138$, $p = 0.025$). Progressive renal dysfunction is accompanied by persistent immune activation and chronic inflammation, leading to increased ADA

activity. Elevated ADA reflects enhanced lymphocyte proliferation and macrophage activation in response to uraemia. Similar observations were reported by Melissinos et al., who found increased ADA activity in patients with chronic renal failure and suggested its role as an indicator of inflammatory activity [11].

Creatinine versus MDA: The present study showed a positive correlation between serum creatinine and MDA ($r = +0.306$, $p = 0.001$), indicating that oxidative stress increases with worsening renal function. Declining kidney function promotes accumulation of uremic toxins and excessive generation of reactive oxygen species, resulting in increased lipid peroxidation and elevated serum MDA concentrations. Dounousi et al. similarly demonstrated that oxidative stress progressively increases with advancing stages of CKD, supporting the findings of the present study [7].

Creatinine versus Calcium: A significant negative correlation was observed between serum creatinine and calcium ($r = -0.194$, $p = 0.017$). As renal function declines, impaired activation of vitamin D reduces intestinal calcium absorption, while phosphate retention further lowers serum calcium concentration through calcium-phosphate complex formation. Consequently, worsening renal dysfunction is associated with progressive hypocalcaemia. Similar observations have been reported in the KDIGO CKD-MBD Guideline and by Moe et al., who described declining serum calcium as a characteristic feature of CKD-MBD [4, 16].

Conclusion

CKD is associated with disturbed mineral metabolism, increased oxidative stress and

chronic inflammation. This study revealed significant increase in Phosphorus, MDA, ADA and a significant decrease in calcium. There is a significant positive correlation between creatinine and Phosphorus, MDA, ADA, significant negative correlation between creatinine and calcium.

The present study demonstrated significant hypocalcaemia, hyperphosphatemia, and elevated serum MDA levels in CKD patients. These biochemical abnormalities reflect CKD-mineral and bone disorder and increased oxidative stress, both of which are associated with an increased risk of vascular calcification and cardiovascular complications. Monitoring these parameters may help identify patients at higher risk and support appropriate clinical management.

Notably, the present study has several limitations. Assessment of serum calcium, phosphorus, MDA, and ADA may aid in identifying CKD-related metabolic abnormalities, monitoring disease progression, and recognizing patients at increased risk of cardiovascular complications.

All participants enrolled in this study were of Andhra Pradesh population, which may limit the generalizability of the findings to other populations. Furthermore, although adenosine deaminase (ADA) primarily acts on adenosine, adenosine concentrations were not measured concurrently in this study, limiting the ability to evaluate the relationship between ADA activity and its physiological substrate. Therefore, additional research involving larger and more diverse populations is needed to confirm our findings and overcome the limitations of this study.

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