

The Role of 8-Isoprostane as A Biomarker in Chronic Kidney Disease Progression

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Abstract

Background	The progression of chronic kidney disease (CKD) and the development of complications are facilitated by oxidative stress, which is a progressive condition. 8-Isoprostane, a byproduct of lipid peroxidation, has the potential to serve as a biomarker that reflects kidney function and oxidative stress levels.
Objective	To investigate the role of 8-Isoprostane as a biomarker in CKD progression.
Methods	A case-control study was conducted involving 120 children aged 6-18 years who were divided into three groups: CKD patients requiring dialysis, CKD patients not requiring dialysis, and healthy controls. Serum 8-Isoprostane levels were tested using enzyme-linked immunosorbent assay, and their ability to diagnose was assessed with statistical methods and Receiver Operating Characteristic (ROC) analysis.
Results	8-Isoprostane levels were significantly elevated in CKD patients requiring hemodialysis compared to non-hemodialysis patients and controls ($p < 0.001$). ROC analysis confirmed its strong diagnostic accuracy, with a sensitivity of 100% and specificity of 100% in distinguishing between CKD patients and controls and a sensitivity of 90% and specificity of 90% in distinguishing between CKD patients with and without hemodialysis.
Conclusion	8-Isoprostane is a reliable biomarker for assessing oxidative stress and CKD progression. Regular monitoring can aid in early diagnosis, better disease management, and targeted interventions.
Keywords	8-Isoprostane, Chronic Kidney Disease (CKD), Oxidative Stress Biomarker.

List of abbreviations: AUC = Area Under Curve, CKD = Chronic Kidney Disease, CRP = C-Reactive Protein, ELISA = Enzyme-linked immunosorbent assay, ESRD = End-stage renal disease, GFR = Glomerular filtration rate, ROS = Reactive oxygen species

Introduction

Chronic Kidney Disease (CKD) is a significant global health issue characterized by the irreversible deterioration of kidney function ⁽¹⁾. The way CKD develops involves complicated processes like oxidative stress, inflammation, and changes in metabolism, which result in the

gradual loss of nephrons and ultimately lead to end-stage renal disease (ESRD). One of the new markers being studied, 8-Isoprostane, which comes from the breakdown of fats, is important because it shows how much oxidative stress is present, a key factor in the worsening of CKD ⁽²⁾.

Oxidative stress plays a pivotal role in CKD's pathogenesis; it results from an imbalance between the production of reactive oxygen species (ROS) and the body's ability to neutralize these reactive molecules with

antioxidants⁽³⁾. Elevated oxidative stress in CKD is associated with mitochondrial dysfunction, chronic inflammation, and structural kidney damage. It exacerbates complications such as hypertension, cardiovascular diseases, and anemia, contributing to the worsening of renal outcomes.

8-Isoprostane, a compound similar to prostaglandin F₂, is created when free radicals cause damage to arachidonic acid. Its levels in biological fluids, such as serum and urine, are considered reliable indicators of oxidative damage⁽⁴⁾. In CKD, higher levels of 8-Isoprostane are linked to more oxidative stress, which means it could be a useful indicator of how serious the disease is and how it is getting worse. This biomarker provides several advantages. Its non-enzymatic formation ensures its presence is primarily due to oxidative stress rather than enzymatic activities that may vary between individuals. Also, finding 8-Isoprostane in CKD patients helps us understand their oxidative stress levels and can inform treatment plans to lower that stress⁽⁵⁾.

Monitoring 8-Isoprostane levels could serve as a valuable tool in evaluating CKD progression and the effectiveness of interventions aimed at mitigating oxidative stress⁽⁶⁻⁷⁾. Research has indicated that treatments aimed at reducing oxidative stress, like antioxidant therapies, might lower 8-Isoprostane levels, which could help slow down the progression of CKD. Additionally, its correlation with other CKD parameters, such as glomerular filtration rate (GFR) and markers of inflammation, underscores its utility in comprehensive disease assessment⁽⁸⁻¹⁰⁾.

