Liver Morbidity in Patients Negative for Overt HBV and HCV Undergoing Maintenance Hemodialysis: a Hospital-based Study

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Research Article

Keywords: end-stage kidney disease, chronic liver disease, ultrasonography, ALT, fatty liver

Posted Date: November 25th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-111341/v1

Abstract

Background: End-stage renal disease (ESRD) is an increasing health problem worldwide. Older age, diabetes and hypertension, acute kidney damage are among some of the factors that play a role in ESRD. This study aims at exploring liver morbidity (LM) among hemodialysis (HD) patients in an endemic country.

Methods: The study included 142 patients aged 12 to 75 years; 53.5% were males. Data were retrieved from files and all participants were examined by abdominal ultrasonography and tested for liver functions and markers and viremia of HCV and HBV.

Results: Three patterns of LM were found in 62 (43.7%); fatty in 30, fibrous in 19 and hepatitis in 13. The duration of renal impairment (p=0.02), duration of hemodialysis (p=0.011), and total dialysis sessions (p=0.007) were associated with LM. ALT and AST >40 IU/L levels were elevated in 9.9% and 9.2% of patients. All 14 patients with high ALT showed evidence of LM (p=0.017) compared to 4 of 13 patients with elevated AST (p<0.001). The ROC curve revealed ALT and AST cut-off points of 16.5 and 25.5 IU/L to discriminate LM. According to the new values, 58.5% and 40.1% of the studied participants had high ALT and AST.

Conclusion: LM is common among EDKD patients undergoing hemodialysis despite the limited role of ALT and AST. The use of ultrasonography and the new lower levels of ALT and AST could improve the screening approach of LM.

Background

Worldwide, end-stage renal disease (ESRD) is an increasing health problem. The main etiology of chronic kidney disease (CKD) may differ in different countries. Common risk factors are aging, diabetes mellitus and hypertension, and chronic use of non-steroidal anti-inflammatory drugs, and acute kidney damage. Polycystic kidney disease is an example of a hereditary cause of CKD [1- 3]. In many Arab countries, obstructive uropathy constitutes a major cause of ESRD (40%) mostly due to renal calculi and schistosomiasis. In endemic areas, infection-related chronic glomerulonephritis is a leading cause of CKD [4]. Other unhealthy lifestyle factors; such as smoking, alcohol and obesity are also associated with CKD and ESRD [5-7]. The association of liver disease with chronic kidney injury is common and infection with blood-borne hepatitis viruses as HBV, HCV is commonly encountered in patients on hemodialysis. Several types of renal diseases have been associated with HBV and HCV; namely mixed cryoglobulinemia, membranoproliferative glomerulonephritis, membranous nephropathy and polyarteritis nodosa [8]. Renal transplantation is associated with reduced survival among HBsAg positive hemodialysis patients. [9] Fortunately, in patients with immune reactive chronic HBV, nucleoside/nucleotide analogues successfully suppress viral replication, decrease morbidity, and transmission in the community [10-11].

Meanwhile, the changes in the lifestyle of the population towards unhealthy habits; namely obesity and sedentary life, have been linked to increase the prevalence of metabolic syndrome (MS). Likewise, the

importance of non-alcoholic fatty liver disease (NAFLD) as one manifestation of MS is appreciated [12]. Nowadays, the association between CKD and NAFLD is of a major concern. Renal impairment is more prevalent in patients with NAFLD while untreated non-alcoholic steatohepatitis (NASH) could progress to cirrhosis and hepatocellular carcinoma (HCC) and increased risk of cardiovascular mortality. Early diagnosis and treatment of NAFLD in CKD patients could ameliorate the cardiovascular risk and delay renal impairment. Current treatment recommendations for nonalcoholic fatty liver disease are limited to weight reduction and treatment of any component of the metabolic syndrome [12-14].

This study is aimed to explore the current status and type of liver morbidity (LM) among patients on chronic hemodialysis using diagnostic tools that are practiced daily in an endemic country for liver disease.

