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A STUDY OF BONE MINERAL DENSITY IN CHRONIC NON-CIRRHOTIC HEPATITIS-C INFECTION

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ABSTRACT

The occurrence of metabolic bone disease in patients with established post-hepatitis cirrhosis has been documented in many previous studies. However, little is known about bone disease in patients with chronic non-cirrhotic viral hepatitis B or C. therefore, the aim of this study was to evaluate bone mass non-invasively using dual energy X-ray bone densitometery (DEXA) in chronic pre-cirrhotic hepatitis-C patients for evidence of excessive bone turnover.

Thirty male patients with chronic hepatitis-C infection in histologically proven non-cirrhotic stages (stage 0-2) were chosen, with age range 24-59 years and mean age 38.6 + 6.4 years, in addition to twenty age-matched healthy control males. Both patients and controls were subjected to: (1) Full history taking and clinical examination (2) Full liver function tests and estimation of serum aminotransferases levels (3) Estimation of serum creatinine, phosphorus, corrected serum calcium and oral glucose tolerance lest (4) hormonal assay including carboy-terminal fragment of parathyroid hormone (PTH-C terminal) and free T3 & T4 (5) hepatitis viral markers: HBs Ag, HBc Ab, HCV-RNA (PCR), all patients were positive to HCV-RNA (PCR) but negative to HBs Ag and HBc-Ab.

(6) CT-guided needle liver biopsy (only for patients) to rule out patients with established cirrhosis (7) DEXA at lumbar spine (LS) as a non-invasive technique, used for evaluation of bone mass.

The study showed that twelve patients 12/30 (40%) had low bone mass (T-score value <-1). There were no significant differences between patients with low bone mass and those with normal bone mass (T-score values >-1), as regards serum albumin levels, Aminotransferases levels and prothrombin time (P> 0.05). Serum phosphorus, corrected serum calcium and parathyroid hormone-carboxy terminal were all normally ranged for all patients irrespective to their bone mass. Bone mass (T-score values) was significantly low in cholestatic patients in comparison to non-cholestatic patients (P<0.01). All cholestatic patients had low bone mass (osteopenia/osteoporosis), while only five out of 23 non-cholestatic patients 5/23 (21.7%) had low bone mass (osteopenia). There were no significant correlation between levels of HCV-viraemia (viral load) and bone mass (T-score values) (P> 0.05), there are no other available published series about such correlation. ***conclusion & recommendation:*** The study showed a significant association between chronic non-cirrhotic hepatitis-C infection and low bone mass. This needs to be confirmed by biological markers of osteopenia through further larger studies. Patients with chronic non-cirrhotic hepatitis-C infection should undergo bone densitometeric assessment; if osteopenic, they should start anti-osteoporotic therapy to avoid major morbidity and mortality which may complicate osteoporosis.

INTRODUCTION & THE AIM OF THE WORK

Previous studies suggest that loss of bone mineral density (BMD) frequently occurs in patients with chronic viral hepatitis presenting with histological evidence of liver cirrhosis. However, little is known about the occurrence of bone disease in non-cirrhotic hepatitis patients (Schiefke et al., 2005). Therefore, it was the aim of this study to evaluate those patients for associated changes in BMD and excessive bone turnover.

Recent studies have reported correlation between chronic hepatitis B or C and osteoporosis even before cirrhotic changes. Both reduced bone formation and increased bone resorption have been found in patients with chronic liver disease, particularly if associated with cholestasis. Reduced

bone formation is assumed to happen in pre-cirrhotic patients, while increased bone resorption is suggested to occur in patients with established liver cirrhosis (Hay, 1995).

The exact pathogenic mechanism of bone disease in chronic non cirrhotic viral hepatitis is unknown. It is likely a multifactorial process; suggested factors are reduced physical activity, low body mass, hypogonadism, vitamin D deficiency and cholestasis (Janes et al. 1995).

The aim of this study was to evaluate patients with chronic non-cirrhotic hepatitis C-infection for associated changes in bone density and evidence of excessive bone turnover; and whether these changes in bone mass are correlated to various virological and biochemical parameters.

SUBJECTS AND METHODS

Thirty male patients with chronic hepatitis-C virus (HCV) infection without histological evidence for liver cirrhosis were selected from Internal Medicine department of Al Hussain university hospital and Al Duaah hospital, with age range 24 –59 years. In addition to twenty age- matched apparently healthy volunteer males. All patients and controls were submitted to the following:

(1) Full history taking and clinical examination.

(2) Laboratory investigations, blood was drawn after overnight fasting, serum was separated and analyzed for:

(i) Serum bilirubin (total, conjugated fraction), serum albumin, prothrombin time, serum aminotrasferases levels (ALT & AST), serum phosphorus, corrected serum calcium, serum creatinine, in addition to oral glucose plasma glucose tolerance test (OGTT) by colorimetric technique (Larry and Karicka, 1996).