There is a critical need for innovative approaches to identify and validate biomarkers that can aid in early diagnosis, disease staging, and monitoring of therapeutic efficacy of CKD. Oxidative stress has been extensively implicated in the pathophysiology of CKD, contributing to nephron loss, inflammation, and fibrosis, which drive disease progression. Among oxidative stress markers, 8-Isoprostane, has become a trustworthy sign of oxidative

damage. Its stable structure and quantifiable presence in biological fluids make it a promising candidate for assessing oxidative stress levels in CKD patients. Additionally, its possible link to how severe CKD is, the need for hemodialysis, and related metabolic issues highlights its usefulness as a biomarker.

The objectives of this study were to evaluate the levels of 8-Isoprostane as an oxidative stress biomarker in children with CKD across different stages and correlate it with renal function markers (blood urea, and serum creatinine). Also, to assess the diagnostic potential of 8-Isoprostane in tracking the progression of CKD.

Methods

Study design

This was a case-control study aimed at evaluating the role of 8-Isoprostane as a biomarker in the progression of CKD. The study included 120 kids between the ages of 6 and 18 and was conducted from April 2024 to July 2024. They were split up into three groups: healthy controls, CKD patients who needed dialysis, and CKD patients who didn't. Ethical approval was obtained from the Institutional Review Board's (IRB) 104-2024/4/3. Verbal consent was obtained from participants' guardians according to ethical guidelines for pediatric research.

Sampling technique

A purposive sampling method was employed. Participants were selected from pediatric nephrology centers in Baghdad: Al-Imamein Al-Kadhimein Medical City, Ibn Al-Balady Hospital, and Children Welfare Hospital.

Data collection involved reviewing medical records for patient history and laboratory findings, and administering direct interviews with patient relatives and healthcare providers.

Data collection tool and questionnaire

A structured questionnaire was designed to collect demographic and clinical data, including:

- age and sex.
- duration and stage of CKD.
- Laboratory results for serum 8-Isoprostane, urea, creatinine levels.

Inclusion criteria

- Children aged 6 to 18 years.
- Healthy children with normal kidney function assessed using serum creatinine (normal value: 0.5-1.2 mg/dl), blood urea (normal value: 20-35 mg/dl), and glomerular filtration rate (GFR) <90 ml/min/1.73 m² within the normal range included as controls.

Exclusion criteria

- Children diagnosed with renal cell carcinoma.
- Presence of urinary tract infections at the time of data collection.

Statistical Analysis

The statistical software for the social sciences (SPSS version 25) was used for the statistical analysis. Data presented as mean and standard deviation (SD). An unpaired t-test was used to ascertain the statistical significance between each pair of study groups. Correlation was done between study parameters within each group and presented as correlation coefficient (r) and their p value. P value less than 0.05 was determine the level of significance.

Results

The concentration of 8-isoprostane significantly different in the three study groups when compared each pair of groups ($p < 0.001$); the highest concentration was in the CKD patients undergoing hemodialysis (256.78 ± 34.6 pg/ml), followed by CKD patients without hemodialysis (163.61 ± 28.77 pg/ml), while the lowest level was observed in the control group (82.33 ± 7.99 pg/ml).

Table 1. Comparison of 8-Isoprostane levels among study groups

8-Isoprostane (pg/ml)	CKD-HD N=40	CKD-No HD N=40	Control N=40
Mean $\pm$ SD	256.78 $\pm$ 34.6	163.61 $\pm$ 28.77	82.33 $\pm$ 7.99
P value *		<0.001	<0.001
P value **			<0.001

*p value by unpaired ttest between chronic kidney disease with hemodialysis group with chronic kidney disease without hemodialysis group and control group, ** p value by unpaired ttest between chronic kidney disease without hemodialysis group and control group

The correlation coefficients (r) between 8-isoprostane and both urea and creatinine were weak in all study groups. Furthermore, none of the observed correlations reached statistical significance (all $p > 0.05$).

