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Liver Enzymes in End Stage Renal Disease Patients Diabetic and Non-Diabetic. Does it Differ than General Population?

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ABSTRACT

Background: Hemodialysis remains the standard therapy for end-stage renal disease (ESRD), the final stage of chronic kidney failure often caused by diabetes mellitus (DM). Evaluating liver enzymes—vital markers of hepatic function—is complicated in ESRD due to uremia, dialysis effects, and accompanying illnesses. The specific contribution of DM to these enzyme changes in ESRD is not well defined. This study aimed to assess liver enzyme levels in hemodialysis patients and distinguish the influence of ESRD alone from ESRD combined with DM.
Methods: A cross-sectional analysis included 140 subjects, comprising 70 ESRD patients and 70 healthy controls. Patients were further stratified into diabetic (n=14) and non-diabetic (n=56) groups. Post-dialysis blood samples were examined for hepatic enzymes, albumin, bilirubin, urea, creatinine, electrolytes, coagulation markers, hematologic parameters, and random blood glucose.
Results: Relative to controls, ESRD patients demonstrated significantly increased aspartate transaminase (AST) ($p=0.012$) and alkaline phosphatase (ALP) ($p<0.001$) levels, together with a pronounced decrease in serum albumin ($p<0.001$). Alanine aminotransferase (ALT) showed a slight, non-significant rise, while total bilirubin remained unchanged. Within the ESRD group, diabetics displayed significantly higher AST ($p=0.017$), ALT ($p=0.003$), ALP ($p=0.013$), and albumin ($p=0.034$) levels compared with non-diabetics. Dialysis adequacy indicators, including urea reduction ratio and Kt/V, were markedly lower in diabetic patients ($p=0.005$ and $p=0.039$, respectively).
Conclusion: Post-dialysis liver enzyme levels are elevated in ESRD, particularly when diabetes is present, compared with healthy individuals. These findings highlight the importance of careful interpretation of liver enzyme data in this population.
Keywords: liver enzymes, diabetic, non-diabetic, end stage renal disease

Abbreviations:
ESRD: End-stage renal disease;
DM: Diabetes mellitus;
HD: Hemodialysis;
CKD: Chronic kidney disease;
HTN: Hypertension;
AST: Aspartate aminotransferase;
ALT: Alanine aminotransferase;
ALP: Alkaline phosphatase;
RBG: Random blood glucose;
URR: Urea reduction ratio;
kt/v: Single-pool Kt/V (a measure of dialysis adequacy);
Na: Sodium; K: Potassium;
INR: International normalized ratio;
PT: Prothrombin time;
Hb: Hemoglobin;
TLC: Total leukocyte count;
PLT: Platelet count;
IRB: Institutional Review Board;
GFR: Glomerular filtration rate;
NAFLD: Non-alcoholic fatty liver disease;
NADPH: Nicotinamide Adenine Dinucleotide Phosphate.

INTRODUCTION

End-stage renal disease (ESRD) is the final stage of chronic kidney disease (CKD) and requires renal replacement therapies such as haemodialysis (HD). Globally, the prevalence of ESRD is increasing, largely due to rising rates of diabetes mellitus (DM) and hypertension (HTN). DM accounts for nearly half of ESRD cases, underscoring the strong link between metabolic disorders and progressive renal failure (1).

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Liver function is commonly assessed by measuring aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP). In ESRD, however, the accuracy of these markers is affected by uremia, dialysis treatment, and multiple comorbidities (2).

Abnormal liver enzyme profiles are frequently observed in ESRD patients. Uremic toxins can interfere with hepatic metabolism, while haemodialysis may alter enzyme activity by removing inhibitory substances (3,4). The independent impact of DM on these alterations remains uncertain. Although DM is known to elevate liver enzymes in otherwise healthy individuals, few studies have examined its role in ESRD, forming the rationale for this investigation (5).

The timing of blood sampling relative to dialysis strongly influences aminotransferase levels. Predialysis samples often show reduced values due to vitamin B6 deficiency and uremic suppression, whereas post-dialysis measurements generally reveal higher levels once inhibitors are cleared (6). Such pre- dialysis reductions suggest that even modest post- dialysis increases may be clinically relevant (7) and do not necessarily indicate intrinsic liver pathology (8).

