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The Clinical Impact of Serum Testosterone Levels in Egyptian Patients with Different Stages of Hepatitis C Virus

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A B S T R A C T

This study was done to discover the relation among total testosterone levels and liver damage in Egyptian patients. Chronic Hepatitis C virus (HCV) infected patients with compensated and decompensated cirrhosis with and without hepatocellular carcinoma (HCC) were enrolled in this study. Serum specimens from patients of forty male and forty female adults had been withdrawn. Total testosterone scales were specified with compare with ten males and ten females' normal people without any known liver damage as control groups. Decreased scales of total testosterone were found in male chronic HCV patients with decompensate cirrhosis and in male chronic HCV patients with compensated and decompensate cirrhosis with HCC. Increased scales of total testosterone were found in male patients with chronic HCV with compensated cirrhosis. There were no considerable changes in the scales of total testosterone in all female patients in this study. Decreased scales of total testosterone were correlated with an increased hazard of liver damage and HCC in male Egyptian patients. No observed alteration in the scales of total testosterone in female Egyptian patients with different degrees of liver damage. There is positive correlation between alpha fetoprotein and male testosterone in patients of chronic HCV with compensated cirrhosis and negative correlation between them in the all others remaining patients, while no correlation between alpha fetoprotein and female testosterone.

Introduction

Males have strikingly increased risk of advanced liver disease [1] , Hepatitis C virus is the main cause of chronic liver disease and cirrhosis, and also liver cancer [2]. Hepatocellular carcinoma (HCC) is the second most common cancer-related death worldwide [3]. Nearly 90 to 95 % of all HCC occur in the context of known and often preventable risk factors, such as chronic viral hepatitis, alcohol abuse, and metabolic disorders. Although several experimental lines of research support a direct role for hepatitis C virus (HCV) in cancer promotion, cirrhosis is the main risk factor for this tumor, whereas other factors like alcohol and tobacco smoking are clearly able to accelerate HCC development [4]. Egypt has the highest prevalence of HCV in the world and the prevalence of HCC is increasing in the last years [5]. Egypt has high prevalence of hepatocellular carcinoma (HCC). It is the 2nd most common cancer site among males and 7th among females (NCI Cancer Registry, 2002-2007). The rising rates of HCC in Egypt are due to the high prevalence of hepatitis B virus (HBV) and hepatitis C virus infection (HCV) (25.9% and 78.5%) among Egyptian population [6]. A strong association between chronic HCV infection and sexual dysfunction [7,8]. In the bloodstream, testosterone is highly protein-bound, with only 2% of the hormone circulating as free testosterone. Sex hormone binding globulin (SHBG) is produced in the liver and binds approximately 40% of testosterone with extremely high affinity. Albumin binds Testosterone with lower affinity and carries approximately 50% [9]. Testosterone is a serious anabolic hormone, with actions on muscle, bone, and hematopoiesis. Numerous of the features of in progress liver disease are like to those seen in hypogonadal men, including sarcopenia, osteoporosis, gynecomastia, and low libido [9]. A German study found that men with low serum testosterone levels were at a higher risk of hepatic steatosis than men with high serum testosterone levels [10]. One expects a similar relation between hepatic steatosis and serum testosterone levels;

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however, this potential relationship has not been extensively investigated [11]. Estrogen levels are frequently elevated in men with cirrhosis. This may reflect increased peripheral aromatization of Testosterone to E2 [13]. The current survey was completed to explore the scales of total testosterone in Egyptian chronic HCV patients with compensate and decompensate cirrhosis with and without HCC.