Patients And Methods

The study included 142 patients with ESRD undergoing maintenance hemodialysis for > 3 months. All were free from evidence of overt HBV or HCV at the time of enrollment. The studied population were selected by a non-random convenience sampling, from two hemodialysis centers (Suez Canal University Hospitals and Ismailia General Hospital) in Ismailia City, Egypt during the period from July 2018 to January 2019.

Ethical Consideration:

After explaining the aim of the study, its nature, and importance, an informed consent was obtained from all participants, and the approved patients were enrolled. The study has also been approved by the ethics committee of the Faculty of Medicine, Suez Canal University, Egypt (Ref. #3680).

Clinical and Laboratory Assessments

Data collected included sociodemographic, clinical, laboratory, as well as the risk factors for blood-borne infections and co-morbid illnesses. Examination with ultrasonography was conducted for the measurement of the morphological parameters (liver size, morphology, surface and echogenicity, and spleen volume, check for ascites) and the hemodynamic parameters (portal vein diameter and mean flow velocity) were also obtained. All ultrasound examinations were performed by a single experienced operator, who was blind to the clinical and laboratory data of the studied participants. The ultrasound was performed before dialysis while the patients were lying supine. The machine used was Sonoace R3 (Samsung Medison, Seoul, Korea) with a curvilinear 2.5-5 MHz transducer.

Methods and sampling:

Two Peripheral venous blood samples were taken, serum was separated and stored at -80°C for testing markers (HCV Ab, HBsAg, HBcAb and HBsAb) and real time PCR. Peripheral mononuclear cells (PMNCs) was separated from the other sample and stored immediately at −80°C. Repeated testing for serological markers of HBV and HCV was also done for all patients to check for seroconversion and to assess

hepatitis B vaccination. In patients with positive HCV Ab, RT-PCR for HCV RNA was performed in the sera to check for overt HCV infection (OCI). If no viremia, the test was repeated in peripheral mononuclear cells (PMNCs) to check for occult HCV infection (OCI). Similarly, RT-PCR for HBV DNA was carried out on the sera of positive HBcAb patients to check for occult HBV infection (OBI).

Study outcomes:

According to the interpretation of the clinical, imaging, and laboratory findings, the liver was considered possibly morbid if there were changes in the liver echogenicity and/or its size, associated with splenic enlargement, dilated portal or splenic veins. Also, the liver is morbid if there is evidence of necro-inflammation of the liver cells (elevated ALT and/or AST) or altered synthetic function (prolonged INR, low serum albumin). The pattern of LM was described as fatty (NAFLD), fibrous, or hepatitis-like pattern. The etiology of liver morbidity was described as (a) viral related (according to results of HBV or HCV serological markers and viremia by RT-PCR for HCV RNA or HBV DNA). (b) NAFLD, diagnosed as fatty liver (if there was bright liver by ultrasonography in the absence of other pathogens and normal liver enzymes) or NASH (if there was steatosis associated with high ALT), (c) Unclassified in absence of the previous two causes. The severity of liver disease was assessed by Child and Pugh scoring system [14]. Interpretation of hepatitis B markers was done according to the criteria of the Center of Disease Control and Prevention, USA [15].

Statistical analysis:

The collected data were managed by the SPSS-version 20 program of statistical analysis. Continuous data were described as range, mean and standard deviation, and qualitative data were summarized by frequencies and percentages. For the analytic data, the Chi-square test was used to detect the differences between qualitative data, while the Student's t-test was used to detect the difference between continuous data. A p-value <0.05 was considered statistically significant. To find out the cut-off values of liver enzymes (ALT and AST) to assess ongoing liver pathology in HD patients, a Receiver Operating Characteristic curve (ROC curve) was constructed and analyzed.

