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Original Article

Effects of Chronic Kidney Disease on Liver Enzymes Activity During Pre and Post Hemodialysis

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Abstract

Background
World wide chronic kidney disease is one of the primary public health problems. This study aimed to find the activity of liver enzymes alanine aminotransferase, aspartate transaminase, alkaline phosphatase, and Gamma-glutamyl transferase in the patient's serum before and after dialysis in chronic kidney disease.

Materials and Methods
This was a case-control study including 68 cases with chronic kidney disease coming for hemodialysis at dialysis centers and 140 healthy individuals as control. Serum samples were used for the analysis of serum urea and creatinine, liver enzymes aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and gamma-glutamyl transferase using Erba Chem-300 liquid chemistry autoanalyzer. Pearson's bivariate correlation analysis and ANOVA were used to correlate variables between the controls and cases. $p < 0.05$ was considered to be statistically significant.

Results
Urea and creatinine levels were significantly higher in both pre and post-hemodialysis as compared to healthy controls with a p-value ($p < 0.001$). Alanine aminotransferase and aspartate transaminase levels were significantly lower in both pre and post-hemodialysis as compared to healthy controls. On the other hand, serum alkaline phosphatase levels were significantly higher in pre and post hemodialysis as compared to healthy control. Moreover, serum gamma-glutamyl transferase levels were significantly higher in pre and post hemodialysis as compared to healthy control.

Conclusion
The study showed differences in the level of liver enzymes in pre and post hemodialysis in chronic kidney disease.

Keywords: *Dialysis, Gamma-glutamyltransferase, Kidney diseases, Liver*

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Introduction

Cases of chronic kidney disease (CKD) on long-standing have progressive and irreversible impairment in renal functions resulting in end-stage renal disease (ESRD) [1]. Worldwide CKD is one of the primary public health problems whose prevalence is varying [2]. The prevalence of CKD in the USA was 13% [3], Beijing China 11.3% [4] and Australia 14% [5]. A study conducted in the eastern part of Nepal shows the prevalence of CKD around 10.6% [6]. Liver enzyme tests detect inflammation and damage to the liver including alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT) [7]. These investigations are useful in diagnosis, follow-up, and effectiveness of treatment [8]. Several studies report that the activity of serum AST is reduced in patients of CKD [9].

Most studies have shown that CKD and hemodialysis (HD) patients have lower serum levels of liver enzymes without renal replacement therapy than those with normal renal function [10]. A study was done by Fine et al. found that in CKD 37% of cases were having high levels of GGT [11]. Fabrizi et al. examined GGT serum levels and reported that there was no significant difference in GGT levels between the hemodialysis (HD) and control [12].

On the other hand, in a CKD patient, renal osteodystrophy may well cause an important elevation in the bone isoenzyme causative to elevated serum ALP level. Therefore, elevated ALP has been related to elevated mortality in pre-dialysis CKD as well as patients on continuation hemodialysis [13]. The objective of this study was to assess the status of serum levels of liver enzymes in CKD patients undergoing HD and compare them with healthy control.

Materials and Methods

This was a case-control study conducted at the Department of Clinical Biochemistry, Manipal Teaching Hospital, Phoolbari, Pokhara, Nepal from 2016 to 2017. The ethical clearance for this study was taken from the ethical committee of the Manipal College of Medical Sciences, before the enrolment of the study subjects. The informed consent was taken from the study subjects for interviews, questionnaires, sample collection. The participant knew their sample were collected for research. The case recruited for this study were the patients with ESRD coming for hemodialysis at Manipal College of Medical Sciences for more than six months. Healthy individuals as control groups having no liver diseases and other acute or chronic diseases served as controls. Those case who were not willing to participate in the study were excluded and few cases, whose post hemodialysis sample could not be collected or who switched to some other dialysis center were excluded from the study. A total of 68 cases with CKD coming for hemodialysis at dialysis centers and 140 Healthy individuals were enrolled as a control.

The sample size for this study was calculated using 95% confidence interval and 80% power. According to literature review [14] it was found that the pre and post dialysis result of ALT were 14.78±0.4 and 17.78±0.3 u/l respectively among 60 samples for each test. Now, the sample size calculation was done using the following formula: $N = (Z_\alpha + Z_\beta)^2 * (1/q_1 + 1/q_0)/ (E/S)^2$, total group size = $N_{total} = N_1 + N_0 = 120$, Proportion of samples in pre test = $q_1 = N_1 / N_{total} = 0.500$, Proportion of samples in post test = $q_0 = 1 - q_1 = 0.500$,Standard normal deviate for $\alpha = Z_\alpha = 1.96$ at 95% CI, Standard normal deviate for $\beta = Z_\beta = 0.8416$ at 80% power. Therefore, 60 and 60 samples for pre and post study. Now adding 10% at calculated sample size then it becomes 66 for each. But the study had taken 68 samples for each.