Furthermore, DM is frequently associated with liver conditions such as non-alcoholic fatty liver disease (NAFLD), steatohepatitis, and cirrhosis, complicating the management of ESRD. Chronic hyperglycemia promotes oxidative stress and inflammation, which aggravate hepatic injury and alter enzyme activity, with insulin resistance playing a key role (9).

Therefore, this study aimed to evaluate liver enzyme levels in ESRD patients receiving haemodialysis and to explore the specific effect of coexisting diabetes mellitus on these biochemical markers.

PATIENTS AND METHOD

This cross-sectional study was designed to evaluate liver enzyme levels in patients with end- stage renal disease (ESRD) undergoing haemodialysis and to assess the influence of concurrent diabetes mellitus (DM). A total of 140 participants were recruited from Benha Teaching Hospital and divided into two groups: 70 ESRD patients and 70 healthy controls free from diabetes or renal disease. The patient group was further separated into diabetic (n=14, all on insulin therapy) and non-diabetic (n=56) subgroups. Inclusion criteria required participants to be 18 years or older, have a confirmed ESRD diagnosis, and receive haemodialysis for at least six months. Exclusion criteria included a Body Mass Index (BMI) above 27 or any illness other than chronic kidney disease that could influence metabolic state or hepatic enzyme activity. Specifically excluded were chronic viral hepatitis, malignancy, haemochromatosis, autoimmune hepatitis, non-alcoholic fatty liver disease, metabolic syndrome, alcoholic liver disease, active smoking, recent surgery, pregnancy, lactation, alcohol intake, or use of hepatotoxic medications such as statins.

The protocol received approval from the Institutional Review Board (IRB) of the Faculty of Medicine, Menoufia University. Written informed consent was obtained from all subjects, ensuring confidentiality and the option to withdraw at any point. Comprehensive data were collected for each participant, including demographic details, medical and medication history, laboratory results, and abdominal ultrasonography findings.

Laboratory investigations for all individuals included measurements of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), serum albumin, total bilirubin, urea, creatinine, sodium (Na), and potassium (K). Coagulation parameters were assessed using prothrombin time (PT) and international normalized ratio (INR). Hematologic tests included hemoglobin (Hb), total leukocyte count (TLC), and platelet count (PLT). Random blood glucose (RBG) was used to evaluate glycemic control, while dialysis adequacy was determined by calculating the urea reduction ratio (URR) and single-pool Kt/V. For ESRD patients, blood specimens were drawn immediately after the haemodialysis session.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 26 (Armonk, NY, USA). The distribution of quantitative variables was checked with the Kolmogorov-Smirnov and Shapiro–Wilk tests, supported by visual inspection. Normally distributed data were presented as mean ± standard deviation, and categorical variables were summarized as counts and percentages. Group comparisons of continuous data used the independent samples t-test for parametric variables or the Mann-Whitney U test for non-parametric data. Associations between categorical variables were examined with the Chi-square or Fisher's exact test as appropriate. A two-tailed p-value <0.05 was considered statistically significant.