Results

The 142 participants aged from 12-75 years, 76 (53.5%) were males, 12 (8.5%) were current smokers and 81 (57%) were living in urban areas. History of previous surgery, dental procedure, and blood transfusion was recalled by 115 (81.0%), 120 (84.5%), and 103 (72.5%) patients respectively. Comorbid hypertension, diabetes mellitus, and renal stones were present in 62 (43.7%) and 11 (7.7%) and 22 (15.5%) of patients, while a family history of liver disease was given by 21 (14.8%). The duration of impaired kidney function (IKF) and the duration of hemodialysis ranged from 1-25 (mean=7.75±5.52) and 1-22 years (mean=6.35±4.89) respectively. Three weekly sessions of hemodialysis were performed in 58.5% patients and twice weekly in 41.5%. The number of dialysis sessions ranged from 104-2652 (mean=820.28±586) along the course of replacement therapy. History of blood transfusion before and after HD was reported

by 23.9% and 10.6% of patients respectively. Anemia was managed by regular erythropoietin in 90.1%) of patients and by iron therapy in 70.4% (Table 1).

Table 1: Comparison between patients with and without liver morbidity regarding sociodemographic characteristics and risk factors.

	n=142	With liver morbidity (n=62)	Without liver morbidity (n=80)	P value
Age mean (years)	44.05±16.78	45.42±16.39	42.99± 16.2	0.97
Male: Female	76:66	32:30	44:36	0.25
Urban: rural	81:61	32:30	49:41	0.095
Previous surgery	115 (81.0%)	49 (79%)	66 (82.5%)	0.49
Previous dental procedure	120 (84.5%)	52 (81.8%)	68 (86.2%)	0.32
Previous blood transfusion	103 (72.5%)	48 (76.4%)	55 (70.1%)	0.27
Previous Schistosomiasis	6 (4.2%)	3 (5.5%)	3 (3.4%)	0.43
Tartar emetic injection	5 (3.5%)	2 (3.6%)	3 (3.9%)	0.64
Previous renal stones	22 (15.5%)	7(12.7%)	15 (17.2%)	0.32
Hypertension	62 (43.7%)	31 (47.3%)	31(41.4%)	0.3
Diabetes mellitus	11 (7.7%)	6 (4.2%)	5 (5.7%)	0.21
Family history of viral liver disease	21 (14.8%)	9 (12.7%)	12 (16.1%)	0.58
Duration of *IKF	7.75±5.52	9±6.12	6.78±4.82	**0.02**
Duration of hemodialysis	6.35±4.89	7.6±5.91	5.38±3.69	**0.011**
Dialysis/week				
Two	59 (41.5%)	24 (38.7%)	35 (43.75%)	0.608
Three	83 (58.5%)	38 (61.3%)	45 (56.25%)	
Number of dialysis sessions	820.28±586	976.26±683.69	699.4±467.1	**0.007**

*Impaired kidney function

Abdominal ultrasonography revealed hepatomegaly in 55 (38.7%) patients. The liver echogenicity was normal in 89 (62.7%), fibrous in 22 (15.5%) and fatty in 31 (21.8%) patients. None had ascites and 10 (7.0%) patients had splenomegaly. Laboratory workup revealed that ALT and AST, serum albumin, and

total serum bilirubin had a range of 4-74, 5-65 IU/L, 2.7-4.7 gm/dl, and 0.2-1.4 mg/dl respectively. Elevated ALT and/or AST were found in 18 (12.67%), high total serum bilirubin in 3 (2.1%) and low serum albumin in 21 (14.8%). Of all, anemia, leukopenia, and thrombocytopenia were recorded in 95.1%, 7 %, and 7.7 % patients. HCV Ab was positive in 15 (10.6%) patients, for the first time in two (1.4% seroconversion). RT-PCR testing for sera of HCV Ab positive patients revealed HCV RNA in the two naïve seroconverted cases, and in the remaining 13, viremia was only evident in PMNCs of 5 cases. Overall, 44 (31.0%) patients were sero-reactive to HBcAb, all proved negative for HBV DNA by RT-PCR. According to the constellation of clinical, imaging, and laboratory data, LM was suggested in 62 (43.67%) patients (Table 2). The pattern of LM was described as NAFLD, fibrous or hepatitis patterns.