Blood was collected from the forearm by venipuncture using a syringe (3ml) and kept in 12"x75" gel tubes. The blood samples were allowed to clot at room temperacture, centrifuged at 4000rpm for about 10 minutes and serum samples were collected. The collected serum samples were either used instantly for the analysis of serum urea and creatinine, liver enzymes AST, ALT, ALP, and GGT using (Erba Mannheim XL- 300) Chemistry auto analyzer or stored in the deep frezer (-20°C) for future analysis. The Reference range employed at our laboratory for Urea is 15-45 mg/dl, Creatinine is 0.7-1.3 mg/dl, AST is 0- 35 IU/l, ALT is 0-45 IU/L, ALP is 53-141 IU/L while that of GGT is 5- 55 IU/L. Statistical analysis was done using SPSS version 22 to compare mean values of serum urea, creatinine, AST, ALT, ALP, and GGT between cases and controls using Student's t-test. Mean ±SD and 95% CI were used to express the results. Pearson's bivariate correlation analysis and ANOVA were used to correlate biochemical variables between the controls and cases. $p < 0.05$ was considered to be statistically significant.

Results

The age and gender distribution of hemodialysis cases and healthy control under study are shown in Table 1. There was no statistically significant difference between the mean ages of the two

groups. When the two groups were analyzed according to sex, a significant difference was observed shown in Table 2. The statistical analysis of serum AST, ALT, ALP, and GGT levels among the prehemodialysis, posthemodialysis, and healthy control are shown in Table 3. Figures 1 and 2 showing the means ± standard deviation for urea and creatinine in pre and post hemodialysis, and Healthy control respectively.

Urea levels were significantly higher in both pre-hemodialysis (137.29±67.65) and post-hemodialysis (57.39 ± 20.67) as compared to healthy controls (23.43 ± 6.94) with a P-value (P < 0.001). Creatinine levels were significantly higher in both pre-hemodialysis (11.48±16.08) and post-hemodialysis (4.27±2.16) as compared to healthy controls (0.91 ± 0.62) with a P-value (P < 0.001). AST levels were significantly lower in both pre-hemodialysis (19.32±10.80) and post-hemodialysis (17.66±8.84) as compared to healthy controls (27.42±10.76), (P < 0.000). No statistically significant difference was observed between the AST values of Pre and Post HD (P = 0.013).

Similarly, serum ALT levels were also significantly lower in both prehemodialysis (26.88± 41.97) and Post hemodialysis (21.96± 11.76) as compared to Healthy control (32.86±16.10) (P < 0.015). No statistically significant difference was observed between the ALT values of Pre and Post HD (P<0.314). On the other hand serum, ALP levels were significantly higher in Prehemodialysis (123.96±66.80) and Posthemodialysis (115.81 ±65.83) as compared to healthy control (88.56±24.97) (P < 0.006). Statistically, a significant difference was observed between the ALP values of Pre and Post HD (P<0.055). Moreover, serum GGT levels were significantly higher in Prehemodialysis (79.60 ± 84.39) and Post hemodialysis (75.80 ±79.77) as compared to healthy control (33.84± 25.60) (P < 0.001). No statistically significant difference was observed between the GGT values of Pre and Post HD (P<0.480).

Table 1: Age of the Hemodialysis case and Healthy control

Parameters	Hemodialysis Cases	Control	P Value
Number (n)	68	140	
Age in Years (mean ± SD)	52.34 ± 14.43	51.42 ± 15.40	0.681
95% CI	(48.85, 55.83)	(48.85,53.99)	
Range in Years	24-84	20-86	
Female (%)	21(30.88)	73(52.14)	

*P value not statistically significant (P>0.05). SD: Standard deviation; 95% CI: Confidence Interval

Table 2: Comparison between gender and groups

Gender	Control	Case	P value	Remarks
Male	67 58.8%	47 41.2%		
Female	73 77.7%	21 22.3%	0.004	Sig
Total	140 67.3%	68 32.7%		

Table 3: Comparison between liver enzymes in pre hemodialysis, post hemodialysis and control subjects

Parameters	Pre Hemodialysis (mean ± SD)	Post Hemodialysis (mean ± SD)	Control (mean ± SD)	p-value ANOVA
AST	19.32 ± 10.80	17.66 ± 8.84	27.42 ± 10.76	<0.001***
ALT	26.88 ± 41.97	21.96 ± 11.76	32.86 ± 16.10	0.015
ALP	123.96 ± 66.80	115.81 ± 65.83	88.56 ± 24.97	0.006*
GGT	79.60 ± 84.39	75.80 ± 79.77	33.84 ± 25.60	0.001*

* Significant *** Highly Significant

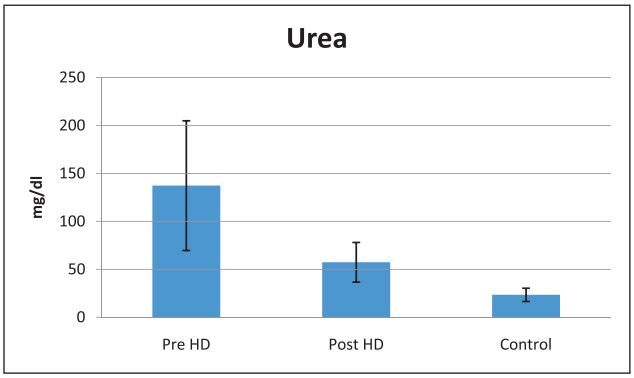

Figure 1: The values are expressed as the means ± SD for serum urea in pre and post HD, and Healthy control