RESULTS

Of 150 initially screened patients, 10 did not meet

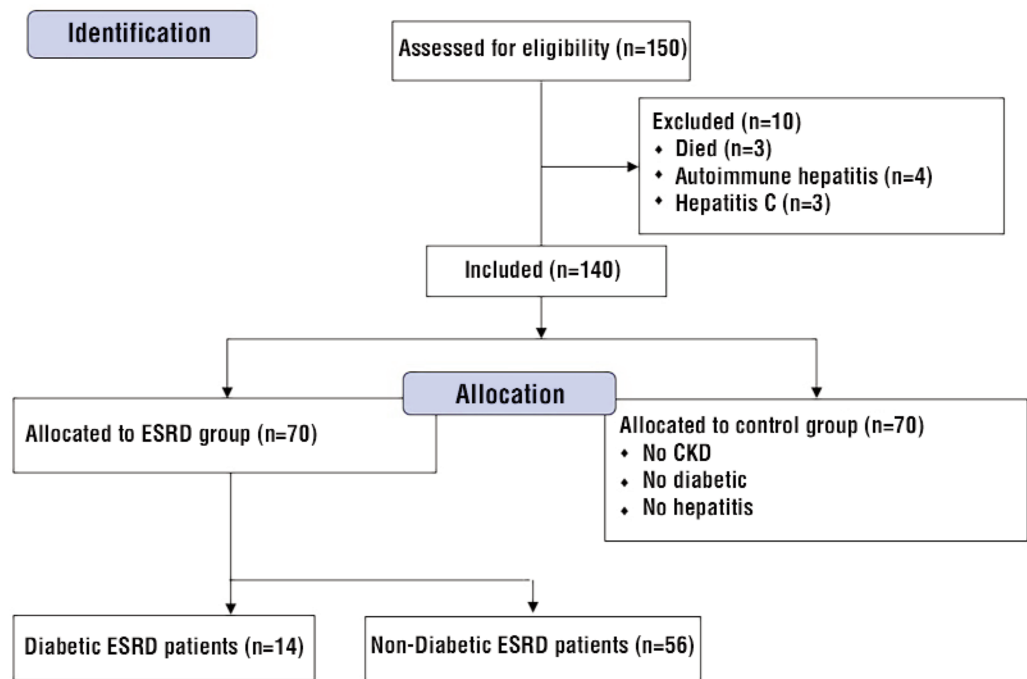

Figure 1 - Flowchart of the enrolled participants.

the inclusion criteria, leaving 140 participants who were enrolled and analyzed (*fig. 1*).

Participants were allocated to an ESRD group (n=70) and a control group of healthy individuals (n=70) free of diabetes or kidney disease. Patients with ESRD were significantly older and had a higher frequency of hypertension than controls ($p<0.001$), whereas gender distribution was comparable. Prothrombin time (PT), international normalized ratio (INR), and random blood glucose (RBG) were all markedly elevated in the patient group (all $p<0.001$). Conversely, hemoglobin (Hb), total leukocyte count (TLC), and platelet count (PLTs) were significantly lower ($p<0.001$, $p=0.007$, and $p<0.001$, respectively; *table 1*).

Evaluation of hepatic and renal parameters showed significantly higher aspartate transaminase (AST) and alkaline phosphatase (ALP) in ESRD subjects ($p=0.012$ and $p<0.001$, respectively) along with a pronounced

Table 1 - Baseline characteristics and laboratory tests of ESRD patients and healthy controls

		ESRD group (n =70)	Control group (n =70)	P value
Age (year)	Mean ± SD Range	48.7 ± 11.8 25 - 70	35.4 ± 9.5 20 – 57	<0.001*
Sex	Male Female	35 (50%) 35 (50%)	33 (47.1%) 37 (52.9%)	0.735
HTN	Yes No	50 (71.4%) 20 (28.6%)	17 (24.3%) 53 (75.7%)	<0.001*
Hb (g/dL)	Mean ± SD Range	8.5 ± 1 6.5 - 11	10 ± 1.5 5.6 – 13	<0.001*
TLC ×103 (cells/μL)	Mean ± SD Range	7.1 ± 2.2 3.6 - 13	8.7 ± 3.2 4 – 16	0.007*
PLT ×103 (cells/μL)	Mean ± SD Range	189.9 ± 28.6 115 - 250	336.5 ± 57.8 213 – 454	<0.001*
PT (seconds)	Mean ± SD Range	12.8 ± 0.7 12.3 - 15.5	12.3 ± 0.1 11.8 – 13	<0.001*
INR	Mean ± SD Range	1.1 ± 0.1 1 - 1.36	1 ± 0.01 1 - 1.2	<0.001*
RBG (mg/dL)	Mean ± SD Range	118.7 ± 51.5 67 - 270	117 ± 17.5 80 – 154	<0.001*

SD: standard deviation, HTN: hypertension, TLC: total leucocytic count, Hb: hemoglobin, PLT: platelets, INR: international normalized ratio, PT: prothrombin time, RBG: random blood glucose, *statistically significant as p value < 0.05.

reduction in serum albumin (p<0.001). Alanine aminotransferase (ALT) and total bilirubin displayed no significant differences. As anticipated, serum urea, creatinine, and potassium were markedly elevated in patients, whereas serum sodium was significantly reduced (all p<0.001; *table 2*).

