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Study of Vitamin D Level in Cirrhotic HCV Patients before and after Transplantation

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ABSTRACT

Background: chronic hepatitis C is a common condition. Transfusion of blood or blood-related products was one of the main routes of HCV transmission. Furthermore, nosocomial infections represent a key source of infection, particularly in some of the high-prevalence countries (such as Egypt, Pakistan and Eastern Europe). In general, prevalence increases with increasing age until peak prevalence at 55–64 years in most regions. At least six HCV genotypes are known, Genotype 4 frequency is the highest from Central Africa to the Middle East. Worldwide people infected with HCV are at an increased risk of developing serious hepatic complications including cirrhosis and hepatocellular carcinoma.

Aim of the Work: the aim of this work is to study vitamin D level in post HCV liver cirrhosis patients before and six months after liver transplantation in addition to chronic HCV patients without cirrhosis.

Patients and Methods: this prospective case control study was conducted on 25 patients. 15 of them with liver cirrhosis due to chronic hepatitis C virus evaluated before and six months after liver transplantation in addition to 10 chronic HCV patients without cirrhosis as control group. Liver cirrhosis or transplantation patients were recruited from Ain Shams specialized hospital liver transplantation unit and chronic HCV patients without cirrhosis were recruited from hepatology outpatient clinic of Ain Shams university hospital in the period from February 2017 to November 2017. Symptoms suggestive of liver disease (e.g. jaundice, bleeding tendency, increased abdominal girth).

Results: this study was conducted on 25 patients. 15 of them with liver cirrhosis due to chronic hepatitis C virus evaluated before and six months after liver transplantation in addition to 10 chronic HCV patients without cirrhosis as control group. Group I: Consists of 15 (60%) patients with post HCV liver cirrhosis before liver transplantation. They were 13 males (86.6%) & 2 females (13.3%). Their mean age was 50.53 ± 4.52. Group II: Consists of the same patients of group I evaluated six months post liver transplantation. Group III: Consists of 10 (40%) patients with chronic HCV without cirrhosis. They were 6 males (60%) & 4 females (40%). Their mean age was 53.0 ± 8.46.

Conclusion: this study concluded that vitamin D deficiency is prevalent among patients with liver cirrhosis. Liver transplantation improves vitamin D level but not to the recommended normal level i.e. vitamin D deficiency or insufficiency can persist after transplantation.

Keywords: Vitamin D level, Cirrhotic HCV Patients, Endoscopic Retrograde Cholangio Pancreatography.

INTRODUCTION

Egypt has the highest prevalence rate of hepatitis C virus (HCV) in the world, making it the most challenging public health problem facing the country [(1)]. Studies showed that 7% of the Egyptian population carry hepatitis C virus (HCV) RNA [(2)]. Liver cirrhosis occurs with untreated chronic hepatitis C virus infection, patients with cirrhosis are susceptible to a variety of complications, and their life expectancy can be markedly reduced, especially in those with acute or chronic liver failures [(3)]. Vitamin D has been associated with chronic liver diseases and it has been reported that low vitamin D status is a common feature in different types of liver diseases [(4)]. According to recent studies , the prevalence of vitamin D insufficiency is higher in patients with chronic liver disease than in general population ranging between 64 and 92 % and it has been also reported that incidence of vitamin D deficiency increases as the liver disease progresses [(4)]. Vitamin D has immunomodulatory effects with direct actions at dendritic cells, monocytes, macrophages, B-cell and T-cell functions considering that vitamin D and vitamin D receptors (VDR) are expressed by several cellular populations of the immune system such as T- helper 1(Th1) and T- helper 2 (Th2) [(4)].

AIM OF THE WORK

The aim of this work is to study vitamin D level in post HCV liver cirrhosis patients before and six months after liver transplantation in addition to chronic HCV patients without cirrhosis.

PATIENTS AND METHODS

This prospective case control study was conducted on 25 patients. 15 of them with liver cirrhosis due to chronic hepatitis C virus evaluated before and six months after liver transplantation in addition to 10 chronic HCV patients without cirrhosis as control group. Liver cirrhosis or