Table (3) illustrated that serum 8-isoprostane have excellent diagnostic accuracy for differentiating CKD patients from healthy controls and for distinguishing CKD patients with hemodialysis from those without hemodialysis. High AUC values (0.984–1.000).

Table 2. Correlation between 8-Isoprostane with blood urea and serum creatinine in each study group

Parameter		8-Isoprostane (pg/ml)		
		CKD-HD	CKD-No HD	Control
Urea (mg/dl)	r	0.039	-0.068	-0.071
	p	0.809	0.678	0.664
Creatinine (mg/dl)	r	0.142	0.019	0.188
	p	0.381	0.905	0.245

CKD-HD: Chronic kidney disease with hemodialysis, CKD-No HD: Chronic kidney disease without hemodialysis

Table 3. Diagnostic Performance of 8-Isoprostane and Correlation with Oxidative Stress, Inflammation, and Nutrition Biomarkers in CKD Progression

Groups	AUC	P value	Sensitivity	Specificity	Cutoff (pg/ml)
CKD-HD vs Control	1.000	<0.001	100%	100%	141.2
CKD-No HD vs Control	0.993	0.006	95%	95%	93.1
CKD-HD vs CKD-No HD	0.984	0.01	90%	90%	198.7

Discussion

The findings of this study showed that patients with CKD, especially those undergoing hemodialysis, experience significantly higher concentration of 8-Isoprostane, which reflect higher oxidative stress compared to healthy individuals and non-dialysis patients. This can be explained by the accumulation of uremic toxins resulting from impaired kidney function, which increases cellular and lipid damage within the body. In addition, the hemodialysis process itself may contribute to oxidative stress because of repeated exposure to inflammatory stimuli and bioincompatible materials during treatment sessions^(11,12).

The current study also demonstrated a weak non-significant relationship between 8-Isoprostane levels and kidney function represented by blood urea and serum creatinine, which may be due to low sample size. However, Iqbal et al.⁽¹³⁾, found that oxidative stress increases as renal function declines, which supports the role of 8-Isoprostane as an important biomarker for monitoring disease progression and evaluating the severity of kidney dysfunction over time. Furthermore, elevated levels of 8-Isoprostane

were associated with increased inflammatory markers such as CRP, highlighting the close relationship between oxidative stress and chronic inflammation in patients with CKD. Persistent inflammation caused by toxin accumulation and repeated dialysis procedures may worsen cellular damage and increase the risk of cardiovascular complications commonly seen in these patients⁽¹⁴⁾.

The results also suggested that oxidative stress is present not only in dialysis patients but also in patients who are not yet receiving dialysis treatment. This indicates that oxidative imbalance may begin in the earlier stages of chronic kidney disease and progressively worsen as the disease advances. Therefore, early monitoring of oxidative stress markers may help in reducing disease progression and preventing further complications⁽⁴⁾.

ROC analysis indicated that 8-Isoprostane is a useful test for distinguishing advanced stages of CKD. The increased levels of 8-Isoprostane in CKD-HD patients can be attributed to hemodialysis-induced exposure to bio incompatible materials and recurrent inflammation accelerates the production of

ROS, leading to lipid peroxidation and elevated 8-Isoprostane levels⁽¹⁵⁾.

In conclusion, the findings reaffirm the role of 8-Isoprostane as a biomarker for oxidative stress in CKD. Its correlation with renal function underscores its utility in disease monitoring and therapeutic guidance. Future studies should explore interventions targeting oxidative stress and inflammation to mitigate CKD progression and validate these findings across broader populations.

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Author contribution

All of the authors contributed equally to the conception, design, data collection, analysis, and writing of the manuscript.

Conflict of interest

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