Table 2: Comparison between patients with and without liver morbidity regarding manifestations of liver disease in 142 studied patients on regular hemodialysis

	n=142	Liver morbidity (n=62)	No liver morbidity (n=80)	P value
Enlarged liver	55 (38.7%)	28 (45.1%)	27 (40.0%)	>0.05
Liver echogenicity				
Normal	93 (62.7%)	13 (21%)	80 (100%)	
Fibrous	19 (15.5%)	19 (30.6%)	0 (0.0%)	NA*
Fatty	30 (21.8%)	30 (48.39%)	0 (0.0%)	
Splenomegaly	10 (7.0%)	8 (12.9%)	2 (2.5%)	0.02
ALT mean	22.3±14.6	26.05±17.544	19.33±11.147	0.01
High ALT (>40 IU/L)	14 (9.9%)	14 (22.58%)	0 (10%)	0.017
AST mean	22.74±12.77	19.58±15.438	23.3±9.158	0.001
High AST (>40 IU/L)	13 (9.2%)	4 (6.45%)	9 (11.25%)	<0.001
S. albumin range	3.89±0.4	3.837±.4013	3.938±.3998	0.59
S. albumin mean	21 (14.8%)	12 (19.35%)	9 (11.25%)	>0.05
Low S. albumin (<3.5 gm/dl)				
S. bilirubin mean	0.55±0.24	0.5829±.26432	0.5294±.21693	
High S. bilirubin (>1.1 mg/dl)	3 (2.1%)	2 (3.22%)	1 (1.25%)	0.48
				>0.05
INR mean	1.05±0.08	1.0460±.06547	1.0581±.08473	1.0
Prolonged INR (>1.3)	1(0.7%)	1 (1.6%)	0	NA*
HB mean	9.78±1.34	9.518±1.1649	9.978±1.4435	0.38
Anemia	135(95.1%)	61 (98.38%)	74 (92.5%)	>0.05
WBC mean	6663±15300	6512±1886	6781±1894	0.49
Leukopenia	10 (7.0%)	6 (9.7%)	4 (5%)	>0.05
Platelet count mean	227542±65635	225822±62426 (9.7%)	228875±6838	0.68
Thrombocytopenia	11 (7.7%)		5 (3.75%)	>0.05

* NA=Not applicable

Elevated ALT and/or AST in 18 (12.67%)

In this study, LM was equally high in patients undergoing dialysis twice and thrice-weekly (p=0.6). The mean number of dialysis sessions throughout the replacement therapy was significantly higher in patients with LM (p=0.007). Similarly, the mean duration of HD and the duration of IKF function were higher in patients with morbid liver. However, the difference between patients with and without LM showed no statistically significant differences regarding age, residence, risk factors, co-morbid illnesses, and family history of liver disease (Table 1).

Comparison of manifestations of liver disease between patients with and without LM:

By ultrasonography, 28 (45.1%) patients with LM showed hepatomegaly compared to 27 (40.0%) without LM (p>0.05). Among patients with LM, fibrous and fatty echo-pattern were present in 19 (30.6%) and 30 (48.39%) compared to none in patients without respectively (p=0.11). Eight (12.9%) patients with LM had splenomegaly compared to 2 (2.5%) without, (p=0.02). The mean ALT values were significantly higher in patients with LM (p=0.01) while the mean of AST was significantly higher in patients without LM (p=0.001). All the 14 patients with high ALT showed evidence of LM (p=0.017) while only 4 of 13 patients with elevated AST had evidence of LM (p<0.001). However, the difference between both groups showed no significant differences regarding serum albumin, total serum bilirubin, INR, anemia, leukopenia, and thrombocytopenia (Table 2).

In this study, the Receiver Operating Characteristic curve analysis (ROC curve) revealed ALT and AST cut-off values, of 16.5 and 25.5 IU/L respectively, could discriminate between patients with and without LM with the diagnostic criteria as shown in Figure 1 and Table 3. ALT and AST cut-off values represent 41.25% and 60.7% of the conventional upper limit of normal (ULN) used in the study labs (40 IU/L). The new cut-off point of ALT has a higher sensitivity and lower specificity (67.7 and 48.75%) compared to AST (50 and 67.5%). However, the two cut-off values have a comparable area under the curve, PPV, NPV, and accuracy.

