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Investigating Serum LDH in Iraqi Patients Undergoing Dialysis for Chronic Kidney Disease

Ahmed A. Saleem[1] *HD*, **Mohammed I. Hamza**[2] *PhD*

[1]Al-Hakim General Hospital, Al-Najaf, Iraq, [2]Dept. of Clinical Biochemistry, College of Medicine, Al-Nahrain University, Baghdad, Iraq

Abstract

Background Chronic kidney disease (CKD) has emerged as a prominent cause of mortality, following cardiac disease and cancer, exhibiting a substantial surge over the past two decades. One biochemical indicator that reflects cellular damage is lactate dehydrogenase (LDH), a key intracellular enzyme involved in the interconversion of pyruvate and lactate during glycolysis. Under normal conditions, LDH remains confined within cells; however, tissue damage can lead to its release into the bloodstream, resulting in elevated serum levels.

Objective To assess the LDH in CKD patients compared with healthy control.

Methods A total forty (40) patient with CKD were studied among them twenty (20) female and twenty (20) male patients and forty (40) healthy as controls, of them were eighteen (18) females and twenty-two (22) males. Their ages (patients and controls) were ranged from (18-70). Blood samples were collected from patients and control to evaluate serum levels of serum LDH and evaluate the routine markers (urea, creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and this was done by spectrophotometry.

Results This result showed the LDH levels in the patients were significantly higher (224.64±113.39 U/L) than in the control group (176.26±38.99 U/L) (P = 0.014). ALT and AST levels in the patients were lower than in the control group, but the difference was not statistically significant for ALT (P = 0.132) and was significant for AST (P = 0.03). The urea, and serum creatinine levels in the patients were all significantly higher than in the control group (P <0.001).

Conclusion Serum LDH levels were significantly elevated in CKD patients undergoing hemodialysis compared to healthy controls, suggesting that LDH may serve as a useful biomarker for tissue damage and disease severity in patients with CKD.

Keywords Chronic kidney disease, lactate dehydrogenase, hemodialysis.

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List of abbreviations: CKD = Chronic kidney disease, ESRD = end-stage renal disease, LDH = Lactate dehydrogenase

Introduction

Chronic kidney disease (CKD) is a major public health concern worldwide, characterized by a gradual and irreversible loss of kidney function. According to the Kidney Disease Improving Global Outcomes (KDIGO) guidelines, CKD is defined by structural or functional abnormalities of the kidney lasting more than three months, with implications for health [(1)]. In advanced stages, particularly end-stage renal disease (ESRD), patients require renal replacement therapy, including dialysis, to survive. In Iraq, the burden of CKD has grown

substantially, driven by increasing prevalence of risk factors such as diabetes mellitus, hypertension, and cardiovascular diseases [2].

Serum lactate dehydrogenase (LDH) levels in patients with CKD on dialysis is a significant area of research, as it relates to metabolic functions and patient outcomes. Elevated LDH levels have been associated with increased mortality risks in hemodialysis patients, indicating a potential biomarker for patient management [3]. A study has showed that serum LDH levels in ESRD patients are significantly higher than in healthy controls, suggesting a metabolic disturbance [4].

Hemodialysis can further elevate LDH levels due to hemoconcentration and enzyme release from blood components during the procedure [2]. Higher baseline LDH levels (>280 U/L) correlate with increased all-cause and cardiovascular mortality in dialysis patients [3].

Monitoring LDH levels may provide insights into patient prognosis and guide clinical decisions in managing CKD patients on dialysis [3,4].

While elevated LDH levels indicate potential risks, it is essential to consider that not all patients with high LDH levels experience adverse outcomes, as individual responses to dialysis and underlying conditions can vary significantly, therefore, this study aimed to evaluate serum levels of LDH and some biochemical parameters in a sample of Iraqi patients undergoing hemodialysis for CKD, and to explore potential associations among these biomarkers, as understanding these biochemical changes may contribute to better monitoring and management of patients on dialysis.