(ii) HBs-Ag, HBc-Ab and HCV-Ab, estimated by enzyme linked immunosorbent technique (ELISA) [Larry and Karicka, 1996].

(iii) HCV-RNA, estimated quantitatively by polymerase chain reaction (PCR) [Larry and Karicka, 1996], using commerical kits from human Inc. Germany by real time ABI prism 7000.

(iv) Hormonal assay: PTH-c terminal, TSH, FT3, FT4 levels; were estimated by radioimmunoassay technique [Larry and Karicka]; using commercial kits from human Inc. Germany.

(3) CT-guided biopsy (only performed for patients), to rule out histological evidence of liver cirrhosis.

(4) Dual enery-x-ray absorptiometery (DEXA) as an ideal non-invasive technique for evaluation of bone mineral density (ie, bone mass) through T-score values analysis in the lumbar spine as a single site selected for assessment of bone mineral density, as about 50% of the lumbar spine is formed of trabecular bone in which osteoporotic changes are more prominent and the Precision is better than in the femoral neck (Verne Joul, 1998)

PATIENTS

All patients had high hepatic aminotransferases enzymes (ALT & AST) ≥ two times the upper limit of the normal levels. They all had positive HCV-Ab (by ELISA-3rd generation) and HCV-RNA (by PCR) with negative HBV serology. Patients were categorized into three groups as regards the level of HCV viremia:

(a) Patients with low viremia: HCV-RNA (PCR) 10^3-10^4 copies /ml.

(b) Patients with moderate viremia: HCV-RNA (PCR) 10^4-10^5 copies/ml.

(c) Patients with high viremia: HCV-RNA > 10^5 COPIER/ml.

Exclusion Criteria for selected patients:

1 - Female patients, for exclusion of postmenopausal osteoporosis.

2 - Patients with history of diabetes mellitus, alcohol abuse, cigarette smoking, or drugs which affect bone metabolism like: heparin therapy, vitamin "A" or "D" therapy or corticosteroid therapy.

3 - Patients with histologic evidence of liver cirrhosis.

4 - Patients with some established endocrine diseases which are characterised by low bone mass eg; impaired glucose tolerance or frank diabetes mellitus,cushing's syndrome and thyrotoxicosis.

5 - patients on combination therapy with interferon (IFN) and ribavirin, as this form of therapy may enhance bone turnover (Shiefk et al, 2005).

6 - patients with concomitant renal impairment.

CONTROLS

They all were apparently healthy males, having normal liver function tests and aminotransferases levels with negative serology for hepatitis B and C viruses. They all were non diabetic, non smoker or alcoholic and matched in age with patients group.

METHODS

1 - CT guided needle liver biopsy:

The biopsy was performed as a reliable technique for exclusion of cirrhotic changes in patients with chronic hepatitis-C infection. Automatic true-cur liver biopsy needle (16-swg.) was used guided by Samaton CT apparatus.

The patients were fasting for about eight hours, their prothrombin concentration was > 60% and their platelets count was > 80% of normal values. The patients were asked to lie in supine position, then the biopsy site was sterilized and 5 ml of xylocain 2% was locally injected: the biopsy was taken while the patients were holding their breath in deep inspiration and the patients were asked to lie on their right side for six hours with one hourly monitoring of his vital signs (Crawford et al; 1998).

(2) Histopathological study

The specimens were fixed in 10% formalin and processed into paraffin blocks, cut by microtome and stained with Hematoxylin, Eosin and Masson trichrome stains for histologic diagnosis of hepatitis and exclusion of cirrhotic changes.

(3) Dual energy x-ray absorptiometery (DEXA):

**Certainly, it is the most widely available technique that is used to measure bone density and to characterize fracture risk sites such as the hip or spine. It is a precise, non-invasive, reproducible fast and low radiation dose technique. Evaluation involved lumbar spine region($L_1 - L_4$), it has an important role in diagnosing and treating osteoporosis. (Kowalchuk, and Dolinka, 1998)

** The DEXA examination was done at Al

** **Diagnosis of osteopenia/osteoporosis was based on world health organization criteria for osteoporosis (Brunder and Shelton, 2002):**

Diagnostic category	T-Score
(1) Normal BMD	≥ - 1
(2) Osteopenia	< -1 and > - 2.5
(3) Osteoporosis	< - 2.5 without fracture
(4) Established osteoporosis	< - 2.5 with fracture

Duaah hospital-Bone Densitometry Unite.

NB: T-score = difference between the registered value and the reference value of mean bone mineral density (BMD in gr/cm2-SD) comparable for sex and ethnicity of young adults at bone metabolic equilibrium (Schiefke, et al; 2005).