Within the ESRD group, subgroup analysis compared diabetics (n=14) to non-diabetics (n=56). The two subgroups were similar in age, sex distribution, and hypertension prevalence. Diabetic patients had significantly higher PT, INR, and RBG values (p=0.006, p=0.003, and p<0.001, respectively), while Hb, TLC, and PLT counts were not significantly different (*table 3*).

Regarding liver enzymes, diabetic ESRD patients showed significantly greater AST, ALT, serum albumin, and ALP levels than non-diabetic peers (p=0.017, p=0.003, p=0.034, and p=0.013, respectively). Total bilirubin remained unchanged between groups, and no significant differences were found in serum urea, creatinine, sodium, or potassium (*table 4*).

Table 2 - Liver function and Kidney function tests of ESRD patients and healthy controls.

		ESRD group (n =70)	Control group (n =70)	P value
AST (U/L)	Mean ± SD Range	26.2 ± 12.1 12 – 59	20.5 ± 5.6 10 – 33	0.012*
ALT (U/L)	Mean ± SD Range	25.1 ± 13.5 10 – 70	20.8 ± 6.2 10 – 35	0.214
S. albumin (g/dL)	Mean ± SD Range	3.9 ± 0.4 2.7 - 4.7	4.3 ± 0.3 3.7 - 4.8	<0.001*
Total bilirubin (mg/dL)	Mean ± SD Range	0.9 ± 0.1 0.6 - 1.3	0.8 ± 0.1 0.7 – 1	0.088
ALP (U/L)	Mean ± SD Range	165.6 ± 94 63.3 – 570	89.3 ± 18.3 60 – 125	<0.001*
S. Urea (mg/dL)	Mean ± SD Range	121.3 ± 32.1 8.5 – 178	25.1 ± 5.7 14 – 43	<0.001*
S. creatinine (mg/dL)	Mean ± SD Range	8.2 ± 2.5 2.2 - 14.2	0.9 ± 0.2 0.6 - 1.3	<0.001*
S. Na (mEq/L)	Mean ± SD Range	135.7 ± 3.6 125 – 146	140.2 ± 2 137 – 144	<0.001*
S. K (mEq/L)	Mean ± SD Range	5.3 ± 0.7 4 - 6.6	4.3 ± 0.3 3.8 - 4.8	<0.001*

SD: standard deviation, AST: aspartate transaminase, ALP: alkaline phosphatase, ALT: alanine transaminase, Na: sodium, K: potassium, *Statistically significant as p value <0.05.

Table 3 - Baseline characteristics and laboratory tests of diabetic and non-diabetic ESRD patients

		Diabetic ESRD group (n =14)	Non-diabetic ESRD group (n =56)	P value
Age (year)	Mean ± SD Range	51.21 ± 9.32 38 – 66	48.04 ± 12.3 25 – 70	0.37
Sex	Male Female	6 (42.9%) 8 (57.1%)	29 (51.8%) 27 (48.2%)	0.766
HTN	Yes No	12 (85.7%) 2 (14.3%)	38 (67.9%) 18 (32.1%)	0.321
Hb (g/dL)	Mean ± SD Range	8.44 ± 1.16 6.5 – 10	8.46 ± 0.91 6.7 – 11	0.867
TLC $\times 10^3$ (cells/µL)	Mean ± SD Range	6.91 ± 2.24 4 – 11	7.2 ± 2.23 3.6 – 13	0.689
PLT $\times 10^3$ (cells/µL)	Mean ± SD Range	186.93 ± 39.84 115 - 245	190.64 ± 25.4 132 – 250	0.811
PT (seconds)	Mean ± SD Range	13.46 ± 1.02 12.3 - 15.5	12.65 ± 0.54 12.3 – 15	0.006*
INR	Mean ± SD Range	1.11 ± 0.11 1 - 1.36	1.04 ± 0.06 1 - 1.32	0.003*
RBG (mg/dL)	Mean ± SD Range	208.36 ± 51.8 90 - 270	96.27 ± 11.77 67 – 132	<0.001*

SD: standard deviation, ESRD: end stage renal disease, TLC: total leucocytic count, HTN: hypertension, Hb: hemoglobin, INR: international normalized ratio, PT: prothrombin time, PLT: platelets, RBG: random blood glucose,
*Statistically significant as p value <0.05.