Table 3: The diagnostic performance of the cut-off values of ALT and AST as assessed by ROC curves

	Cut-off	P value	AUC*	Sensitivity	Specificity	PPV	NPV	Accuracy
ALT	16.5	0.047	0.6	67.70%	48.75%	50.60%	66.10%	57%
AST	25.5	0.006	0.63	50%	67.50%	54.40%	63.50%	60%

In this study, 44 (31%) were HBcAb positive, all showed no HBV DNA viremia. In the two centers of the study, all HD patients (who were HBsAg negative) were candidates for hepatitis B vaccination following the decision of hemodialysis. Of all, protective HBsAb titer (≥10mIU/ml) was found in 131 (92.25%); including 43 (30.3%) related to infection and 88 (62%) as a result of vaccination. The remaining 11 patients were non-immune; one (0.7%) had isolated HBcAb and 10 (7%) were non-reactive to hepatitis B markers (susceptible group). The frequency of HBcAb was significantly higher in patients with LM

(40.3%) compared to patients without (23.75%), p=0.044. HCV Ab was positive in 15 (10.6%) patients, 11 (17.7%) with LM and 4 (5%) without, p=0.025. Of 15 HCV Ab positive patients, the two patients with overt HCV and the five with occult HCV had evidence of LM.

The interpretation of HBV markers revealed that liver morbid patients had an insignificantly higher frequency of infection-related immunity (38.7%), significantly lower vaccination-related immunity (53.2%), and insignificantly higher frequency of susceptible patients (6.45%) compared to patients without LM. The pattern of response to hepatitis B vaccination showed a good response (>100 mIU/ml) in the majority of patients (80.3%), fair response (10-100 mIU/ml) in 17 (12%), and non-response in 11 (7.7%) patients. In all the studied populations, the geometric mean concentration and median values of HBsAb were 167.1 and 324 mIU/ml respectively. However, no statistically significant difference was found between patients with and without LM regarding the pattern of response to vaccination, its geometric mean concentration and median (p>0.05) (Table 4).

Table 4: Interpretation of hepatitis B markers

	Total	With liver morbidity N=62	Without liver morbidity N=80	P-value
Infection related immunity	43 (30.3)	25 (40.3)	18 (22.5)	>0.05
Vaccination related immunity	88 (62.0)	33 (53.2)	55 (68.75)	<0.005
Isolated HBcAb	1 (0.7)	0 (0)	1 (1.25)	*NA
Susceptible	10 (7.0)	4 (6.45)	6 (3.4)	>0.05
HBcAb positive	44 (31.0%)	25(40.3%)	19 (23.75%)	0.044
HBsAb titer pattern				
>100 IU/L	114 (80.3%)	52 (83.9%)	73 (91.25%)	>0.05
10-100 IU/L	17 (12.0%)	5 (8.1%)	12 (15%)	
<10 IU/L	11 (7.7%)	5 (8.1%)	6 (7.5%)	
** GMC	167.1	173.0	162.0	>0.05
Median	324	316.0	328.5	>0.05
HCV Ab positive	15 (10.6%)	11(17.7%)	4 (5%)	0.025
HCV RNA in ***PMNCs in 15 HCV Ab positive	5	5	0	-

*NA = Not applicable

**GMC=Geometric mean concentration

***PMNCs=peripheral mononuclear cells

Discussion

Patients with ESKD are liable to infection with hepatitis viruses due to impaired cellular immunity. Repeated hospitalization, exposure to invasive procedures, and blood transfusion are among the risk factors [17-19]. For a long time, hemodialysis was reported as one of many predictors for infection with HCV and HBV. Currently, the prevalence of viral hepatitis is declining in hemodialysis units in Egypt and many other countries, due to better infection control, hepatitis B vaccination, and updates in the

management of anemia. Moreover, Egypt has adopted a national wide program for screening and updated therapy for HCV and HBV [20].

In HD patients, screening for hepatitis viruses is usually made by periodic testing of hepatitis markers [21]. In the study settings, new infection with HCV is infrequently discovered despite the segregation of patients according to their infection status [22]. Unfortunately, many of such patients did not recall manifestation of acute hepatitis and their liver enzymes were mostly below the conventional ULN (40 IU/L).