(4) Statistical analysis:

Data were summarized as mean ± SD. Comparisons between means were performed by the use of student's T-test. Differences between proportions were estimated by the Chi – square test. Anova test was used to compare means in more than two groups of patients. Person's correlation coefficient was used for estimation of the level of association between two variables: A result was considered significant if $P < 0.05$.

RESULTS

** Data obtained were statistically analysed and tabulated in (table 1-8).

Serum phosphorus, corrected total serum calcium, renal function profile, oral glucose tolerance test, thyroid hormones, carboxy-terminal parathyroid hormone fragment, were all within normal range for all patients (table 8).

Table (1): Statistical comparison between controls and patients; as regards biochemical profile, prothrombin time and aminotransferases levels.

Variables	Group	Mean	SD	Min.	Max	T-rest	
						P	Sig
AST (0-40 U/L	Patients **(No=30)** Controls **(No=20)**	84.33 24.20	27.12 5.17	48 16	168 43	<0.001	H.sig.
ALT (0-40 U/L	Patients Controls	98.85 28.30	31.44 5.78	55 18	192 42	<0.001	H.sig.
Total serum Bilirubin (0.2-1)mg/dl	Patients Controls	1.98 0.52	1.14 0.07	0.70 0.40	5.2 0.70	<0.005	H.sig.
Serum Albumin (3.5-5)mg/dl	Patients Controls	3.68 4.34	0.61 0.23	2.8 3.9	4.6 4.8	<0.001	H.sig.
Prothrombin Time **(12-14)** second	Patients Controls	15.12 11.20	2.05 0.70	13 10	18 13	<0.001	H.sig.

There were statistically significant differences, between controls and patients as regards levels of AST, ALT, total serum bilirubin, and serum albumin as well as prothrombin time (P < 0.01).

Table (2): Statistical comparison between controls and patients as regards T-score vales at lumbar spine, measured by DEXA

T-Score	Mean	± SD	Min	Max	T – test	
					P	Sig
Patients: No = 30	-1.35	0.442	-3.5	0.5	<0.05	Sig
Controls: No = 20	- 0.04	0.628	- 1.55	0.95		

There was statistically significant higher values of T-Score at lumbar spine in controls in comparison to patients

Table (3): Comparison between cholestatic and non-cholestatic patients, as regards serum bilirubin (total and conjugated fraction) and T-Score values at lumbar spine.

Variable	Non-cholestatic patients :No=23 (conjugated bilirubin< 50% of Total bilirubin).				Cholestatic patients: No =7 (conjugated bilirubin > 50% of Total bilirubin).			
	Mean	SD	Min	Max	Mean	SD	Min	Max
Total serum bilirubin (0.2 – 1mg/dl)	19	0.55	0.7	2.8	3.40	1.33	0.60	5.20
Direct(Conjugated) bilirubin (up to 0.25)	0.4	0.18	0.20	0.60	2.20	0.82	1.00	3.50
T-Score values	-0.922	0.234	-2.3	0.51	-2.624	0.545	-3.5	-2.1
T- test:	P < 0.01 (Sig)							

There was a statistical significant difference between cholestatic and non cholestatic patients regarding T-score values which was significantly lower in cholestatic than non-cholestatic patients (P < 0.01).

Table (4): Distribution of diagnostic categories of bone density at lumbar spine (LS) region, measured by DEXA in both cholestatic and non-cholestatic patients.

Diagnostic category of bone density.	Non-cholestatic patients: No = 23/30 (76.7%)	Cholestatic patients: No = 7/30 (23.3%)
Normal BMD (T-score ≥ - 1)	18/23 (78/3%)	Non (0%)
Osteopenia (T-Score<-1and>- 2.5)	5/23 (21.7%)	4/7 (57.9%)
Osteoporosis (T-score < -2.5)	Non (0%)	3/7 (42.1%)
Chi square test: P < 0.005 (highly sig.)		

There were highly significant differences between cholestatic and non-cholestatic patients, regarding distribution of different bone density categories, measured by DEXA at lumbar spine (LS) region.

Table (5):Statistical comparison between patients with low T-score values and those with normal T-score values, as regards serum levels of aminotransferases.

variables	Patients with normal Tscore values No=18/30 (60%)				Patients with low T-score values No = 12/30 (40%)				T-test	
									P	sig.
	Mean	SD	Min	Max	Mean	SD	Min	Max		
AST level	76.4	12.23	49	128	79.1	10.14	51	136	>0.05	N.sig
ALT level	94.8	18.56	62	216	96.2	20.33	64	210		

There were no significant difference between patients with normal T – score values and those with low T- score values, as regards levels of AST & ALT.