Table 4 - Liver function and kidney function tests of diabetic and non-diabetic ESRD patients

		Diabetic ESRD group (n =14)	Non-diabetic ESRD group (n =56)	P value
AST (U/L)	Mean ± SD	34.64 ± 16.3	24.04 ± 9.86	0.017*
	Range	12 – 59	12 – 55	
ALT (U/L)	Mean ± SD	31.71 ± 13.84	23.5 ± 13.08	0.003*
	Range	17 – 62	10 – 70	
S. albumin (g/dL)	Mean ± SD	3.75 ± 0.24	3.92 ± 0.45	0.034*
	Range	3.3 - 4.1	2.7 - 4.7	
Total bilirubin (mg/dL)	Mean ± SD	0.88 ± 0.18	0.89 ± 0.14	0.811
	Range	0.6 - 1.3	0.7 - 1.3	
ALP (U/L)	Mean ± SD	206.5 ± 112.17	155.37 ± 87.07	0.013*
	Range	122 – 570	63.3 – 398	
S. Urea (mg/dL)	Mean ± SD	117.64 ± 30.95	123.59 ± 29.15	0.502
	Range	47 – 160	57 – 178	
S. creatinine (mg/dL)	Mean ± SD	7.24 ± 3.47	8.43 ± 2.12	0.235
	Range	2.2 - 14.2	4.5 – 13	
S. Na (mEq/L)	Mean ± SD	134.67 ± 3	135.93 ± 3.7	0.194
	Range	129 - 139.6	125 – 146	
S. K (mEq/L)	Mean ± SD	5.17 ± 0.66	5.39 ± 0.66	0.287
	Range	4 - 5.9	4.12 - 6.6	

SD: standard deviation, AST: aspartate transaminase, ALP: alkaline phosphatase, ALT: alanine transaminase, K: potassium, Na: sodium, *Statistically significant as p value <0.05.

Univariate linear regression identified age, platelet count, PT, INR, RBG, serum albumin, serum urea, and serum sodium as significant predictors of AST. Each one-unit rise in age, PT, INR, RBG, and serum urea corresponded to AST increases of 0.24 (0.113–0.365), 4.35 (1.58–7.12), 35.7 (10.1–61.3), 0.05 (0.006–0.09), and 0.04 (0.008–0.07), respectively. In contrast, one-unit decreases in platelet count, serum albumin, and serum sodium were linked to AST elevations of 0.02 (0.04–0.004), 4.15 (8.07–0.22), and 0.79 (1.22–0.35), respectively. Multivariate analysis retained age as the only independent predictor, where each one-unit increase corresponded to a 0.17 (0.01–0.322) rise in AST (*table 6*).

For ALT, univariate analysis showed that PT, INR, RBG, serum albumin, total bilirubin, and urea reduction ratio (URR) were significant determinants. Increases of one unit in PT, INR, RBG, and total bilirubin were associated with ALT elevations of 6.16 (3.1–9.21), 41.5 (12.7–70.3), 0.07 (0.02–0.11), and 27.3 (13.1–41.5), respectively. Conversely, one-unit reductions in serum albumin and URR predicted ALT increases of 5.2 (9.6–0.79) and 0.25 (0.51–0.002), respectively. In the multivariate model, serum albumin and URR remained independent predictors, with each one-unit decrease linked to ALT elevations of 10.3 (17.3–3.5) and 0.25 (0.5–0.03), respectively (*table 6*).

DISCUSSION

A total of 140 participants were included in this investigation, consisting of 70 end-stage renal disease (ESRD) patients and 70 age-matched healthy controls who were free of diabetes, renal impairment, or any hepatic disorder that might influence enzyme levels.