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transplantation patients were recruited from Ain Shams specialized hospital liver transplantation unit and chronic HCV patients without cirrhosis were recruited from hepatology outpatient clinic of Ain Shams university hospital in the period from February 2017 to November 2017. **The study was approved by the Ethics Board of Ain Shams University and an informed written consent was taken from each participant in the study.** ***Patients with chronic liver disease were identified according to the following:*** History and Clinical stigmata suggestive of liver cirrhosis i.e. (bleeding tendency, jaundice, gynecomastia, lower limb oedema, ascites and splenomegaly), laboratory changes of liver cell failure i.e. low albumin level, increased serum bilirubin level and INR, radiological data implying hepatic affection i.e. (cirrhotic liver, splenomegaly and ascites). ***All patients were subjected to the following Full medical history taking with special stress on:*** Symptoms suggestive of liver disease (e.g. jaundice, bleeding tendency, increased abdominal girth). ***Thorough clinical examination including:*** General examination with stress on stigmata of chronic liver disease (gynecomastia, lower limbs oedema, ascites, bruises and other signs of bleeding tendency), local abdominal examination of liver, spleen and for presence of ascites, BMI for all subjects included. ***Laboratory investigations including:*** Liver function tests: Bilirubin, total serum protein, serum albumin, prothrombin time and INR, complete Blood Count including white blood cells, platelet count and haemoglobin concentration, renal function tests: serum creatinine, serum sodium, potassium, calcium, phosphorus, serum alpha feto protein (AFP), HBs Ag, HCV Ab, HB Core Ab (IgG and IgM), estimation of serum vitamin D level (25 hydroxycholecalciferol) was done on blood samples taken from the patients after 12 hours fasting by using ELISA technique. ***Imaging and radiological studies including:*** Abdominal ultrasound with special comment on parenchyma of liver, whether there is any focal lesion and it's size, presence or absence of ascites, portal vein diameter, splenic size, splenic vein diameter, and presence of venous collaterals. ***Exclusion criteria:*** Patients under corticosteroid treatment or hormonal therapy as oral contraceptive pills, patients under multi-vitamins or vitamin D treatment, patients with chronic kidney disease, patients with liver cirrhosis due to other causes than HCV, patients with condition leading to bone disease. ***Inclusion criteria:*** In order to be included, patients had to fulfill the following criteria: a diagnosis of post HCV liver cirrhosis based on clinical or ultrasonographic signs, liver transplantation with follow up at least 6 months after transplantation, patient age is 18 years or more. ***Statistical analysis:*** Statistics were done using the mean, standard deviation and chi-square test using the software program SPSS V.20.

RESULTS

Table (1): Gender in patients and control groups

Gender			Cases	Control	Total
Male		**N**	13	6	19
		%	86.7%	60.0%	76.0%
Female		**N**	2	4	6
		%	13.3%	40.0%	24.0%
Total		**N**	15	10	25
		%	100.0 %	100.0%	100.0 %
Chi-square	**X^2**		**2.339**		
	P-value		**0.126**		

P. value obtained on comparing gender in the three groups of patients group I (pre transplant patients), group II (post transplant patients) and group III (chronic HCV patients without cirrhosis as control group).

Table (2): Comparison between MELD score in patients and control groups

		Mean	±	S.D	ANOVA test	p. value		
MELD score	**Pre**	17.67	±	4.17	48.892	0.001*	P1	0.001*
	Post	9.67	±	2.13			P2	0.001*
	Control	6.90	±	0.74			P3	0.025*

P1: Pre & Post; P2: Pre & Control; P3: Post & Control
ANOVA test was used for comparison between the three groups, group I, group II and group III.

P1is the p. value between group I and group II with statistical significant difference (p. value 0.001), P2 between group I and group III with statistical significant difference (p. value 0.001) and P3 between group II and group III with statistical significant difference (p. value 0.025).

Table (3): Comparison between vitamin D level in patients and control groups

		Mean	±	S. D	ANOVA test	p. value		
Vitamin D	Pre	9.80	±	1.03	55.980	0.001*	P1	0.001*
	Post	19.87	±	2.04			P2	0.001*
	Control	37.30	±	4.41			P3	0.001*

P1 is the p. value between group I and group II with statistical significant difference (p. value 0.001), P2 between group I and group III with statistical significant difference (p. value 0.001) and P3 between group II and group III with statistical significant difference (p. value 0.001).

Table (4): Comparison between sodium level in patients and control groups

		Mean	±	S. D	ANOVA test	p. value		
Sodium	Pre	134.73	±	3.33	11.838	0.001*	P1	0.002*
	Post	139.80	±	3.10			P2	0.001*
	Control	142.40	±	5.97			P3	0.125

P1 is the p. value between group I and group II with statistical significant difference (p. value 0.002), P2 between group I and group III with statistical significant difference (p. value 0.001) and P3 between group II and group III with no statistical significant difference.