Table (6): Statistical comparison between patients with normal T-score values and those with low T-score values, as regards serum albumin and prothrombin time.

Parameter	Patients with normal T-Score (≥ - 1): No. = 18/30				Patients with low T-score (< -1): No. = 12/30				T-test	
	Mean	± SD	Min	Max	Mean	± SD	Min	Max	P	sig
Serum Albumin (3.2–5) g/dl.	3.81	0.53	3.00	4.8	3.75	0.32	2.9	4.6	>0.05	N.sig
Prothrombin time (12-14) sec.	13.88	0.30	12	15	14.02	0.42	13	17	>0.05	N.sig

There were no statistically significant differences between patients with normal T-score values and those with low T-score values, regarding serum albumin and prothrombin time.

Table (7): Correlation between levels of HCV viremia and T-score values in patients group.

Variables	Patients with low viremia				Patients with moderate viremia				Patients with high viremia			
	No = 8/30 (26.7%)				No = 15/30 (50%)				No = 7/30 (23.3%)			
HCV-RNA (PCR) copies /ml	103 – 104				104 – 105				< 105			
T-score values	Mear	SD	Min	Max	Mear	SD	Min	Max	Mear	SD	Min	Max
	-1.32	1.026	-2.5	0.12	-1.36	1.41	-3.5	0.56	-1.34	1.408	-2.9	0.44
Anova test	P > 0.05											

There was no significant correlation between levels of HCV viremia and T-score values in patient with chronic non-cirrhotic HCV infection. (P<0.05).

Table (8): Statistical comparison between controls and patients with low bone mass regarding corrected serum calcium, phosphorus and PTH-c terminal levels.

Variable	Controls No. = 20	Patients with low bone mass No. = 12/30 (40%).	T-test	
			P	sig
Corrected serum calcium (mg/dl)	- 9.36 ± 0.412	9.44 ± 0.358	> 0.05	N.sig
Serum phosphorus (mg/d)	- 4.81 ± 0.395	4.62 ± 0.320	> 0.05	N.sig
PTH-c terminal (p gm/ml)	119.243 ± 32.11	128.64 ± 48.725	> 0.05	N.sig

There were statistically insignificant differences between patients with low bone mass and controls as regards corrected serum calcium, serum phosphorus and PTH – c terminal levels.

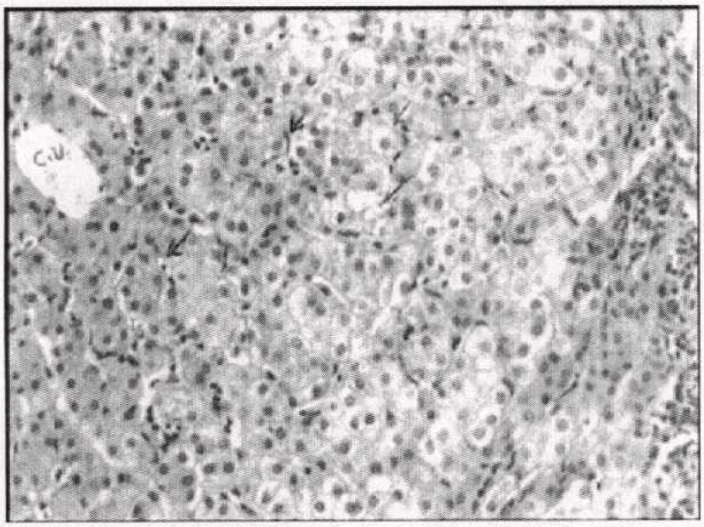
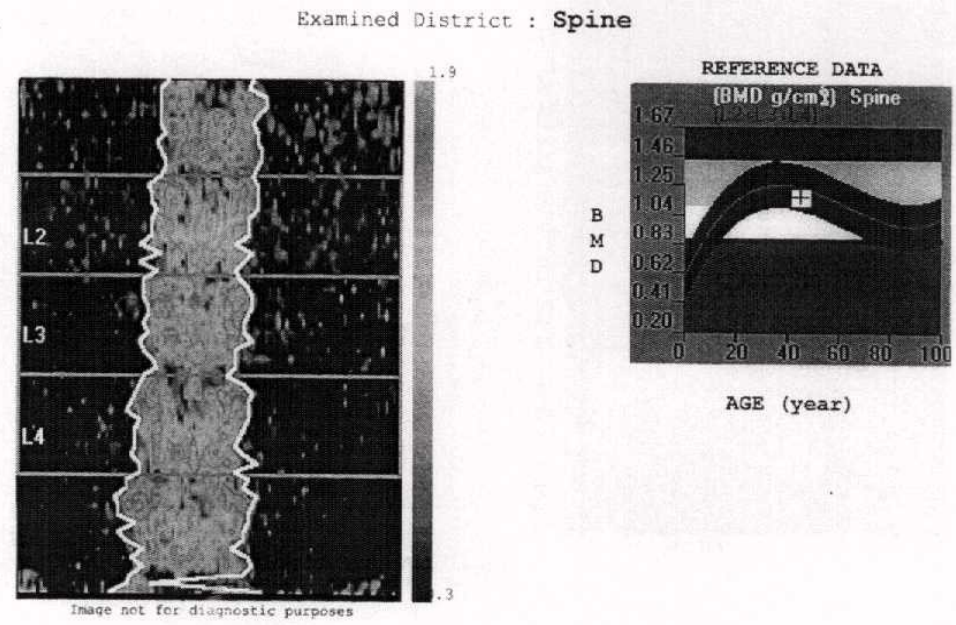