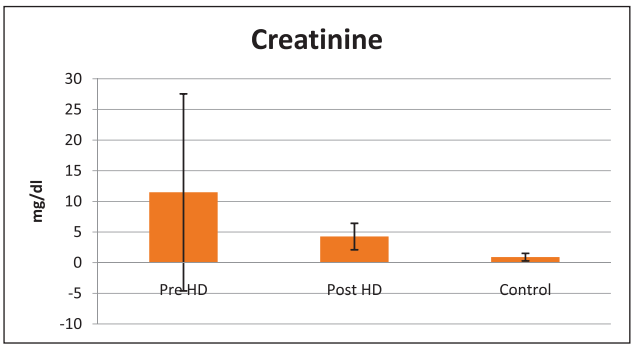

Figure 2: The values are expressed as the means ± SD for serum creatinine in pre and post HD, and Healthy control

Discussion

Patients with CKD have increased chronic co-morbidities which may be coexisting or develop later during the progression of diseases to ESRD. So these patients require regular laboratory investigation to exclude such diseases. Therefore liver enzymes have an important role in the diagnosis and monitoring of liver damage in CKD. On the other hand, in CKD kidney fails to functions because of which metabolic end

products cannot be removed from the blood which ultimately causes ESRD and such that they have to go for dialysis or renal transplantation [1]. Different constituents in the blood are increased, decreased, or removed during hemodialysis. Thus we carried out the current study to assess liver enzymes AST, ALT, ALP and GGT among Prehemodialysis, posthemodialysis, and healthy control, and to see if there are any differences in liver enzymes between them. Furthermore, to the best of our knowledge, no such study has been reported from Nepal to date. The study showed that there is a significant decrease in serum AST, ALT, and an increase in ALP and GGT activity among CKD patients before and after HD patients as compared with the healthy control group.

During this study, it was observed that CKD is more common in males than in a female with the age group of 24-84 years with a Mean age of 52.34 years. A similar study showed that male is affected more with age group ranging from 40 to 60 years in CKD [15]. The common reasons that may attribute are Diabetes Mellitus, Glomerulonephritis, Hypertension, or some other age-related changes that happen after advancing age. According to our study, there is a significant decrease in serum AST, ALT activity among CKD patients before and after hemodialysis as compared with healthy control. Our study is similar to a study conducted by Ray et al. to see the relationship between CKD and liver enzymes [10]. A study done in the year 2015 by Ray et al. had similar results for AST and ALT who concluded that in CKD the level of serum aminotransferase was low with and without end-stage renal disease and the levels become further lower as the disease of CKD advances [10].

This decreased activity of aminotransferase could be because of the following reasons, A study conducted by Ono et al. concludes that low serum pyridoxine level is the reason for low aminotransferase, [16] but another study conducted by Gressner et al. concludes that there are no effects of pyridoxine on aminotransferase [17]. Another study conducted by Huang et al. concludes that a higher level of homocysteine level may lead to lower aminotransferase levels in CKD [18]. Another study concludes that a low level of aminotransferase could be due to interference caused by a uremic toxin or ultraviolet absorbing components during the detection of aminotransferase in the blood of CKD [19]. According to our study, there is a significant increase in serum ALP activity among CKD patients before and after hemodialysis (HD) as compared with healthy control.

Serum ALP is one of the investigations in liver function tests that help diagnose obstructive jaundice in subjects without CKD however this may not be true in a patient on dialysis in CKD. Through different researches, it has now been known that serum ALP is raised in patients with CKD and is associated with increased mortality [20] which is similar to our study. On the other hand, ALP is also produced from different tissues including bone, it has been seen in few studies that serum ALP is raised in CKD patients without any liver disease which may be because of high−turnover in bone disorder [21,22]. According to another study, there is a significant increase in the level of ALP in CKD because of an increase in osteoblastic differentiation [21]. According to our study, there is a significant increase in serum GGT activity among CKD patients before and after HD as compared with the healthy control group. Our study is similar to a study conducted by Isabella Ramos de Oliveira Liberato et al[23]. The elevated level of serum GGT in CKD undergoing Hemodialysis might be due to the use of drugs or due to the progression of CKD or diabetes mellitus, which can cause steatohepatitis [24] or malnutrition inflammation-atherosclerosis syndrome, that was seen in patients undergoing dialysis with CKD because of systemic arterial hypertension or diabetes mellitus [25]. So far there are only a few studies that have been done to assess the effects of Hemodialysis in CKD on serum GGT [23,12] because of this to know the exact causes of changes in the level of GGT further studies are needed.

Conclusion

Our results showed differences in the level of liver enzymes in pre and post hemodialysis in chronic kidney disease. Differences in the serum level of liver enzymes before and after hemodialysis can potentially be used as markers hepatic damage due to aggregation of metabolic wastes in the blood of patients with chronic renal failure.

Conflicts of interests: None

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