Materials and methods

The current survey is a retrospective observational cross-sectional study on patients who visited National Hepatology and Tropical Medicine Research Institute (NHTMRI) from the attendants of outpatient clinic and from inpatients in the time between January 2017 and May 2017. 80 patients were enrolled in the study. Data like age and sex were collected by using a questionnaire and clinical data were extracted from the patient's records. The overall 100 cases were classified into five equal groups; group I normal people without any known liver damage, group II patients with chronic HCV with compensated cirrhosis, group III patients with chronic HCV with decompensate cirrhosis, group IV HCV patients with compensated cirrhosis complicated by HCC, and group V HCV patients with decompensate cirrhosis complicated by HCC. All groups of patients were diagnosed and classified by physicians of NHTMRI from inpatients clinics according to their medical reports and were diagnosis according to their liver function tests, ultrasonography, computed tomography and liver biopsies to confirm the cirrhosis while the control people were chosen by physicians of NHTMRI from the Patients families of inpatients and outpatient clinics and were undergo to liver function tests and virological markers to confirm that they were without any liver damage, and all the above results did not mention since these results were out of the focus of the study. All The containment criterions were patients without HBV infection, without weed, tobacco or alcohol booze. Blood specimens for the measure of serum total testosterone scales were withdrawn by venipuncture completed between 8:00 - 11:00 AM. Serum total testosterone scales were calculated utilizing the Coat-A-Count total testosterone kit (Siemens Diagnostics Inc., Los Angeles, CA, USA). HCC patients were diagnosed with biomarker alpha-fetoprotein (alpha-fetoprotein $\geq$ 800) by the method of the electrochemiluminescence immunoassay "ECLIA" Cobas e 602 immunoassay analyzers, Cobas, Roche, US and also by abdominal computed tomography (CT) and ultrasonography.

Results

Risk factors were highly prevalent among cases groups as regard HCV Ab, alcohol booze, weed tobacco and past history of liver disease than the control group (**Table 1**).

All studied groups were matched for age and sex and the difference in between were statistically non considerable (**Table 2**).

All studied groups were matched for regard serum testosterone (**Figure 1**) and alpha fetoprotein and the difference in between were statistically considerable (**Table 3**). Values are represented as mean $\pm$ SD of 20 subject/group. P values were significant at <0.05 compared to control.

Table 1: Risk factors among the studied groups.

	Cases N=80		Control=20	
	No	**(%)**	**No**	**(%)**
Anti-HCV				
Positive	80	100	0	0
Negative	0	0	20	100
Cigarette smoking				
No	80	100	20	100
Yes	0	0	0	0
Alcohol drinking				
No	80	100	20	100
Yes	0	0	0	0
Past liver disease history				
No	0	0	20	100
Yes	80	100	0	0

HCV, Hepatitis C virus.

Table 2: Demographic characteristics of all studied groups.

Groups		I (normal healthy people without any known liver damage	II (patients with chronic HCV with compensated cirrhosis)	III (patients with chronic HCV with decompensate cirrhosis)	IV (HCV patients with compensated cirrhosis complicated by HCC)	V (HCV patients with decompensate cirrhosis complicated by HCC)	Statistical test of significance
Sex	Male	10	10	10	10	10	Chi-square 0
	Female	10	10	10	10	10	
Age Mean ± SD P value (compared to control group)		59.2 ± 12.1	57.2 ±11.3 0.966 NS	58.1±9.8 0.966 NS	58.7 ±7.8 0.966 NS	59.3 ±10.3 0.966 NS	ANOVA test(f) 0.141

HCV, Hepatitis C virus; HCC, Hepatocellular carcinoma; SD, Standard Deviation; NS, non significant.

Table 3: Serum total testosterone and alpha-fetoprotein levels among the studied groups.

Groups	I (normal healthy people without any known liver damage	II (patients with chronic HCV with compensated cirrhosis)	III (patients with chronic HCV with decompensate cirrhosis)	IV (HCV patients with compensated cirrhosis complicated by HCC)	V (HCV patients with decompensate cirrhosis complicated by HCC)
Mean Alpha fetoprotein (ng/ml) ± SD P value (regard to control group)	16.2 ±4.1	67.2 ±12.1 0.001 HS	213.1±17.8 0.001 HS	1007±77.8 0.001 HS	995.3±100.2 0.001 HS
Mean Total testosterone in male patients (ng/ml) ± SD P value (regard to control group)	4.86 ±0.767	14.2±0.45 0.001 HS	0.728±0.464 0.001 HS	0.741±0.422 0.001 HS	0.672±0.382 0.001 HS
Mean Total testosterone in female patients (ng/ml) ± SD P value (regard to control group)	0.534±0.131	0.43±0.115 0.07 NS	0.446±0.112 0.07 NS	0.381±0.093 0.07 NS	0.419±0.099 0.07 NS

HCV, Hepatitis C virus; HCC, Hepatocellular carcinoma; SD, Standard Deviation; HS, highly significant; NS, non significant.