Evaluation revealed that ESRD patients demonstrated significantly higher aspartate aminotransferase (AST) and alkaline phosphatase (ALP) values, while alanine aminotransferase (ALT) showed a mild, non-significant increase. Conversely, serum albumin

Table 5 - Urea-creatinine ratio and kt/v of diabetic and non-diabetic ESRD patients

		Diabetic ESRD group (n =14)	Non-diabetic ESRD group (n =56)	P value
Urea reduction ratio (%)	Mean ± SD	62.11 ± 7.48	69.98 ± 13.2	0.005*
	Range	49 - 76.4	45.8 - 93.7	
kt/v	Mean ± SD	1.18 ± 0.21	1.36 ± 0.3	0.039*
	Range	0.9 - 1.7	0.7 - 1.93	

SD: Standard deviation.

Table 6 - Univariate and multivariate linear regression analysis of different factors for prediction of changes in AST and ALT in the studied patients.

AST	Univariate regression analysis		Multivariate regression analysis	
	β (95% CI)	P value	β (95% CI)	P value
Age	0.24 (0.113 – 0.365)	<0.001*	0.17 (0.01 – 0.322)	0.037*
PLT	-0.02 (-0.04 - -0.004)	0.019*	-0.42 (-4.72 – 3.87)	0.846
PT	4.35 (1.58 – 7.12)	0.002*	0.92 (-2.99 – 4.83)	0.642
INR	35.7 (10.1 – 61.3)	0.007*	9.36 (-21.9 – 40.7)	0.555
RBG	0.05 (0.006 – 0.09)	0.023*	0.01 (-0.02 – 0.05)	0.384
S. albumin	-4.15 (-8.07 – -0.22)	0.038*	0.01 (-0.04 – 0.06)	0.630
S. Urea	0.04 (0.008 – 0.07)	0.013*	-0.51 (-1.05 – 0.03)	0.063
S. Na	-0.79 (-1.22 - -0.35)	<0.001*	0.03 (-0.02 – 0.07)	0.284
ALT				
PT	6.16 (3.1 – 9.21)	<0.001*	5.13 (-0.03 – 10.3)	0.05
INR	41.5 (12.7 – 70.3)	0.005*	12.3 (-29.2 – 53.9)	0.555
RBG	0.07 (0.02 - 0.11)	0.008*	-0.01 (-0.08 – 0.06)	0.774
S. albumin	-5.2 (-9.6 - -0.79)	0.021*	-10.3 (-17.3 - -3.5)	0.004*
Total bilirubin	27.3 (13.1 – 41.5)	<0.001*	14.9 (-4.87 – 34.7)	0.137
Urea reduction ratio	-0.25 (-0.51 - -0.002)	0.048*	-0.25 (-0.5 - -0.03)	0.029*

SD: Standard deviation.

and sodium were notably lower in the patient group. As anticipated, levels of urea, creatinine, and potassium were markedly elevated in ESRD, whereas total bilirubin did not differ between groups.

Earlier studies examining hepatic enzyme activity (AST, ALT, ALP) in ESRD have yielded conflicting findings, often influenced by whether blood specimens were taken prior to or following hemodialysis. Some reports indicate lower enzyme concentrations in pre-dialysis samples, whereas others describe significant elevations in post-dialysis measurements.

In partial agreement with the present findings, Latiwesh et al. (10) assessed 53 chronic kidney disease (CKD) patients on maintenance hemodialysis and 50 healthy individuals, noting a significant rise in ALP (p=0.01) but non-significant reductions in AST and ALT among patients.

Comparable results were reported by Manju et al. (11), who found significantly decreased AST and ALT coupled with a pronounced elevation in ALP in CKD cases compared with controls (p<0.05), which they linked to disease severity, concurrent illnesses, and dialysis-associated influences.

Consistently, Fabrizi et al. (12) observed markedly lower AST (p=0.00001) and ALT (p=0.00001) levels in a pre-dialysis CKD cohort of 407 subjects compared with 431 healthy counterparts.