In this study, the possibility of liver morbidity (LM) was evident in 62 (43.7%) and three patterns are described; NAFLD followed by fibrous and hepatitis patterns. Of 30 patients with NAFLD, 25 showed fatty liver, mostly with hepatomegaly and normal ALT. All had no evidence of overt or occult HCV or HBV despite sero-reactivity to HBcAb in 6 (24%). In the other 5 candidates, the elevation of ALT permits the diagnosis of NASH. Worldwide, NAFLD represents the most common cause of CLD particularly after successful prevention and control of hepatitis viruses and the increasing prevalence of obesity and sedentary life [23, 24]. The association between CKD and NAFLD is of major concern because renal impairment is reported more in patients with NAFLD. Early diagnosis and treatment of NAFLD in CKD patients could ameliorate the cardiovascular risk and delay renal impairment [25, 26].

The second most frequent pattern of LM was the fibrous liver diagnosed in 19 patients. They included two cases of overt HCV, five had occult HCV and four were positive for HBcAb without viremia. The third category was the hepatitis pattern affecting 18 patients, 5 with NASH previously discussed, and 13 with normal liver texture. All had no evidence of overt or occult HCV and the majority has been exposed to hepatitis B infection with no residual viremia.

During the study, the US was of great help to evaluate the presence and type of liver morbidity. The diagnosis of liver cirrhosis and fatty liver by US has been reported to correlate with liver tissue elastography. Furthermore, the US reliably documents moderate to the severe fatty liver compared to histopathology. Ultrasonography is still the imaging technique of choice for diagnosis of fatty liver in clinical settings and screening of population [27-29].

In this study, the diagnostic performance of ALT was more consistent with LM compared to AST. All the 14 patients with elevated ALT had evidence of LM compared to only 4 of 13 with elevated AST. In the latter cases, the rise in AST could be due to injury in other organs [30]. The limited role of liver enzymes, encountered in the assessment of LM, was also reported by many studies in patients with CKD and/or hemodialysis. Low ALT levels have been attributed to hemodilution, vitamin B6 deficiency, uremic toxins, or presence of blood components that absorb ultraviolet light [31]. Moreover, a ROC curve showed ALT and AST cut-off values of 16.5 and 25.5 IU/L respectively to discriminate patients with LM. According to the new values, 58.5% and 40.1% of the studied participants had high ALT and AST values compared to 9.9% and 9.2% when the conventional ULN was used. While the cut-off values of ALT have a higher sensitivity and lower specificity (67.7 and 48.75%) compared to AST (50 and 67.5%), both have a comparable PPV and NPV. Unfortunately, the accuracy of the AUC of either enzyme is considered low. The

cut-off values of ALT and AST, shown in this study, were very close to 17 and 24 IU/L reported in 90 patients on continuous ambulatory peritoneal dialysis with viral hepatitis. However, our ALT cutoff was lower than 24 IU/L that reported among 202 HD patients with HCV [32, 33].

In the present study, patients with LM and low serum albumin showed no evidence of decompensation clinically or by the Child-Pugh scoring system. Hypoalbumenia in ESKD patients has been attributed to many factors as low dietary protein, decrease synthesis, or inflammation. Many studies suggested unfavorable prognosis in such patients particularly those with type 2 diabetes mellitus [34, 35].

Liver morbidity among our HD patients was significantly associated with the duration of renal impairment (p=0.02), the duration of maintenance hemodialysis (p=0.011) as well as the total number of dialysis sessions (p=0.007). The association between these factors with LM has not been previously reported. The study also revealed exposure to HBV and HCV in 31% and 10.6% of the studied population. Interestingly, the same three factors discussed were significantly associated with HCV infection but not with HBV (not included in results). The duration of hemodialysis, as a risk factor for overt and occult HCV infection, has been previously appreciated in HD patients [36-40]. As shown in this study, the absence of association between the duration of hemodialysis and exposure to HBV was also reported by others [41-42]. In the setting of the study, newer patients are planned to undergo three dialysis sessions weekly while the two sessions were related to patients who were admitted earlier for dialysis, had residual kidney function, less complication or were residing away from the hospital. Although studying the risk factors of infection with hepatitis viruses was not among the study objectives, none of the classical risk factors was associated with LM; namely blood transfusion, surgery or dental procedures. They either did not show association or carried an odds ratio <1. This changing pattern could be attributed to the inclusion of participants who were intended to be free from overt infection with hepatitis viruses. Other factors include the use of sensitive tools for screening of hepatitis markers and better management of anemia [43, 44].