Fig. 1 This figure represents histopathological feature of one of the studied patients with chronic active HCV infection that shows diffuse hepatocyte degeneration in the entire hepatic lobule, associated with lymphocytic infiltration. Some hepatocytes are multinucleated reflecting regeneration process. No fibrous tissue is seen in the hepatic lobules. This feature is consistent with chronic active non-cirrhotic HCV infection.



Densitometry Data

R.O.I.	BMD (ROI) (g/cm²)	(Zscore Ref.) (g/cm²)	Area (cm)²	BMC (g)	ZScore	TScore
L2	1.159	[1.03 -1.34]	10.8	12.474	-0.14 (-2%)	-0.18 (-3%)
L3	1.190	[1.12 -1.46]	10.8	12.880	-0.57 (-8%)	-0.74 (-10%)
L4	1.151	[1.07 -1.40]	12.2	14.025	-0.52 (-7%)	-0.67 (-9%)

Fig. 2: Dual energy x-ray absorptiometery (DEXA) -bone densitometery- revealed: lumbar vertebrae (L_2–L_4) showing bone mineral density (BMD) of (1.151-1.190 g/cm2) with an average T-score of (-0.74 – 0.18) denoting normal BMD.

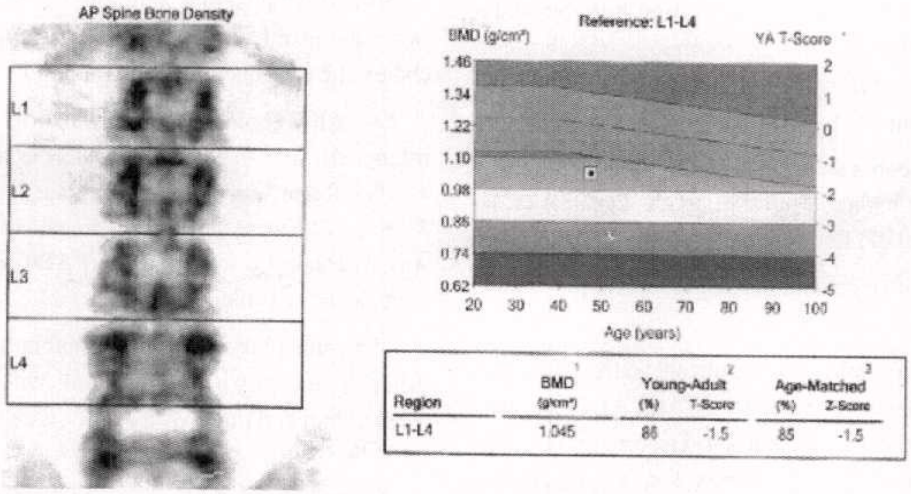
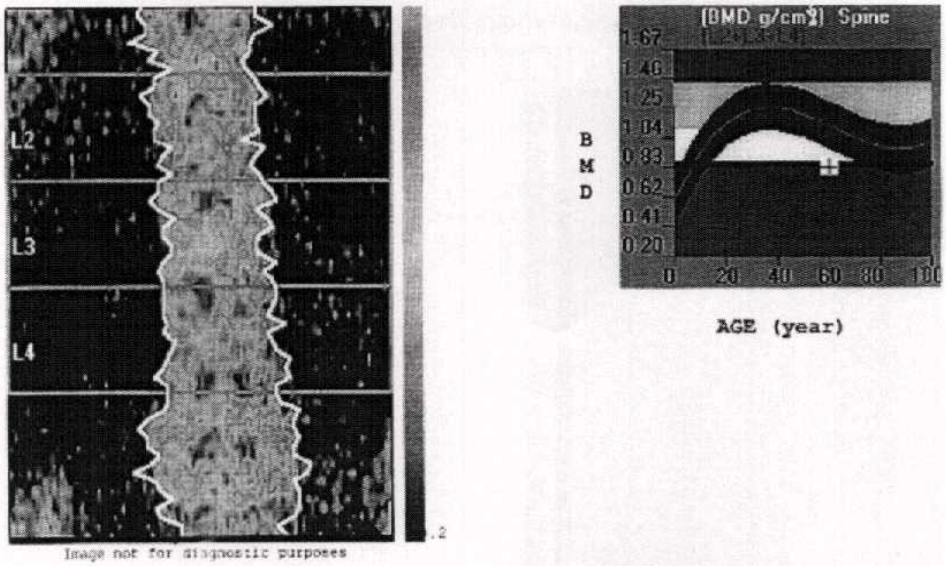