DISCUSSION

Vitamin D after synthesis in the skin or receiving through the meal is metabolized to the active metabolite calcitriol in the liver and kidney. Since a part of vitamin D is metabolized in the liver, some studies suggested that vitamin D deficiency might be associated with certain liver diseases. A high prevalence of vitamin D deficiency can be observed in patients with liver cirrhosis [(5)]**.** It is well established that compromised liver function will affect an individual's ability to synthesize vitamin D [(6)]**.** Chronic hepatitis C infection is one of the main causes of liver disease including liver cirrhosis [(7)]**.** Lower vitamin D levels have been observed in chronic hepatitis C patients with advanced fibrosis compared to those with mild or absent fibrosis. A recent meta-analysis has reported that the diagnosis of advanced liver fibrosis was doubled when plasma vitamin D levels were ≤ 10 ng/mL. Additionally, sustained virological response rates were twice in those patients with serum vitamin D levels > 20 ng/mL [(8)]**.** The incidence of severe vitamin D deficiency (<25ng/mL) increases with worsening synthetic liver dysfunction and consequences of vitamin D deficiency include liver disease progression, infection, and graft failure. Vitamin D deficiency is endemic among all patients with cirrhosis listed for transplantation [(9)]**.** The aim of this study was to estimate vitamin D level in post HCV liver cirrhosis patients before and six months after liver transplantation in comparison to chronic HCV patients without cirrhosis. Our study was conducted on a total of 25 patients. All were recruited from Ain Shams specialized hospital in the period from February 2017 to November 2017. They were divided into three groups: **group I** which consists of post HCV liver cirrhosis screened before liver transplantation (*pre transplant group*), **group II** which consists of the same patients of group I evaluated six months post liver transplantation (*post transplant group*) and **group III** which consists of chronic HCV patients without cirrhosis as *control group*. In this study, male patients were 19 (76%) and female patients were 6 (24%). This reflects the male predominance in the incidence of liver cirrhosis. This can be explained by the fact that men are more likely to be infected with HCV [(10)]**.** In this study, the mean of Child Pugh score in pre transplant patients (group I) was 9.67 which decreased six months post liver transplantation in group II to 5.27 with p. value 0.001 as shown in table 3. This agrees with ***David et al.*** [(11)] who stated that Child score decreased post liver transplantation from 10.43 pre transplant to 6.39 post liver transplantation with p. value 0.002. Also MELD score in pre transplant patients (group I) was 17.67 while in post liver transplant patients (group II) it was 9.67 with p. value 0.001 as shown in table 4. This agrees with ***Yung-Chang et al.*** [(12)] who stated that MELD score decreased from 18.47 in pre transplant patients to 9.73 after liver transplantation with p. value 0.023. In this study, there is highly significant statistical difference between pre transplant patients (group I) and post transplant patients (group II) as regard total bilirubin which decreased from 3.37 mg/dl pre transplant to 1.26 mg/dl post transplantation with p. value 0.001 as shown in table 7. This agrees with ***Charlotte et al.*** [(6)] study which was conducted on 20 patients with liver cirrhosis with a mean follow up period of six months after liver transplantation who proved a statistical

significance difference between total bilirubin level decreasing from 3.46 mg/dl at screening pre transplantation to 1.32 mg/dl post transplantation with p. value 0.005. There was a statistical significant difference between group I (pre transplant patients with liver cirrhosis) and group III (control group of chronic hepatitis patients without cirrhosis) as regards INR which was 1.52 in patients with cirrhosis and 1.32 in chronic hepatitis patients without cirrhosis with p. value 0.014 as shown in table 8. These results agree with ***Peng et al.*** [(9)] who proved a statistical significant difference as regards INR between chronic hepatitis without cirrhosis patients and liver cirrhosis patients with p. value 0.012. The mean sodium level in in pre transplant patients (group I) was 134.7 mg/dl and in post liver transplant patients (group II) was 139.8 mg/dl as shown in table (9). This agrees with ***Jana et al.*** [(13)] study which was conducted on 143 patients with liver cirrhosis, they undergone liver transplantation with a mean follow up period of six months and stated that serum sodium increased post liver transplant from 135 mg/dl pre transplant to 140 mg/dl in post transplant patients. This was explained by activation of the renin-angiotensin system that occurs in liver cirrhosis and increased aldosterone level which promotes the reabsorption of sodium and water by acting on the kidney leading to decreased serum sodium that is improved after liver transplantation. There was a statistical significant difference between pre and post liver transplant patients as regards haemoglobin which increased from 11.15 g/dl in pre transplant patients (group I) to 12.40 g/dl in post liver transplant patients (group II) as shown in table 10. This agrees with ***Diogo et al.*** [(14)] who stated that haemoglobin increased post liver transplant from 10.8 g/dl pre transplant to 12.7 g/dl post liver transplantation. This was explained by impaired coagulation and increased bleeding tendency in patients with liver cirrhosis in addition to splenic sequestration of red blood cells due to portal hypertension induced hypersplenism and viral- and toxin-induced bone marrow suppression that improves after liver transplantation. This result disagrees with ***Ben et al***. [(15)] who stated that there is no significant difference between pre and post transplantation haemoglobin. There was a statistical significant difference between pre and post liver transplant patients as regards calcium level which increased from 8.33 mg/dl in pre transplant patients (group I) to 8.79 mg/dl in post liver transplant patients (group II) to be almost as normal persons in whom serum calcium ranges from 8.5 to 10.5 mg/dl as shown in table 12. This agrees with ***Lucilene and Maria*** [(16)] who stated that calcium level improved post liver transplantation and increased from 8.2 mg/dl pre transplant to 9 mg/dl post transplant. There was a statistical significant difference between pre and post liver transplant patients as regards serum albumin which increased from 2.85 g/dl in pre transplant patients (group I) to 3.91 g/dl in post transplant patients (group II) as shown in table 6. This agree with ***Peng et al.*** [(9)] who stated that albumin level improved post liver transplantation and increased from 2.9 g/dl pre transplant to 4.1 g/dl post transplant.

CONCLUSION

This study concluded that vitamin D deficiency is prevalent among patients with liver cirrhosis. Liver transplantation improves vitamin D level but not to the recommended normal level i.e. vitamin D deficiency or insufficiency can persist after transplantation.

CONFLICTS OF INTEREST

There are no conflicts of interest.

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