Multiple explanations have been advanced for the reduced AST and ALT activities observed in hemodialysis populations. Suggested mechanisms include clearance of aminotransferases during dialysis sessions, suppression of enzyme activity due to increased lactate and rapid NADPH consumption, inhibition by circulating uremic toxins, and frequent pyridoxine (vitamin B6) deficiency, which is vital for aminotransferase production (13,14).

In contrast, Nazana et al. (8) demonstrated that hemodialysis can raise hepatic enzyme levels, though post-dialysis measurements typically remain within normal reference limits. They emphasized that applying standard upper-limit thresholds might lead to under-recognition of liver disease in these patients. Among their 60 participants, AST values above the upper limit of normal increased from 51.7% before dialysis to 81.7% afterward, while ALT elevations rose from 10.0% to 16.7% (p=0.01). Ratios of AST/ULN and ALT/ULN were also significantly higher following dialysis.

Similarly, Oliveira Rebarto et al. (15) assessed 40 hemodialysis patients both before and after treatment and reported significant post-dialysis rises in hematocrit, aminotransferases, and gamma- glutamyl transferase, attributing these changes to hemodilution and fluid redistribution during the dialysis process.

Among the ESRD cohort, individuals with diabetes showed significantly higher levels of AST, ALT, serum albumin, and ALP than those without diabetes, whereas total bilirubin, urea, creatinine, sodium, and potassium remained comparable between the two subgroups.

Based on current literature, this appears to be the first investigation to directly contrast liver enzyme patterns between diabetic and non-diabetic ESRD patients, offering a novel evaluation of these biochemical markers within these specific populations.

Even though no earlier research has specifically examined diabetic ESRD patients, several studies have assessed liver enzyme changes in broader diabetic populations. Murtadha et al. (16), for instance, observed significantly higher AST and ALT values in both type 1 and type 2 diabetic individuals compared with healthy controls, providing detailed subgroup data.

Similarly, Choudhary et al. (17) identified a pronounced elevation of ALP among diabetic patients relative to controls, alongside a notable increase in ALT within the diabetic group.

Consistent with these findings, Islam et al. (5) reported that abnormal liver enzyme activity (ALT, AST, ALP) occurred far more frequently in type 2 diabetic subjects than in non-diabetic participants, with 61.2% of diabetic patients exhibiting at least one enzyme above the reference threshold compared with only 37.1% of controls.

The underlying mechanisms for these abnormalities likely relate to diabetes-associated hepatic conditions, including non-alcoholic fatty liver disease (NAFLD) and steatohepatitis, which induce hepatocyte damage and inflammation, thus elevating AST and ALT (18).

Higher ALP levels may indicate combined hepatic or bone metabolic disturbances, both of which are frequently intensified by the metabolic derangements present in diabetes (19).

The rise in serum albumin detected among diabetic ESRD patients might be attributed to enhanced liver synthetic activity or altered protein turnover linked to diabetic metabolic changes (20).

In partial support of these observations, Soleymanian et al. (21) reported significantly greater serum albumin and creatinine concentrations among diabetic patients in a sample of 532 individuals on maintenance hemodialysis.

However, in contrast to our findings, they did not observe a significant difference in ALP levels, which could be attributed to variations in patient demographics, dialysis techniques, or treatment protocols.

Evaluation of clinical and demographic variables demonstrated that ESRD participants were significantly older, displayed a higher frequency of hypertension, and showed elevated Prothrombin Time (PT), International Normalized Ratio (INR), and Random Blood Glucose (RBG).

Conversely, hemoglobin (Hb), total leukocyte count (TLC), and platelet (PLT) values were markedly lower in the ESRD cohort, while the sex distribution remained comparable to that of healthy controls.

Similar demographic trends were observed by Manju et al. (11), who examined hepatic and pancreatic enzymes (AST, ALT, ALP, GGT, amylase, lipase) in 100 CKD patients and 100 healthy subjects and reported no significant differences in age or sex distribution.

Variations in age-related findings across studies may stem from sample size limitations or differing recruitment strategies.

Hypertension is a frequent and often inadequately controlled comorbidity in ESRD, affecting approximately 50-60% of hemodialysis patients and up to 80-90% in some reports (22,23).