Fig. 3: Dual energy x-ray absorptiometery (DEXA) -bone densitometery- revealed: lumbar vertebrae showing total bone mineral density (BMD) of 1.045 g/cm2 with a T-score of – 1.5 denoting osteopenia with increased fracture risk at this region.



Densitometry Data

R.O.I.	BMD (ROI) (g/cm²)	(Zscore Ref.) (g/cm²)	Area (cm)²	BMC (g)	ZScore	TScore
L2	0.876	[0.92 -1.23]	11.8	10.331	-1.31 (-19%)	-2.02 (-27%)
L3	0.885	[1.01 -1.35]	11.9	10.571	-1.73 (-26%)	-2.52 (-33%)
L4	0.753	[0.96 -1.29]	13.5	10.135	-2.26 (-33%)	-3.10 (-41%)

Fig. 4:Dual energy x-ray absorptiometery (DEXA) -bone densitometery- revealed: lumbar vertebrae showing BMD of (0.753 – 0.885 g/cm2) with a T-score of (-2.02 – -3.10) denoting osteoporosis with increased fracture risk.

Analysis of results

** The biochemical parameters of liver function (serum albumin, total serum bilirubin and prothrombin time) as well as serum aminotransferases levels were statistically higher in patients group than control group (P <0.005) (table 1).

** T-score values at the lumbar spine (Ls) were statistically higher in control group than patients group (P < 0.05) [table 2].

** Twelve patients 12/30 (40%) had low bone mass(T-score values <-1).

** There were no significant differences in serum aminotransferases (AST & ALT) levels between patients with normal T-score values (T-score ≥ - 1) and those with how T-score values (T-score<-1); P> 0.05 [table 5].

** Regarding serum bilirubin (total and conjugated fraction); patients were grouped into two groups (1) non-cholestatic group (conjugated bilirubin fraction <50% of total serum bilirubin. (2) Cholestatic group (conjugated bilirubin fraction > 50% of total serum bilirubin. T score values was significantly lower in cholestatic than non – cholestatic patients (P < 0.01) [table 3].

** All cholestatic patients were either osteopenic 4/7 = 57.9% or osteoporotic (3/7 = 42.1%). Regarding to non-cholestatic patients, only 5/23 (21.7%) were osteopenic, no patient 0/23 (0%) was osteoporotic and 18/23 (78.3%) had normal bone density (Table 4).

** Serum albumin and prothrombin time did not differ significantly between patients with normal T-score values and those with low T-score values (P > 0.05) [Table 6].

Finally there was insignificant correlation between viral load (levels of HCV - viremia) and bone mass (T-score values) (P > 0.05) [Table 7].

DISCUSSION

Hepatic osteodystrophy is a term that identifies metabolic bone disease, which occurs on top of chronic liver disease. Although osteoporosis (loss of bone mass) is seen to be the commonest metabolic bone disease that may complicate chronic liver disease, the potential for osteomalacia (defective mineralisation of bone matrix ie, osteoid,) exists (Hay, 1995).

The prevalence of osteoporosis in patients with chronic liver diseases varies between 10 – 60%, the highest prevalence is observed in cholestatic disorders and alcoholic liver disease (Bonkovsky et al; 1990 and Gallego – Rojo et al., 1998). It has been suggested that reduced bone formation occurs early in pre-cirrhotic patients with chronic viral hepatitis, while increased bone resorption occurs late in patients with advanced (cirrhotic) liver disease (Hay, 1995).

Many previous studies reported loss of bone mass in chronic cirrhotic liver disease. However, little in known about metabolic bone disease in patients with chronic non-cirrhotic hepatitis in whom osteoporosis remains unrecognized (Schiefke et al., 2005).

The most precise, but invasive, technique for diagnosis of osteopenia is bone biopsy. Urine pyridinoline & hydroxyprolin and serum aminoterminal-procollagen III are non-invasive biochemical indicators of bone turnover but they have been shown to be of limited predictive value of osteapenia. The only reliable non invasive detective technique of bone density in dual energy x-ray absorptiometery (DEXA) [Bonkovsky et al., 1990]

In our study we used T-Score as an accurate criterion for estimation of low bone mass in comparison to other inaccurate criteria e.g. Z-score criterion which ignore the age of patients as an independent risk factor for low bone mass [bonkovsky et al., 1990]

Because osteoporotic changes is more prominent in region with high trabecular bone proportions, lumbar spine (LS) region was selected as a solitary site for estimation of bone mass (trabecular bone forms about 50% of Ls but about 30% of femoral neck), therefore bone of LS has faster renewal rate and better precision on DEXA than femoral neck' (Verne Joul, 1998).

Most of risk factors for osteoporosis have been eliminated in our study as all patient were males, nonalcoholic, non smoker, had normal renal and endocrine glands functions with no history of drugs which affect bone metabolism, so the detected loss of bone mass was likely attributed to chronic liver disease. T-score values (bone mass) at lumbar spine (LS) were significantly higher in controls in comparison to patients ($P < 0.05$) [Table 2].

Schiefke et al; 2005 found that bone mineral density (BMD) was significantly reduced in 25/43 (56%) of non-cirrhotic patients with hepatitis B or C infection. This goes with our result as 12/30 (40%) of patients with chronic non-cirrhotic patients with hepatitis-C infection had low BMD. The discrepancy between the prevalence of patients with low bone mass in both studies may be attributed to the racial factor and the involvement of patients with chronic hepatitis –B infection in the former study which may be more complicated with osteopenia than hepatitis-C infection.

There were no significant differences in serum aminotransferases (AST & ALT) levels, albumin levels, and prothrombin times; between patients with normal bone mass (T-score values ≥ -1) and those with low bone mass (T-score values < -1); ($P > 0.05$) [Table 5,6]. This goes with was reported by (Masaki et al., 1998) that there are no standard laboratory measurement of liver function that could predict the diagnosis of low bone mass in patients with chronic liver disease. We found that 7/30 (23.3%) of patients with non-cirrhotic hepatitis–C infection were cholestatic; they had statistically significant lower bone mass (T-score values) than non-cholestatic patients ($P < 0.01$) [Table 3]. While all cholestatic patients had low bone mass (T-score values) [Table 4], only 5/23 (21.7%) of non-cholestatic patients had low bone mass. So, the frequency of osteopeina/osteoporosis in cholestatic patients was significantly higher than that in non-cholestatic patients ($P < 0.005$) [Table 4].

This is consistent with what was reported by (Janes et al., 1995) that both reduced bone formation and increased bone resorption have been found in chronic, particularly cholestatic, liver disease. The

cause of reduced bone mass in chronic cholestatic liver disease is not well understood, it seems to be multifactorial. The most important factor is that unconjugated bilirubin is suggested to have an inhibitory effect on osteoblast proliferation, other suggested factors include: hypogonadism, vitamin D and K deficiency, low body mass index and reduced physical activity (Trantwein et al., 2000 and Hay, 2003). Bone density improves in patients with chronic cholestatic liver disease of viral origin after liver transplantation (Hay, 2003).

There were insignificant differences between patients with low bone mass and controls as regards levels of corrected serum calcium, serum phosphorus and carboxy-terminal fragment of parathyroid hormone (PTH-C terminal) ($P > 0.05$) [Table 8]. This goes with what was reported by (Monegal et al., 1997), that elevated serum PTH mainly reflecting advanced liver disease with histologically proved cirrhosis which is not the case of patients involved in our study, who had histologically proven chronic non-cirrhotic hepatitis-C infection. PTH-c terminal is a degradation product of PTH with a long plasma half life (6 – 12 hours) and in the presence of normal renal function it is considered as an index of chronic PTH hypersecretion that occurs in severe chronic liver disease secondary to hypocalcemia and vitamin D deficiency (defective absorption and 25 hydroxylation in the liver), it falls markedly after liver transplantation.

Although osteomalacia is unusual in chronic liver disease, it may be present in chronic cholestatic liver disorders, it is important to measure vitamin D levels in patients with cholestatic liver disease, if low, vitamin D replacement can easily correct associated osteomalacia (Hay, 1995)

Conclusion and Recommendation:

The study revealed a significant association between chronic non-cirrhotic hepatitis-C infection and osteopenia. Further and larger studies to identify biochemical markers of osteopenia are required to confirm this association. Patients with chronic non-cirrhotic hepatitis-C infection should be considered for routine bone densitometeric assessment early in the pre-cirrhotic course of the disease, if osteopeia is found, anti-osteoporotic therapy should be started to avoid osteoporotic complications which result in major morbidity and mortality.