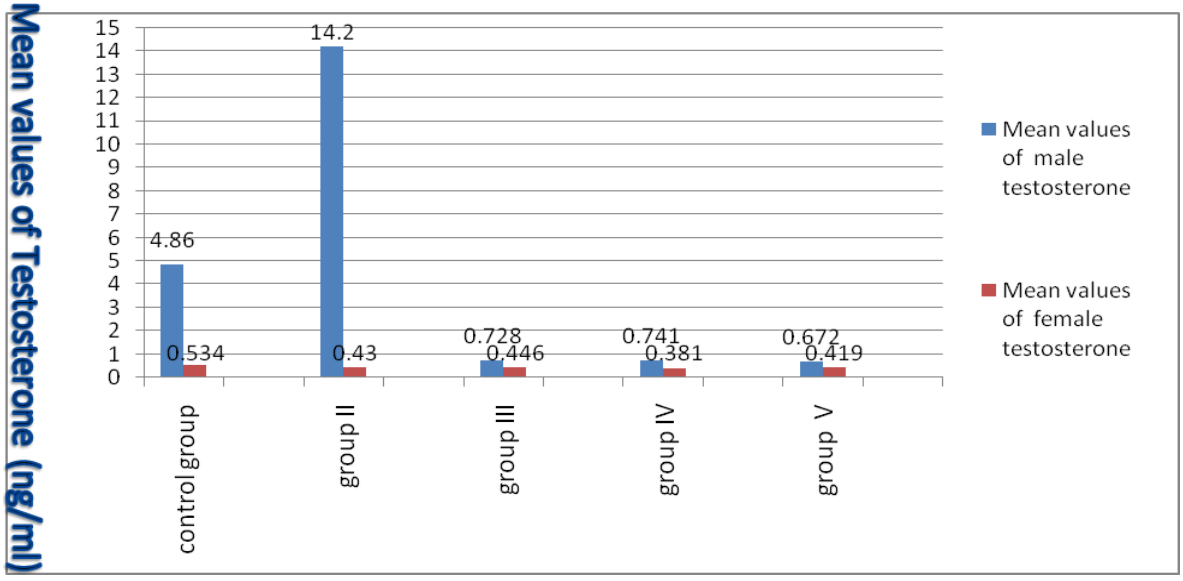

Fig. 1: Serum testosterone levels in all studied groups.

Total testosterone level was increased in males with chronic HCV with compensated cirrhosis (group II) compared to normal people (group I). On the other hand total testosterone levels were decreased in male HCC patients with chronic HCV with decompensate cirrhosis (group V). Also, it was decreased in male, HCC patients with chronic HCV patients with compensated cirrhosis (group IV) and decreased also in male complicated chronic HCV patients with decompensate cirrhosis (group III). No observed change in total testosterone level in all female patients**.** Tumor marker alpha-fetoprotein level was markedly elevated among patients with hepatocellular carcinoma (group IV & V) and significantly elevated in both HCV compensate and decompensate cirrhotic liver patients (groups II and III). Both of decompensate cirrhotic group (group III) and hepatocellular groups (group IV and group V) are higher than normal subjects group (group I) and higher than group of chronic HCV with compensate cirrhosis (group II). There is positive correlation between alpha fetoprotein and male testosterone in group II and negative correlation between them in the others groups, while no correlation between alpha fetoprotein and female testosterone (**Figure 2**).