The extended PT and INR values documented in ESRD are primarily linked to reduced hepatic synthetic capacity and the accumulation of uremic toxins, both of which disrupt the production and function of clotting factors. Hemodialysis may further influence these coagulation parameters (24).

Additionally, high random blood glucose is frequently observed in ESRD-especially in diabetic individuals-owing to insulin resistance, inadequate glycemic regulation, and the disturbed glucose metabolism characteristic of renal impairment (25).

The decreases in hemoglobin, total leukocyte count, and platelet numbers observed in ESRD are well-known hematologic complications. These abnormalities are primarily driven by diminished erythropoietin production, chronic inflammation, and impaired bone marrow activity, illustrating the complex metabolic and hematologic derangements typical of advanced kidney disease (26).

Our results showing high serum urea and creatinine align with the observations of Latiwesh et al. (10), who similarly documented significantly increased levels of these parameters in CKD patients compared with healthy subjects ($p<0.05$).

Such elevations reflect the profound reduction in renal clearance and excretory ability that accompanies ESRD and progressively worsens as the glomerular filtration rate (GFR) declines (27).

In subgroup analyses, diabetic ESRD patients exhibited markedly higher PT, INR, and random blood glucose values than non-diabetic counterparts, even though the two groups were comparable in age, sex distribution, and hypertension prevalence.

No significant differences were noted in hemoglobin, total leukocyte count, or platelet levels between these subgroups.

The increased PT, INR, and random blood glucose observed in diabetic ESRD patients are probably the result of sustained hyperglycemia, insulin resistance, and the chronic inflammatory state characteristic of diabetes.

Additional contributors may include coagulation abnormalities, medication effects, and other metabolic disturbances commonly linked to diabetic conditions (28).

Our analysis also showed that diabetic ESRD patients had significantly lower urea reduction ratio (URR) and Kt/V values compared with non-diabetic patients.

This investigation is among the first to directly contrast these key indicators of dialysis adequacy between the two groups.

Similarly, Baloochi Beydokhti (29) evaluated 33 patients (16 diabetic, 17 non-diabetic) using Kt/V >1.2 and URR >65% as adequacy benchmarks and found that URR was below 65% in all diabetic participants compared with 41.2% of non-diabetics. In the same study, a Kt/V above 1.2 was achieved by 64.7% of non-diabetics but only 31.3% of diabetics, indicating better dialysis efficacy among non- diabetic patients.

Regression analysis revealed age as the most significant predictor of elevated AST concentrations, suggesting that older individuals are more susceptible to liver enzyme abnormalities.

This association may be explained by age-related reductions in hepatic function, cumulative liver insults, or slower metabolic clearance of toxins.

Furthermore, the higher prevalence of comorbidities such as cardiovascular disease, diabetes, and hypertension in older patients may heighten hepatic susceptibility, thereby promoting AST elevation, a recognized indicator of hepatocellular damage (30).

Further modeling showed that decreased serum albumin and reduced URR were independent predictors of higher ALT values, indicating their potential role in monitoring liver status.

Low albumin usually reflects malnutrition or impaired hepatic protein synthesis, conditions frequently encountered in ESRD as a result of persistent inflammation and fluid overload (31).

Similarly, a reduced URR indicates inadequate clearance of metabolic waste during dialysis, which can impose hepatic stress and lead to ALT elevation (32).

The main limitations of this work are its single-center design and modest sample size, which may limit the broader applicability of the results.

Future multi-center studies with larger participant numbers are needed to validate these findings and to establish more precise liver enzyme reference values in ESRD, especially among diabetic patients.

Including additional parameters such as gamma-glutamyl transferase (GGT), HbA1c, and lipid profiles would enhance the scope and robustness of future investigations.

CONCLUSION

ESRD patients warrant re-evaluation, and the established upper normal limits may need revision. More extensive research is required to validate these findings. These results could potentially alter the clinical interpretation of liver enzyme levels during the routine monthly follow-up of ESRD patients, particularly those with diabetes, and in other clinical contexts.

Conflicts of Interest: Not applicable

Source of Funding: Not applicable

Ethics Approval

Ethical approval for this study was obtained from the Institutional Review Board (IRB) at the Faculty of Medicine, Menoufia University.

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