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دراسة كثافة العظام فى مرضى الالتهاب الكبدى الفيروسى من النوع (ج) الغير مصحوب بتليف فى الكبد

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ثبت من خلال الدراسات السابقة وجود علاقة بين نقص كثافة العظام وتليف الكبد الذى يحدث كأحد مضاعفات الإصابة بالالتهاب الكبدى الفيروسى. إلا أنه لا يتوفر الكثير من المعلومات عن وجود خلل فى كثافة العظام فى مرضى الالتهاب الكبدى الفيروسى (ب) أو (ج) الغير مصحوب بتليف فى الكبد.

لذلك كان الهدف من هذه الدراسة تقييم كثافة العظام بطريقة غير نفاذية (باستخدام جهاز قياس كثافة العظام ذو الأشعة السينية مزدوجة الطاقة فى مرضى الالتهاب الكبدى الفيروسى (ج) فى مرحلة ما قبل التليف الكبدى للتأكد من وجود نقص فى كثافة العظام لديهم.

وقد تم اختيار ثلاثين مريضاً من الذكور المصابين بالالتهاب الفيروسى الكبدى (ج) الغير مصحوب بتليف كبدى (من خلال الفحص الهيستوباثولوجى) ، تراوحت أعمارهم بين 24 – 59 سنة وكان متوسط أعمارهم 38.6 سنة بالإضافة إلى عشرين من الذكور الأصحاء المتوافقين فى العمر مع مجموعة المرضى وذلك كمجموعة ضابطة. وقد تم إخضاع كل من مجموعة المرضى والمجموعة الضابطة للآتى:

1 – استقصاء التاريخ المرضى والفحص الإكلينيكى الشامل.

2 – الاختبارات المعملية الكاملة التى تعكس وظائف الكبد وإنزيمات الكبد فى الدم.

3 – قياس معدلات الكرياتينين الفوسفور والكالسيوم المصحح وكذلك منحنى السكر فى الدم.

4 – قياس هرمونات الغدة الدرقية وهرمون الغدة الجار – درقية ذو النهاية الكربوكسيلية.

5 – قياس دلائل الفيروس الكبدى ب ، ج (ثم اختيار المرضى السلبيين لدلائل الفيروس الكبدى (ب) والإيجابيين لدلائل الفيروس الكبدى (ج).

6 – أخذ عينة كبدية إبرية موجهة بواسطة الأشعة المقطعية (فقط للمرضى الذين شملهم البحث).

7 – تقييم كثافة العظام بواسطة جهاز قياس كثافة العظام ذو الأشعة السينية مزدوجة الطاقة وذلك فى منطقة الفقرات القطنية.

وقد أظهرت الدراسة ما يلى: -

** 40% من المرضى أظهروا نقص فى كثافة العظام.

** لم يكن هناك فارق ذو أهمية إحصائية بين مجموعة المرضى ذوى كثافة العظام المنخفضة ومجموعة المرضى ذوى كثافة العظام الطبيعية بالنسبة لمستويات الألبيومين وإنزيمات الترانس – أمينيز فى الدم وكذلك بالنسبة لزمن البروثرومبين.

** كانت مستويات الفوسفور والكالسيوم المصحح وهرمون الغدة الجار – درقية ذو النهاية الكربوكسيلية فى الدم جميعها فى المعدل الطبيعى فى كل المرضى بصرف النظر عن كثافة العظام لديهم.

** وجود نقص فى كثافة العظام ذو أهمية إحصائية فى المرضى الذين أظهروا ارتفاع فى نسبة البليروبين المتزاوج بالمقارنة بالذين كان لديهم نسبة البليروبين المتزاوج طبيعية.

** جميع المرضى الذين كان لديهم ارتفاع فى نسبة البليروبين المتزاوج كان لديهم نقص فى كثافة العظام بينما فقط 21.7% من المرضى الذين كان لديهم نسبة طبيعية البليروبين المتزاوج أظهروا نقص فى كثافة العظام.

** لم يكن هناك علاقة إحصائية ذات أهمية بين مستويات الحامض النووى الفيروس الكبدى ج (RNA) وكثافة العظام فى مرضى الالتهاب الكبدى (ج) الغير مصحوب بتليف فى الكبد.

الخلاصة والتوصيات:

أظهرت الدراسة وجود علاقة ذات أهمية إحصائية بين الالتهاب الكبدى الوبائى (ج) الغير مصحوب بتليف فى الكبد ونقص كثافة العظام. وهذه النتيجة تحتاج لتأكيدها من خلال الدلالات الحيوية التى تشير إلى نقص كثافة العظام، وذلك من خلال دراسات مستقبلية على نطاق أوسع.

يجب على مرضى الالتهاب الكبدى الفيروسى من النوع (ج) الغير مصحوب بتليف فى الكبد تقييم كثافة العظام لديهم، وفى حالة وجود نقص فيها يجب أن يأخذوا العلاج المناسب لها وذلك حتى يتجنبوا المضاعفات المرضية والمميتة لوهن العظام.