In this study, the frequency of HBcAb and HCV Ab were significantly higher in patients with LM (40.3% and 17.7%) compared to patients without (23.75% and 5%). Furthermore, sera of 44 HBcAb positive patients proved non-viremic when tested by RT-PCR for HBV DNA. However, to exclude OBI in the study cohort, sera, and liver tissues of all patients should be tested regardless of their HBcAb status [44]. In the setting of this study, all our HBsAg negative patients were candidates for hepatitis B vaccination and protective HBsAb titer (≥10mIU/ml) were found in the majority (92.3%). However, 10 patients (7%) were susceptible to infection and will be further considered for the second course of vaccination. In the immune group following infection (30.3%), it is not exactly known when this infection had occurred. Infection after successful vaccination has been reported and usually results in reactivity to HBcAb and boosting the titer of HBsAb [45]. The efficacy of hepatitis B vaccination of HD patients in this study who were negative to HBcAb (62%) is comparable to 69% reported in a large meta-analysis study [46].

The Study Limitation

It is worth noting that the etiology of liver morbidity is not the same. Furthermore, the tools used in this study reflect our everyday practice in a country that is endemic for viral and parasitic infections affecting the liver as well as NAFLD. Also, due to limited resources, hepatitis B vaccine was given to all HBsAg negative candidates without testing for HBcAb or HBsAb and in patients who did not show reactivity to HBsAg, a yearly booster dose is given. Besides, the evaluation of hepatitis B vaccination in the studied participants did not reflect a certain schedule after immunization. One of the present study limitations was testing for occult HCV and HBV only in patients exposed to HCV and HBV and did not include the others who were negative for HCV Ab or HBcAb.

In Conclusion

Liver morbidity of different causes has been shown in a considerable proportion of patients undergoing hemodialysis. The most common type was NAFLD, followed by fibrous liver and hepatitis. Among the studied population who were proposed to be free from active HBV and HCV, new overt HCV and occult HCV was diagnosed while no evidence of occult infection was present. The study also presented a satisfactory response to hepatitis B vaccination. The limited role of liver enzymes in the detection of liver morbidity in hemodialysis patients was contradicted by the usefulness of ultrasonography by delineating any change in the echo-pattern of the liver. However, the new cut-off values of ALT and AST revealed in this study could improve their diagnostic outcomes.

Recommendation:

Further validation study is recommended to assess the diagnostic values of ALT and AST is among hemodialysis patients. Efforts should be directed to improve the lifestyle of HD patients to prevent and treat fatty liver disease. Meanwhile, occult infection with HBV and/or HCV among patients and health care workers is recommended to track the source of new infections.

Declarations

Funding

This project was funded by the Deanship of Scientific Research, Jouf University, Kingdom of Saudi Arabia, project # (37/440).

Ethics approval and consent to participate

The study was performed in line with the 1975 Declaration of Helsinki and was approved by the Ethics Committee of the faculty of medicine, Suez Canal University, Egypt (ref. #3680).

Authors Contributions:

Conception and design of study: AA, RK, WO, IT, HO, RL, MR. Acquisition of data: laboratory or clinical/literature search: WO, IT, HO, RL, MR. Analysis and interpretation of data collected: RK, WO, IT, HO,

RL, MR. Drafting of article and/or critical revision: AA, RK, WO, IT, HO, RL, MR. Final Approval: AA, RK, WO, IT, HO, RL, MR.

Competing interest:

There are no conflicts of interest.

Availability of data:

All the data generated in this study are available from the head of the research group on reasonable grounds.