Methods

This case control study was included 80 participants age ranged from 18 to 70 years, consisted of patients diagnosed as CKD, all patients are under hemodialysis compared to 40 healthy persons as controls were enrolled serially in the study. The control subjects were taken from the same socioeconomic population who matched for their age and body mass index (BMI) with the cases. All persons in control group were having normal kidney function. All the participants notified about the goals of the study, and informed. All patients were attended from Al-Hakim General Hospital (Dialysis Unit) and Al-Najaf Teaching Hospital in Al-Najaf. Patients and controls were with a comparable age.

Exclusion criteria

Patients with cardiovascular disease, liver disease, diabetes disease, thyroid disease, leukemia or elderly patient above 70 years.

Sample collection

Five mL of blood were taken from each patient and control; serum was centrifuged at 2000 rpm for 5-10 min. The levels of serum LDH, urea, creatinine and some of liver enzymes including alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were measured.

Measurement of LDH

This test is measured by a colorimetric spectrophotometer.

Principle

LDH is an oxidoreductase enzyme that catalyzes the reversible oxidation of lactate to pyruvate using NAD+ as hydrogen acceptor. The equilibrium favors the conversion of pyruvate to lactate at pH 7.4–7.8. The decrease in absorbance at 340 nm is directly proportional to LDH activity.

$$\text{Lactate} + NAD^+ \overset{LDH}{\longleftrightarrow} \text{Pyruvate} + \text{NADH} + H^+$$

Calculation

$$\text{Serum Copper conc. (U/dL)} = \frac{\Delta A_{sample}}{\Delta_{min}} * 8095$$

Statistical analysis

Data analysis was performed using statistical package for social sciences software version 22 (SPSS Inc. Chicago, Illinois, United States). The Shapiro Wilk normality test was used to determine whether the studied parameters

follow a Gaussian distribution. Categorical variables were expressed as frequencies and proportions. Proportions were compared using the chi-square (x2) test. Expressed report data as mean standard deviation (SD) for continuous variables. Tukey's Post Hoc tests were applied for multiple comparison after analysis of variance (ANOVA) test. Scores were analyzed correlation between variables by Pearson correlation analysis. In addition, receiver operating characteristic (ROC) was used to evaluate the area under the curve (AUC). The best cut-off point for the studied signs was also calculated sensitivity and specificity. A P value less than 0.05 was considered significant statistically [5].

Results

Demographic parameters

The distribution of sex within both groups was relatively balanced. In the patient group, there is an equal split between males and females. In the control group, there is a slight male predominance with 55% males and 45% females. However, there was no significant difference P >0.05 in the distribution of sex between the groups. show this in figure (1).

Regarding age; the mean age of the patients was (44.68±16.19 years) and of the control group (46.95±15.03 years) with no significant difference (P = 0.522) as shown in figure (2).

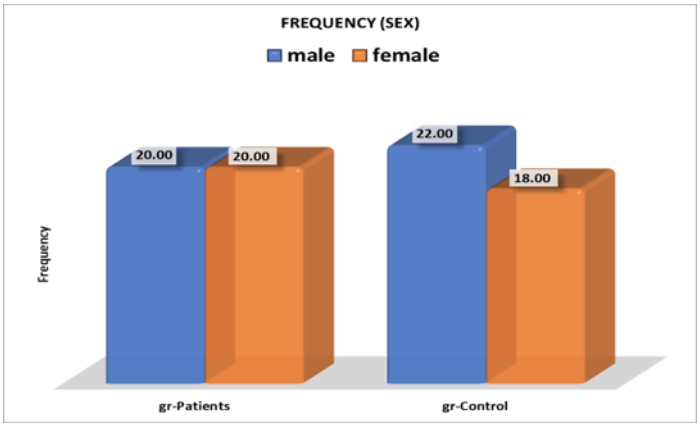

Figure 1. Sex distribution between the groups

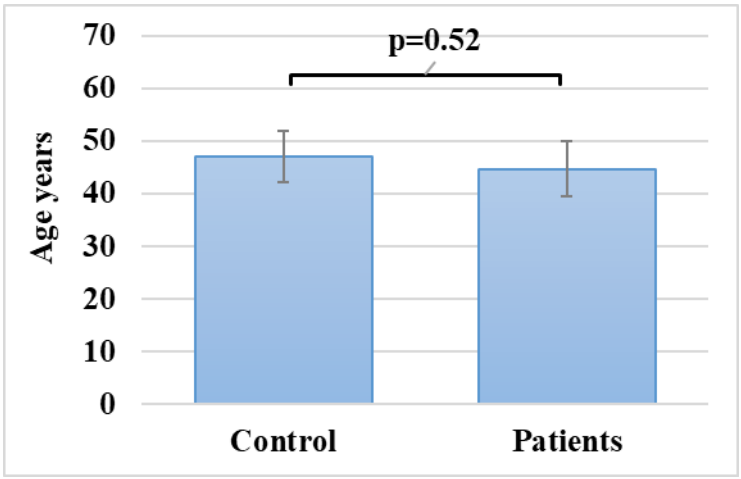

Figure 2. Bar chart for means & 95%Confidence interval error bars of (Age) of both study groups

The BMI of the patients was significantly lower (23.79±3.97) than that of the control group (27.19±3.82) (P <0.001) as shown in figure (3).

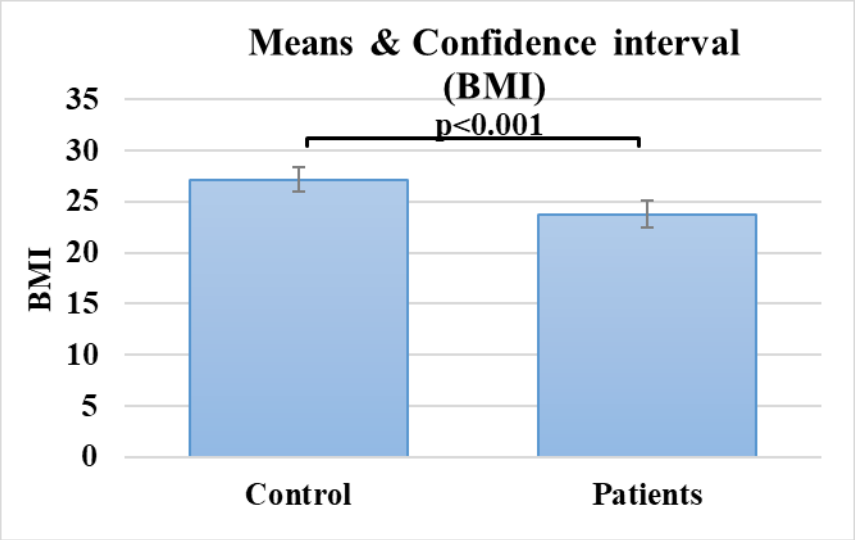

Figure 3. BMI In both study groups

Biochemical parameters

LDH

As shown in table (1) and figure (4), LDH levels in the patients were significantly higher (224.64±113.39 U/L) than in the control group (176.26±38.99 U/L) (P = 0.014).

ALT and AST

ALT and AST levels in the patients were lower than in the control group, but the difference is not statistically significant for ALT (P = 0.132) and was significant for AST (P = 0.03) (Table 1).

Blood urea and serum creatine

The urea, and serum creatinine levels in the patients were all significantly higher than in the control group (P <0.001 for both) (Table 1).

Table 1. presents a comparison of various health parameters between chronic kidney disease patients on hemodialysis and a control group

Variables	Statistic	Min	Max	Range	Median	Mean± SD	SEM	p-values
LDH (U/L)	Patients	105.24	623.32	518.08	194.09	224.64± 113.39	18.16	0.014
	Control	89.04	250.95	161.91	174.05	176.26± 38.99	6.24	
ALT(U/L)	Patients	9.30	70.00	60.70	20.00	23.48± 12.49	2.00	0.132
	Control	14.0	41.00	27.00	28.00	27.10± 8.07	1.29	
AST(U/L)	Patients	12.0	41.00	29.00	22.00	22.63± 7.93	1.27	0.030
	Control	16.0	40.00	24.00	27.00	26.65± 8.13	1.30	
(Urea) mg/dL	Patients	72.00	227.0	155.0	124.0	126.33± 33.94	5.43	<0.001
	Control	11.00	44.00	33.00	27.00	27.53± 7.97	1.28	
(S. Cr) mg/dL	Patients	4.72	14.80	10.08	8.40	8.98± 2.44	0.39	<0.001
	Control	0.55	1.10	0.55	0.86	0.86± 0.13	0.02	

The parameters are presented as mean values with standard deviations, SEM=Standard error of the mean and the significance of the differences between the two groups is indicated by p-values using students t-test

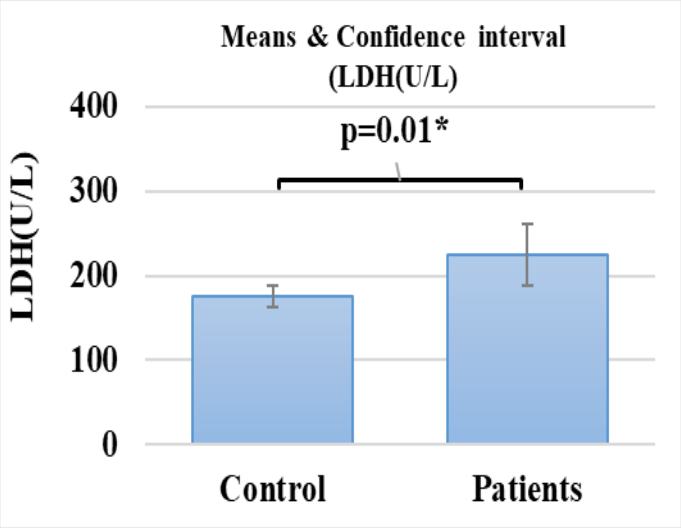

Figure 4. LDH in both study groups

When Pearson correlation was done between LDH with measured liver enzymes (ALT and AST), and with renal function parameters (urea and creatinine), there was insignificant correlation with each one of these parameters in both groups (patients and controls) (P value >0.05) as shown in table (2).

Table 2. Pearson correlation coefficient between the lactate dehydrogenase and other studied parameters in patients and control groups

Parameter		LDH (U/L)	
		Control group	Patients
Age (yr)	r	-0.03	-0.09
	p	0.85	0.57
BMI (kg/m^2)	r	0.03	-0.11
	p	0.84	0.50
ALT (U/L)	r	-0.01	-0.02
	p	0.95	0.91
AST (U/L)	r	-0.05	-0.19
	p	0.75	0.25
Urea (mg/dl)	r	0.06	-0.02
	p	0.70	0.89
Creatinine (mg/dl)	r	0.02	-0.06
	p	0.91	0.70

Discussion

LDH is a crucial enzyme present in almost all cells of the human body, primarily found in the cytoplasm [3]. The highest concentrations of LDH are observed in organs like the heart, liver, lungs, kidneys, skeletal muscle, red blood cells, and lymphocytes [4]. Elevated LDH levels are associated with severe diseases, tissue damage, and multiple organ failure. LDH plays a significant role in kidney diseases, particularly CKD. In patients with CKD, LDH levels can serve as a biomarker for early renal damage [5].

No significant correlation was found between LDH and age in either group ($p < 0.05$). However, a previous study suggests that LDH levels tend to increase with age, possibly due to age-related comorbidities and physiological changes [6].

CKD patients exhibited significantly lower BMI ($p < 0.001$), likely reflecting protein-energy wasting and catabolic imbalance. Muscle wasting may contribute to increased LDH leakage from skeletal muscle. While high BMI is generally associated with better survival in HD patients, some studies suggest that acute illness and inflammation may have a more substantial impact on CKD progression than BMI alone [7].

In the current study, the observed significant increase in LDH levels among CKD patients undergoing HD ($p = 0.014$) aligns with findings from prior research. LDH is a cytoplasmic enzyme released during cellular damage, and its elevation in CKD patients is often attributed to multiple factors including uremic toxicity, oxidative stress, and the mechanical stress of dialysis itself.

Elevated LDH levels have been associated with kidney damage, particularly in diabetic kidney disease [8], and are frequently observed in ESRD patients, potentially due to the HD process itself [9].

A study in by 2021 Ryu et al. [10] highlighted that elevated LDH levels in incident HD patients were independently associated with increased all-cause mortality, suggesting that LDH may serve as a prognostic biomarker in this population. The authors proposed that LDH reflects systemic inflammation and cellular turnover, both of which are heightened in advanced CKD and during HD. Furthermore, in 2022, Fang et al. [11] reported a positive correlation between LDH levels and corrected QT (QTc) interval prolongation in maintenance HD patients, indicating that elevated LDH may also be linked

to cardiovascular risk in this group. These findings support the notion that LDH elevation is not merely a biochemical anomaly but may have clinical implications in the management and risk stratification of CKD patients on dialysis. LDH levels in CKD patients undergoing HD have been shown to correlate with changes in liver enzymes, particularly AST and ALT, suggesting a shared metabolic or tissue injury pathway. A study published in Clinics found that patients with CKD undergoing HD exhibited lower AST and ALT levels, while LDH levels were often elevated. The authors suggested that LDH elevation may reflect tissue damage or metabolic stress, whereas reduced aminotransferases could be due to pyridoxine deficiency or hemodilution effects common in HD patients [12]. Similarly, another study emphasized that good liver function is crucial in CKD, and alterations in AST and ALT levels may accompany shifts in LDH, especially in the context of anemia and systemic inflammation during dialysis [13]. In an Iraqi cohort study, researchers observed that LDH levels were elevated in CKD patients on HD, while AST and ALT levels remained within the lower normal range, reinforcing the idea that LDH may serve as a more sensitive marker of cellular stress or injury in this population [14].

Regarding correlation between LDH and blood urea, current results showed no significant correlation in both patients and control group. Elevated BUN has been independently associated with adverse renal outcomes and anemia in CKD [15,16]. Vanholder et al. [17] emphasized that while urea is a marker of uremic retention and dialysis adequacy, it also exerts direct toxic effects, including oxidative stress and apoptosis, particularly at concentrations typical in CKD patients. However, LDH, a cytoplasmic enzyme released during tissue injury, may reflect broader cellular damage rather than renal clearance efficiency alone. This distinction is important because LDH elevation may result from muscle breakdown, inflammation, or dialysis-induced hemolysis, rather than directly from impaired nitrogen metabolism as indicated by blood urea levels.

Although serum creatinine levels were markedly higher in CKD patients ($p < 0.001$), LDH did not significantly correlate with creatinine ($p > 0.05$), suggesting that LDH elevation may occur independently of renal clearance failure. Nonetheless, LDH is considered a sensitive biomarker for renal tubular injury and may better reflect early or ongoing damage compared to creatinine, which often lags in response [18]. A study by Tang et al. [19] investigated the association between LDH and diabetic kidney disease and found that while LDH levels were elevated in patients with impaired renal function, the correlation with serum creatinine was not consistently significant, indicating that LDH may reflect broader tissue injury or metabolic stress rather than glomerular filtration efficiency alone.

In conclusion, serum LDH levels were significantly elevated in CKD patients undergoing hemodialysis compared to healthy controls, suggesting that LDH may serve as a useful biomarker for tissue damage and disease severity in patients with CKD.

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Author contribution

Both authors had made a substantial, direct, and intellectual contribution to the work, and approved it for publication.

Conflict of interest

The authors declare there is no conflict of interest.

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Correspondence to Dr. Ahmed A. Saleem
E-mail: ahmedaltorfi45@gmail.com
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