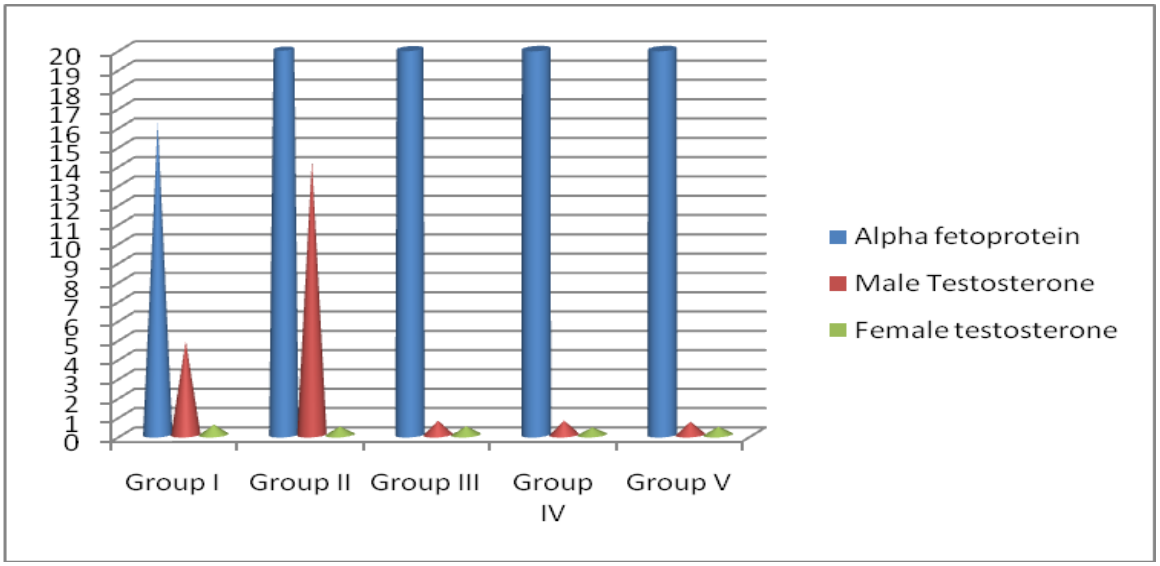

Fig. 2: The relation between alpha fetoprotein and Serum testosterone levels (male and female) in all studied groups.

Discussion

This study revealed that the high scales of serum total testosterone were correlated with the HCV-infected group with compensate cirrhosis among male patients. This correlation between serum testosterone and HCV infection has been kept even after predominant the effect of HBs Ag carrier status, anti-HCV positive, alcohol booze, weed tobacco, past liver disease history [15]. On the other side, this survey shows no considerable alteration in the scales of total testosterone in all female patients. Few surveys have scanned the correlation between testosterone and HCV infection and even little have classified the potential link between testosterone and HCV patients [16,17]. A cross-sectional survey in male veterans with chronic HCV, serum samples were gained to detect total serum testosterone and do the FibroSURE-ActiTest. The correlation between total testosterone and hazard of in progress hepatic fibrosis (F3 and F3/F4) and inflammatory action (A3 and A2/3) detected by the FibroSURE-ActiTest was estimated. The technique implied this correlation between testosterone and HCV infection is yet in general hazy. Mean total serum testosterone was considerable higher in advanced fibrosis cases and advanced inflammatory action cases. Total testosterone in the upper tertile was correlated with an even major raised hazard of advanced fibrosis than advanced inflammatory action [1]. One possible explanation is total serum testosterone is correlated with a raised hazard of both advanced fibrosis and inflammatory action in HCV-infected men. Testosterone scales may be serious in the pathogenesis of HCV-related advanced liver disease [1]. The current survey shows lower serum testosterone level among HCC with compensate and decompensate cirrhosis and among HCV patients with decompensate cirrhosis groups than other groups and the difference in between are statistically significant among male patient while it is not evident among female patients. Another study also reported depressed testosterone scales have been informed in up to 90% of males being estimated for liver transplantation. The extent of the slide in serum testosterone correlates with the riskiness of liver disease [12,13].

Serum testosterone is decreased up to 90% of men with cirrhosis, with scales drops as liver disease advances, extra lately, it was explained that decreased testosterone in men with cirrhosis is correlated with increased mortality [9]. Also *Grossmann M et al [2012]* [12] reported that there was a considerable correlation between testosterone scales and mortality in men with liver disease. The pathogenesis of hypogonadism in decompensate cirrhotic patients is sophisticated and not well illustrated. It includes both a gonadal and a hypothalamic-pituitary dysfunction, which is shown in lab trials by a decrease in gonadotropins (FSH and LH), total testosterone and FT serum scales. A decreased plasma scales and offspring rate of testosterone in cirrhosis of the liver and that the technique of the hypogonadism is perhaps secondary to hypothalamic-pituitary inhibition rather than to primary testicular dysfunction [14]. In current survey increase serum levels of testosterone were correlated with early phase of liver diseases and the decreased levels of serum testosterone were correlated with developing of liver diseases and with an increased hazard of developing HCC, this may be due to that many clinical sequelae of advanced liver disease, such as anemia, sarcopenia, bone disease, and gynecomastia are also seen in hypogonadism. Therefore, low testosterone levels may contribute to at least some of these manifestations [12].

Conclusion

The values of total testosterone were reduced in males HCC patients with compensate and decompensate cirrhosis and reduced in males chronic HCV with decompensate cirrhosis. It was elevated in males of chronic HCV with compensate cirrhosis, while there was no significant changes in the values of total testosterone scales in female patients. There was a significant correlation between total testosterone scales and the degrees of risk of liver damage in males Egyptian patients.

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