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Figures

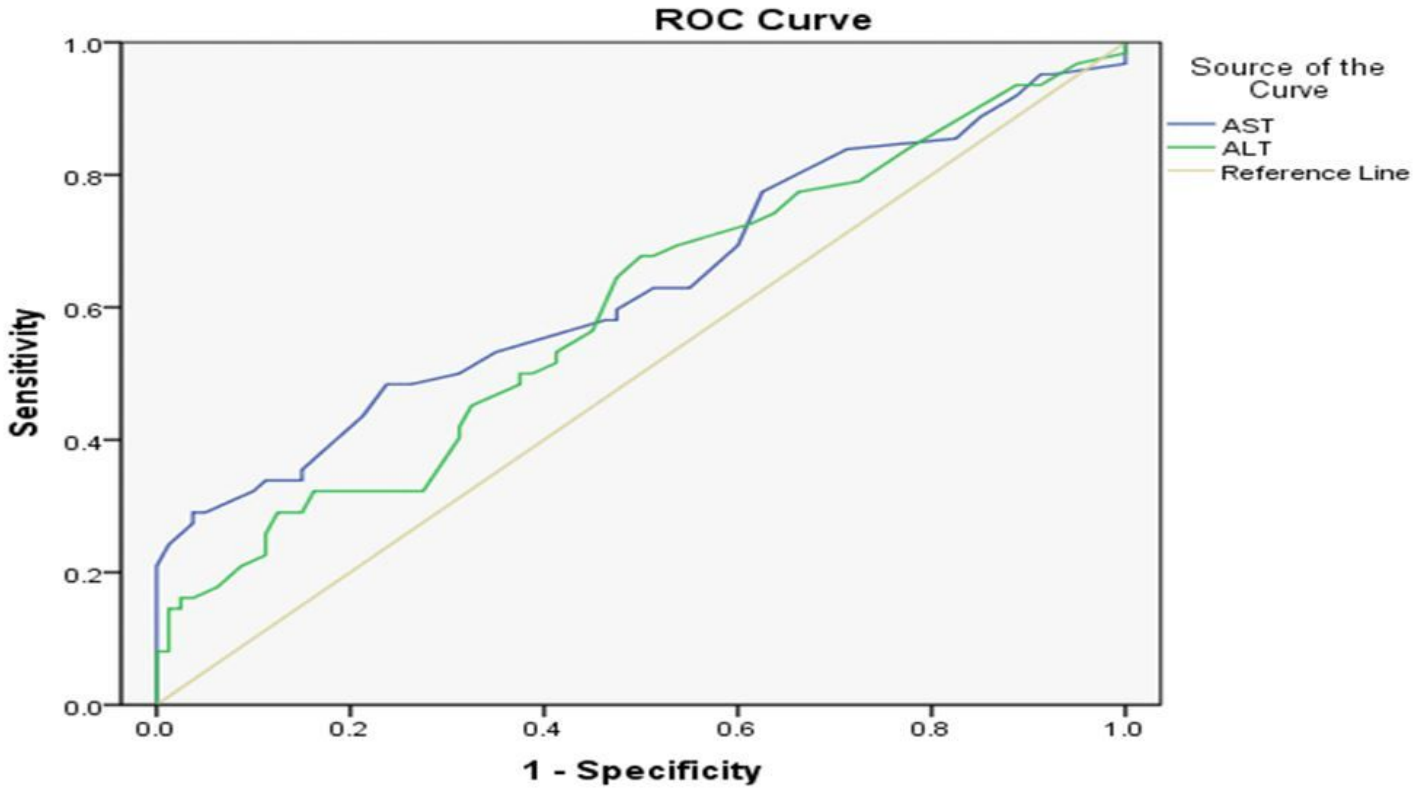

Figure 1

ROC curve of the levels of ALT and AST in 142 hemodialysis patients. At cut-off points of 16.5 and 25.5 IU/L, ALT and ALT could respectively differentiate between patients with and without liver morbidity better than the conventional ULN used in the study. ROC: Receiver operating characteristic; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase.