RESULTS

Tables & Figures

The children enrolled in this study were divided into four groups:

- Group I: 25children with metabolic liver disease.
- Group II: 25 children with autoimmune hepatitis.
- Group III: 25 children with viral hepatitis.
- Group IV: 25 normal children (control group).

Table (1): Comparison of age among the different studied groups.

Variable	Group I "n=25"	Group II "n=25"	Group III "n=25"	Group IV "n=25"	F	p
Age (Ys.)					0.81	0.36
Range	7-15	7-16	6-16	7-16		
Median	11	12	11	11		
Mean	10.95	11.81	11.52	11.45		
S.D.	2.30	3.00	2.80	2.282		

This table shows no statistical significant difference among the different studied groups regarding the mean of age (P 0.36).

Table (2): Sex distribution of the studied groups.

Variable	Group I "n=25"	Group II "n=25"	Group III "n=25"	Group IV "n=25"	X^2	p
Sex					1.03	0.41
Male	12(48.0%)	12(48.0%)	15 (60.0%)	13 (52.0%)		
Female	13 (52.0%)	13 (52.0%)	10(40.0%)	12 (48.0%)		

The table shows that there was no statistical significant difference in sex distribution among the different studied groups (P 0.41).

Table (3): Clinical variables of the diseased groups.

Symptoms and signs	Group I "n=25"		Group II "n=25"		Group III "n=25"	
	No.	%	No.	%	No.	%
Anorexia	14	56.0	0	0	0	0
Jaundice	10	40.0	18	72.0	9	36.0
Hematemesis	0	0.0	3	12.0	8	32.0
Edema of LL.	7	28.0	5	20.0	3	12.0
Abdominal pain	16	64.0	0	0.0	15	60
Abdominal enlargement	17	68.0	16	64.0	16	64.0
Hepatomegaly	20	80.0	18	72.0	17	68.0
Splenomegaly	15	60.0	9	36.0	11	44.0
Ascites	10	40.0	7	28.0	9	36.0

This table shows that the most frequent clinical presentation in metabolic liver disease group (group I) was hepatomegaly (80%) followed by abdominal enlargement (68%), abdominal pain (64%) ; while in AIH group (group II) jaundice and hepatomegaly (72%) was the most frequent presentations followed by abdominal enlargement (64%) . In chronic viral hepatitis group hepatomegaly (68%) was the most frequent presentation followed by abdominal enlargement (64%), abdominal pain (60%), jaundice (36%) and hematemesis (32%). Splenomegaly was most frequent among cases of group I (60%) followed by group III (44%) and lastly group II only 9 cases had splenomegaly (36%).

Table (4): Nutritional assessment of the diseased groups by BMI.

BMI	No	%
5th percentile	6	8.0%
10 th percentile	11	14.66%
25 th percentile	21	28.0%
50 th percentile	32	42.66%
75 th percentile	5	6.66%
Total	**75**	

BMI: Body Mass Index

This table demonstrates the distribution of the diseased groups according to the BMI as a measure of nutritional assessment. On the basis of Egyptian growth charts 2002 only 32 cases (42.66%) were at the 50th percentile, 21 cases (28%) were at the 25th percentile, 11 cases (14.66%) were at the 10th percentile, 8 cases (10.66%) were at the 5th percentile and 3 cases (4%) were at the 75th percentile.

Table (5): Liver function test of the studied groups.

Liver function tests	Group I "n=25"	Group II "n=25"	Group III "n=25"	Group IV "n=25"
Total bil. (mg/dl)				
Range	0.35-19.1	0.32-22.37	0.39-23.85	0.6-0.97
Median	1.9	4.1	2.8	0.8
Mean	5.33	8.76	8.21	0.786
S.D.	6.77	9.54	9.53	0.102
Direct bil. (mg/dl)				
Range	0.04-11.3	0.09-15.99	0.13-15.14	0.1-0.4
Median	0.9	2.4	1.5	0.25
Mean	4.23	6.62	6.11	0.2665
S.D.	6.28	7.96	8.17	0.091
AST(U/L)				
Range	25-798	42.7-1302	37-311	19.5-35.3
Median	88	205	90	25.9
Mean	233.52	336.45	132.71	25.845
S.D.	207.92	316.31	84.51	4.516
ALT(U/L)				
Range	23-669	40.9-871	26-279	19.9-32.4
Median	65.1	148	62	26.2
Mean	152.70	262.17	106.63	27.27
S.D.	145.70	228.35	80.86	3.717
T-ALP(U/L)				
Range	91-634	119-1085	69.6-283	16.48-130.4
Median	208	217	202	100.4
Mean	271.60	312.52	103.66	85.059
S.D.	147.41	205.62	84.28	38.014
GGT(U/L)				
Range	6.3-460	4.2-246	12-142.6	26.7-35.11
Median	98	87	74.9	30.75
Mean	123.74	108.81	118.29	30.4675
S.D.	93.73	68.04	6.45	2.180
PT(Sec.)				
Range	12.7-30.6	12-84	12-26.6	11.9-12.95
Median	14	18.1	16.5	12.4
Mean	16.91	23.03	18.29	12.404
S.D.	6.39	14.01	6.45	0.276
PC (%)				
Range	23.9-100	8-100	17.5-100	97-102
Median	75	51.7	56.9	100
Mean	65.17	53.22	63.90	99.65
S.D.	27.27	20.87	25.38	1.137
S.Albumin(g/dl)				
Range	1.1-4.2	2-4.4	1.9-4.5	2.95-4.5
Median	3	3.2	3	4.1
Mean	3.28	3.21	3.14	4.045
S.D.	0.99	0.71	0.62	0.343

Normal values: AST up to 50U/L ALT up to 45U/L Albumin 3.7-5.5 g/dl

T-ALP up to 126 U/L GGT up to 76 U/L

Table (5) shows the mean value and standard deviation of liver function tests of the different studied groups . The highest levels of total bilirubin (8.76 ± 9.54 mg/dl), direct bilirubin (6.62 ± 7.96mg/dl), AST (336.45 ± 316.31U/L), ALT (262.17 ± 228.36U/L), T-ALP (312.52 ± 205.62U/L) and PT (23.03 ± 14.01 sec) were found in group II (AIH group). While gamma glutamyl transpeptidase was highest in group I (metabolic liver disease group) (123.74 ± 93.73 U/L). The lowest level of serum albumin was in group III (virus hepatitis group) (3.14 ± 0.62 g/dl) and the least PC was in group II (53.22 ± 20.87%).

Table (6): Ultrasonographic findings of the studied groups.

Ultrasonographic findings	Group I "n=25"		Group II "n=25"		Group III "n=25"	
	No.	%	No.	%	No.	%
Hepatomegaly	25	100.0	21	84.0	20	80.0
Splenomegaly	19	76.0	13	52.0	16	64.0
Ascites	15	60.0	9	36.0	12	48.0

This table shows that hepatomegaly was the most frequent ultrasonographic finding in metabolic liver disease group (group I) (100%), followed by AIH group (group II) (84%).Also splenomegaly was most frequent in (group I) followed by group III (64%).

Table (7): Liver biopsy findings of the diseased group.

Liver biopsy findings	Group I "n=25"		Group II "n=25"		Group III "n=25"	
	No.	%	No.	%	No.	%
Cirrhotic	11	44.0	13	52.0	17	68.0
Non cirrhotic	14	56.0	12	48.0	8	32.0

This table shows the distribution of the three diseased groups according to the liver biopsy findings, while the percentage of liver cirrhosis was highest in group III (17 cases) (68.0%) followed by group II (13 cases) (52.0%) and the least was in group I (11 cases) (44.0%).

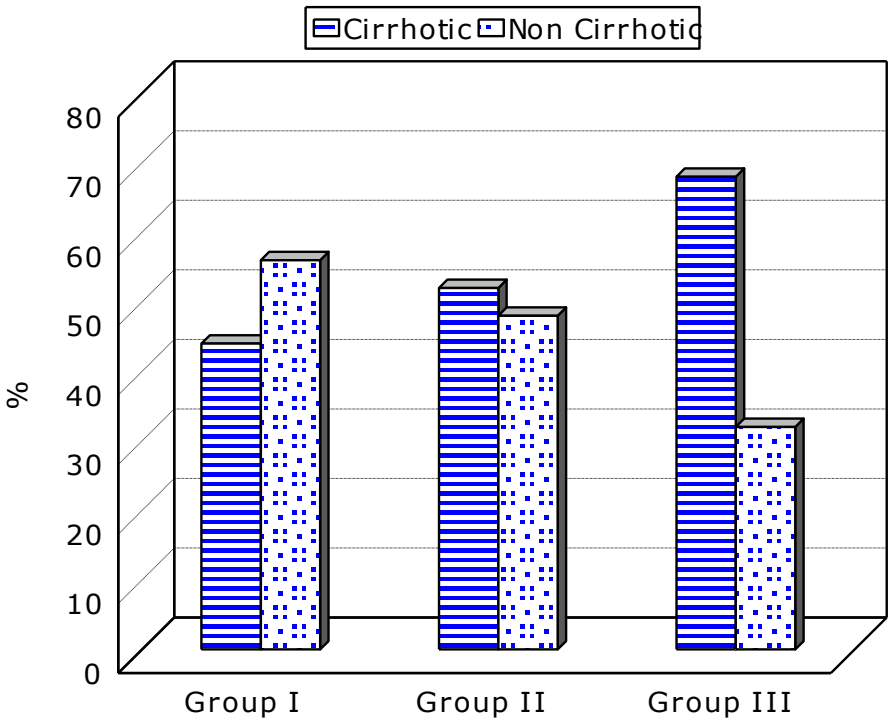

Fig.(1): Liver biopsy finings of the diseased group .

Table (8): Biochemical markers of bone turnover in different studied groups.

Bone turnover markers	Group I "n=25"	Group II "n=25"	Group III "n=25"	Group IV "n=25"	F	P
Osteocalcin (ng/mL)						
Range	10.8-46.6	6.44-48.4	8.11-43.2	2.3-12.65	19.85	0.002**
Mean	18.28	19.34	20.81	7.14		
S.D.	9.04	9.71	9.04	3.09		
B-ALP(U/L)						
Range	10.5-32.1	10.5-52.9	10.6-59.6	8.2-16.8	13.9	0.001**
Mean	27.23	32.60	29.34	11.06		
S.D.	5.93	6.67	8.34	1.85		
DPd (nM/mM)						
Range	5.6-23.5	6.1-50	8.7-45.2	2.3-7.4	22.9	0.0001**
Mean	11.63	18.06	12.26	5.03		
S.D.	4.73	9.09	8.82	1.51		

** High significance difference

This table illustrates the distribution of the studied groups according to the mean values of the biochemical markers of bone turn over ; where the highest level of serum osteocalcin was in group III (20.81 ± 9.04 ng/ml) followed by group II (19.34 ± 9.71 ng/ml) and group I (18.28 ± 9.04 ng/ml). Alkaline phosphatase bone isoenzyme (B-ALP) was highest in group II (32.60 ± 6.67U/L) followed by group III (29.34 ± 8.34U/L) and group I (27.23 ± 5.93U/L). The deoxypyridinoline (DPd) was highest in group II (18.06 ± 9.09nM/mM) followed by group III (12.26 ± 8.82 nM/mM) and group I (12.63 ± 4.73 nM/mM). There is high statistical significance difference between the four studied groups as regard the changes of the serum level of osteocalcin, B-ALP and urinary level of DPd ($P>0.001$).

Table (9):Serum osteocalcin level in different studied groups.

Variable	Group I "n=25"	Group II "n=25"	Group III "n=25"	Group IV "n=25	F	p
Osteocalcin (ng/mL)						
Range	10.8-46.6	6.44-48.4	8.11-43.2	2.3-12.65	19.85	0.002**
Mean	18.28	19.34	20.81	7.14		
S.D.	9.04	9.71	9.04	3.09		

** High significance difference.

Waller-duncan of F-test

	Group I	Group II	Group III
Group II	N.S.		
Group III	N.S.	N.S.	
Group IV	Sig.	Sig.	Sig.

N.S. Non Significance Sig. Significance

Waller-duncan of F-test shows no statistical significant difference between the three diseased groups regarding the serum level of osteocalcin, meanwhile there was significance difference between groups (I, II, III) and group (IV) (control group).

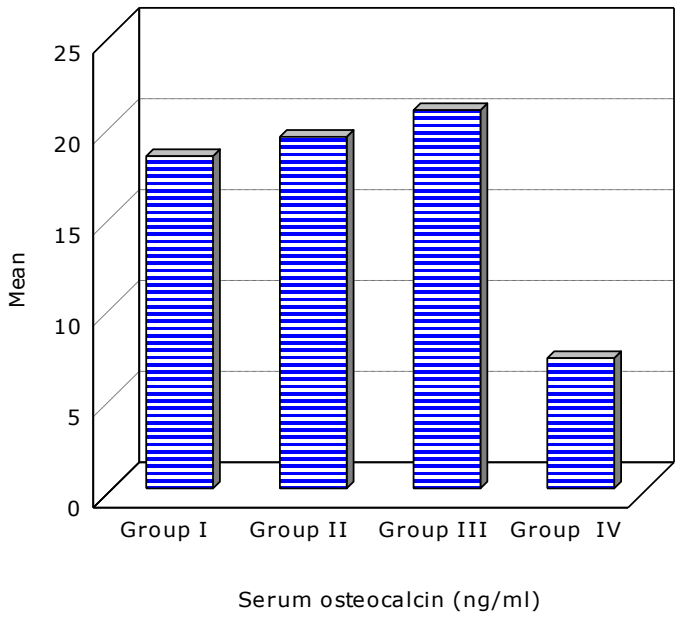

Fig.(2): Serum osteocalcin level in different studied groups

Table (10): Serum osteocalcin (ng/ml) in cirrhotic and non cirrhotic patients in different groups.

Variable	Group I "n=25"	Group II "n=25"	Group III "n=25"	Group IV "n=25"	F	P LSD
Cirrhotic						
Range	13.9-46.6	14.1-48.4	12.9-43.2	2.3-12.65	16.25	0.001*
Mean	21.643	24.398	22.67	7.14		IV # other gps.
S.D.	11.880	9.704	8.807	3.09		
Non cirrhotic						
Range	10.8-15.73	6.44-24.5	8.11-23.4	-	2.65	0.21
Mean	13.196	12.52	15.77			N.S.
S.D.	1.833	4.80	5.56			
t,	4.52	6.25	3.98	-		
p	0.002*	0.001*	0.012*			

ANOVA test was done to demonstrate the relation between the four studied groups regarding the level of serum osteocalcin according to the presence or absences of liver cirrhosis . There was high statistical significance difference between the diseased groups whether having liver cirrhosis or not and the control group .Meanwhile in each of the diseased groups there was a statistical significant difference between group of patients had liver cirrhosis and those did not regarding the level of serum osteocalcin (P>0.001).

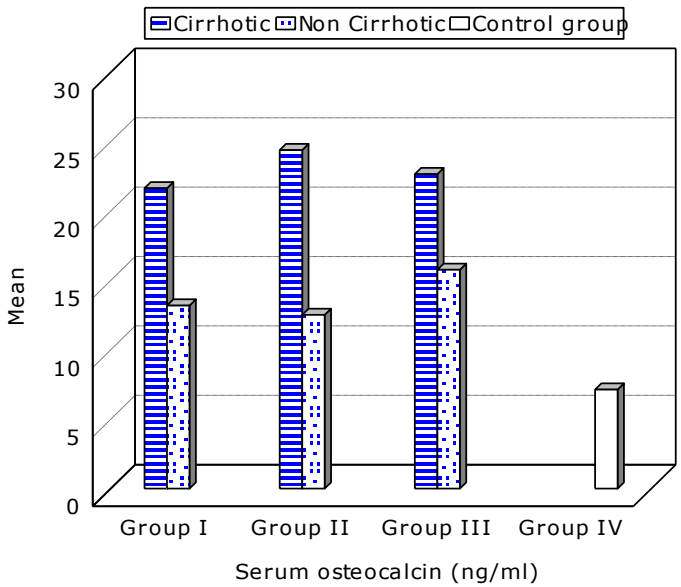

Fig. (3): Serum osteocalcin (ng/ml) in cirrhotic and non cirrhotic patients in different groups

Table (11): Osteocalcin level in patients having liver cirrhosis and those did not and the control group

Variables	Cirrhotic "n=41"	Non – Cirrhotic "n=34"	Control "n=25"	F	p
Osteocalcin (ng/mL) Range Mean S.D.	8.16-48.4 21.45 8.83	6.44-56.6 15.75 8.86	2.3-12.65 7.14 3.09	25.9	0.001**

Waller-duncan of F-test

	cirrhotic	Non cirrhotic
Non Cirrhotic	Sig.	
Control	Sig..	Sig.

Sig. Significance

Regarding the level of serum osteocalcin, Waller-duncan of F-test shows statistical significant difference between groups of patients was having liver cirrhosis and those did not .In the same time both groups had a high significant difference between both of them and the control group.

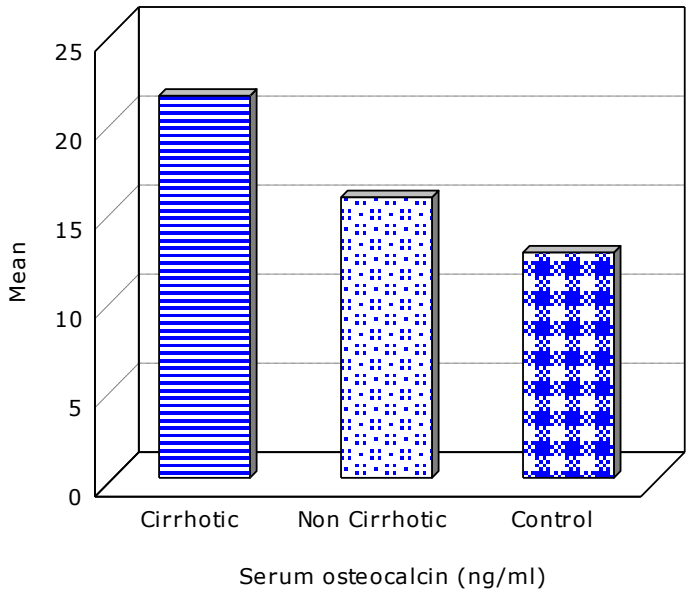

Fig.(4): Osteocalcin level in patients having liver cirrhosis and those did not and the control group

Table (12): Serum B- ALP in different studied groups.

Variable	Group I "n=25"	Group II "n=25"	Group III "n=25"	Group IV "n=25"	F	p
B-ALP(U/L)						
Range	10.5-32.1	10.5-52.9	10.6-59.6	8.2-16.8		
Mean	27.23	32.60	29.34	11.06	13.9	0.001**
S.D.	5.93	6.67	8.34	1.85		

** High significance difference .

Waller-duncan of F-test

	Group I	Group II	Group III
Group II	N.S.		
Group III	N.S.	N.S.	
Group IV	Sig.	Sig.	Sig.

N.S. Non Significance Sig. Significance

Waller-duncan of F-test shows no statistical significant difference between the three diseased groups regarding the serum level of bone alkaline phosphatase isoenzyme B-ALP, meanwhile there was significance difference between groups (I, II, III) and group (IV) (control group).

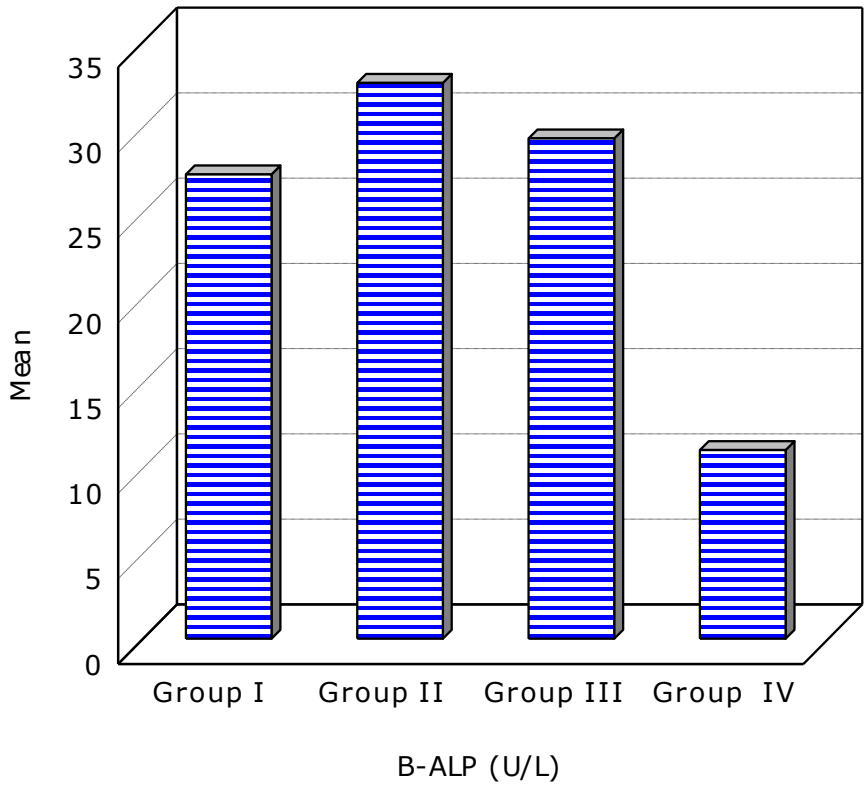

Fig.(5): Serum B- ALP in different studied groups.

Table (13): B-ALP (U/L) in cirrhotic and non cirrhotic patients in different groups.

Variable	Group I "n=25"	Group II "n=25"	Group III "n=25"	Group IV "n=25"	F	p
Cirrhotic Range Mean S.D.	14.6-32.1 18.943 4.964	13.1-52.9 24.100 14.650	11.2-59.6 23.41 12.109	8.2-16.8 11.06 1.85	9.52	0.0032* IV # other gps.
Non cirrhotic Range Mean S.D.	10.5-17.8 13.101 1.976	10.5-28.3 17.83 6.34	10.6-29.8 17.31 7.26	-	2.06	0.32 N.S.
t, p	2.65 0.035*	3.03 0.029*	2.71 0.036*	-		

ANOVA test was done to demonstrate the relation between the four studied groups regarding the level of serum B-ALP according to the presence or absences of liver cirrhosis. There was high statistical significance difference between the diseased groups (groups I & II and III)whether having liver cirrhosis or not and the control group(group IV) .Meanwhile in each of the diseased groups there was a statistical significant difference between group of patients had liver cirrhosis and those did not regarding the level of serum B-ALP (P>0.001).

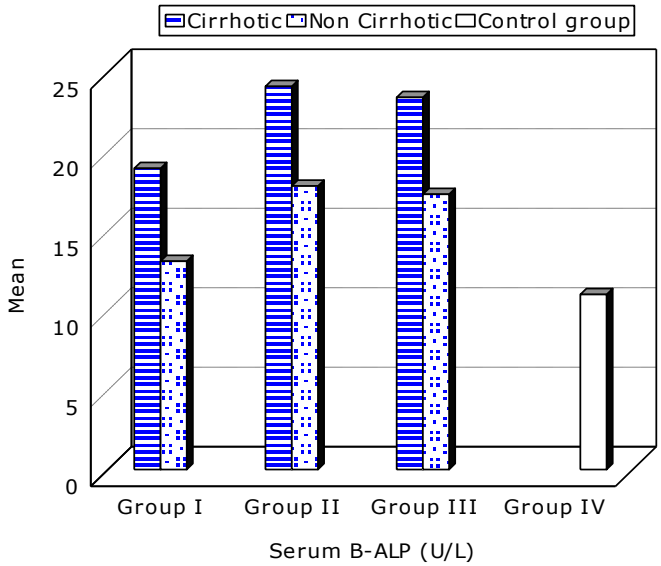

Fig. (6): B-ALP(U/L) in cirrhotic and non cirrhotic patients in different groups.

Table (14) B-ALP level in patients having liver cirrhosis and those did not and the control group

Variables	Cirrhotic "n=41"	Non – Cirrhotic "n=34"	Control "n=25"	F	p
B-ALP(U/L)					
Range	10.5-63.46	9.6-52.9	8.2-16.8		
Mean	24.34	19.11	11.06	10.73	0.012*
S.D.	15.82	9.69	1.85		

Waller-duncan of F-test

	cirrhotic	Non cirrhotic
Non cirrhotic	Sig.	
control	Sig.	Sig.

Sig. Significance

Waller-duncan of F-test shows statistical significant difference between groups of patients was having liver cirrhosis and those did not .Meanwhile both groups had a high significant difference regarding the level of serum bone alkaline phosphatase (B-ALP) and the control group.

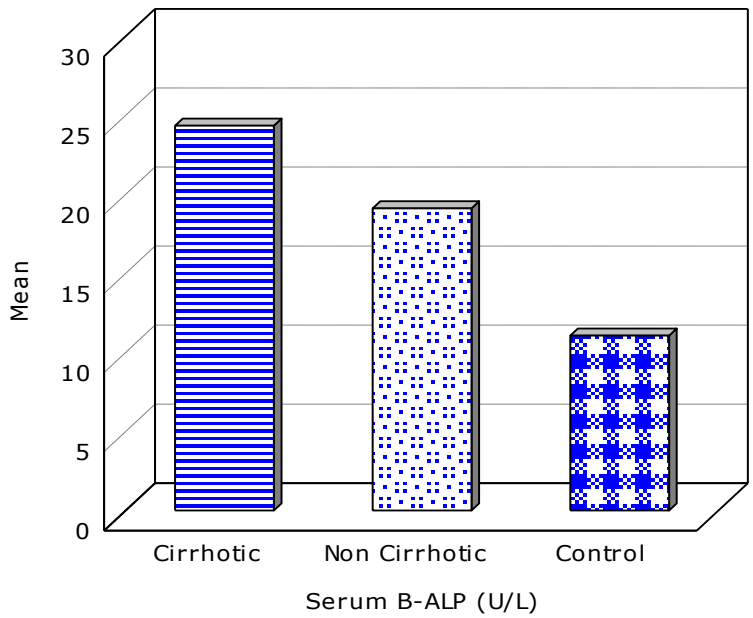

Fig. (7): Serum B-ALP level in patients having liver cirrhois and those did not and the control group

Table (15): Deoxypyridinoline (DPd) level in different studied groups.

Variable	Group I "n=25"	Group II "n=25"	Group III "n=25"	Group IV "n=25"	F	p
DPd (nM/mM)						
Range	5.6-23.5	6.1-50	8.7-45.2	2.3-7.4		
Mean	11.63	18.06	12.26	5.03	22.9	0.001**
S.D.	4.73	9.09	8.82	1.51		

** High significance difference

Waller-duncan of F-test

	Group I	Group II	Group III
Group II	Sig.		
Group III	N.S.	Sig.	
Group IV	Sig.	Sig.	Sig.

N.S. Non Significance Sig. Significance

Waller-duncan of F-test shows statistical significant difference between group II (AIH) in one hand and group I and group III on the other hand regarding the level of DPd, in the same time there was significance difference between groups (I, II, III) and group (IV) (control group).

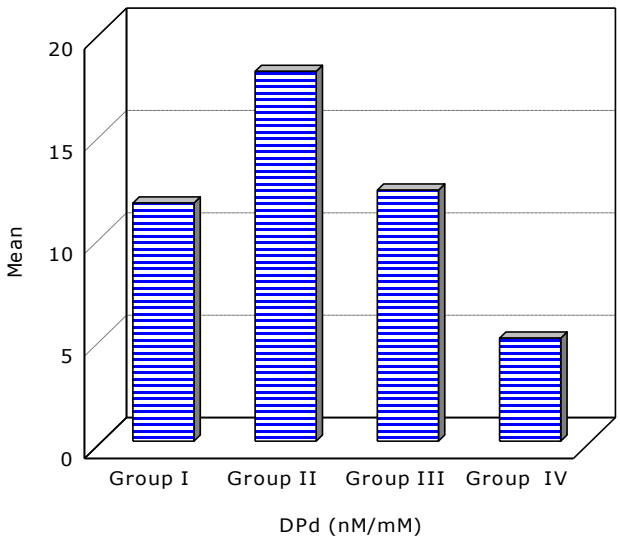

Fig. (8): Deoxypyridionnlin (DPd) level in different studied groups

Table (16): DPd (nM/mM) in cirrhotic and non cirrhotic patients in different groups.

Variable	Group I "n=25"	Group II "n=25"	Group III "n=25"	Group IV "n=25"	F	p
Cirrhotic						
Range	8.75-23.5	10.7-50	10.4-45.2	2.3-7.4	9.87	0.021* IV # other gps.
Mean	14.696	20.131	20.62	5.03		
S.D.	4.302	9.852	8.549	1.51		
Non cirrhotic						
Range	5.6-15.2	6.1-13.3	8.7-18.7	-	2.65	0.31 N.S.
Mean	9.385	10.21	12.99			
S.D.	2.549	2.42	3.40			
t,	3.12	5.65	4.06			
p	0.021*	0.001*	0.0039*			

ANOVA test was done to demonstrate the relation between the four studied groups regarding the level of DPd according to the presence or absences of liver cirrhosis. There was high statistical significance difference between the diseased groups (groups I & II and III) whether having liver cirrhosis or not and the control group (group IV) .Meanwhile in each of the diseased groups there was a statistical significant difference between group of patients had liver cirrhosis and those did not regarding the level of DPd (P>0.001).

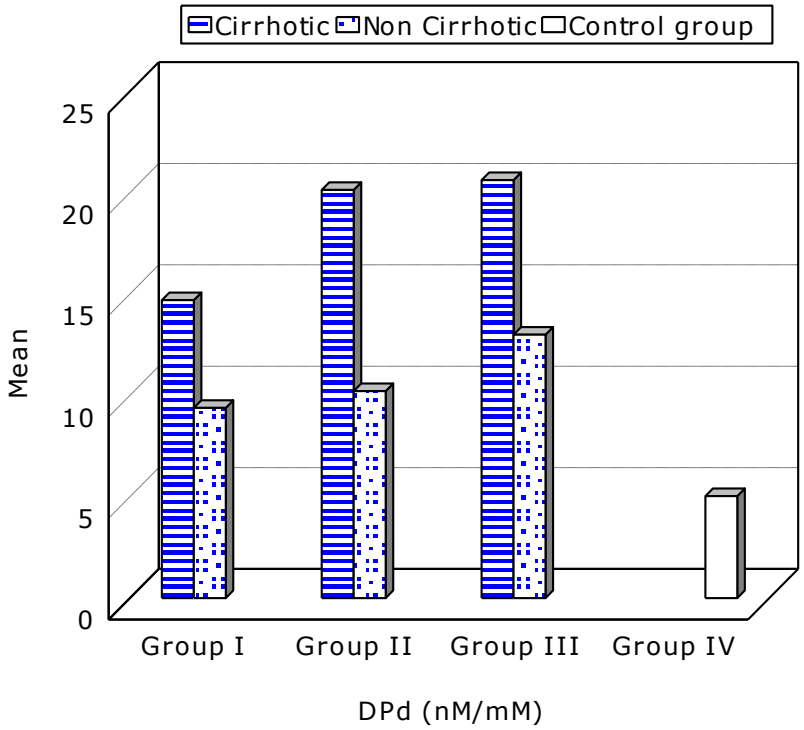

Fig. (9): DPd (nM/mM) in cirrhotic and non cirrhotic patients in differnt groups

Table (17): DPd level in patients having liver cirrhosis and those did not and the control group.

Variables	Cirrhotic "n=41"	Non – Cirrhotic "n=34"	Control "n=25"	F	p
DPd (nM/mM)					
Range	7.1-50	5.6-50	2.3-7.4	21.47	0.0015**
Mean	16.25	13.53	5.03		
S.D.	8.06	7.55	1.51		

Waller-duncan of F-test

	cirrhotic	Non cirrhotic
Non cirrhotic	Sig.	
control	Sig.	Sig.

Sig. Significance

Waller-duncan of F-test shows statistical significant difference between groups of patients was having liver cirrhosis and those did not .Meanwhile both groups had a high significant difference regarding the level of deoxypyridinoline (DPd) and the control group.

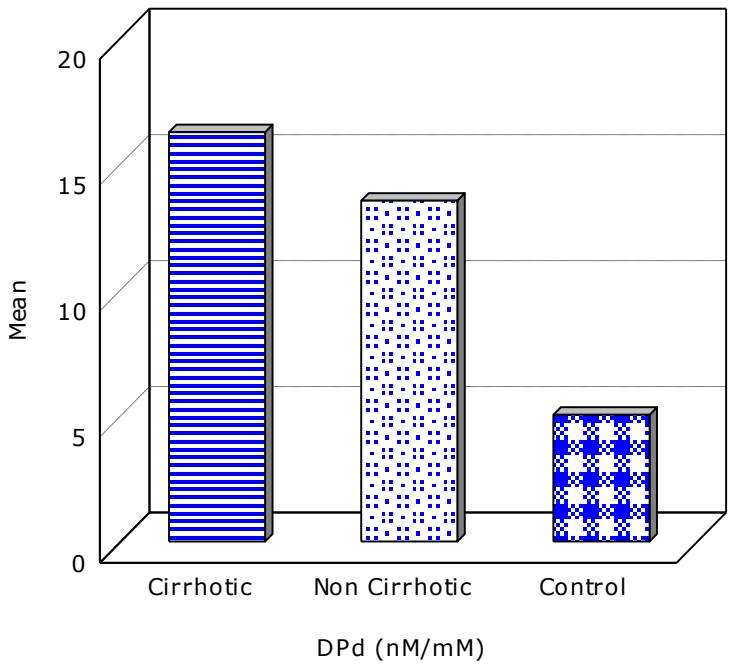

Fig.(10):DPd level in patients having liver cirrhosis and those did not and the control

Table (18): Correlation between bone markers and liver function tests.

Variables	Osteocalcin	B-ALP	DPd
Total bilirubin r p	 0.261 >0.05	 0.042 >0.05	 -0.005 >0.05
AST(U/L) r p	 -0.073 >0.05	 -0.018 >0.05	 0.095 >0.05
ALT(U/L) r P	 0.016 >0.05	 -0.020 >0.05	 0.026 >0.05
T-ALP(U/L) r P	 0.024 >0.05	 0.364 0.02*	 0.135 >0.05
GGT(U/L) r P	 -0.134 >0.05	 -0.071 >0.05	 -0.002 >0.05
Serum albumin r p	 -0.477 0.019*	 -0.575 0.012*	 -0.42 0.015*
Prothrombin activity (%) r P	-0.335 0.02*	-0.392 0.028*	-0.367 0.014*

* Significance difference
r = correlation coefficient

This table shows the correlation between the changes in biochemical markers of bone turnover (osteocalcin, B-ALP and DPd) and the changes of liver function tests. There is negative moderate correlation between the level of serum albumin and the bone markers but there is no statistical significance difference, meanwhile there is a statistical significance difference between the level of T-ALP and B-ALP with positive moderate correlation. Also there is a statistical significance between the changes in prothrombin concentration and the osteocalcin level with negative moderate correlation between them (p=0.01).

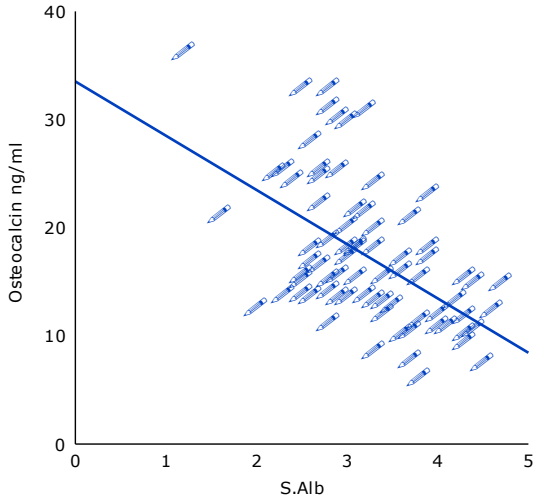

Fig.(11): Correlation between S. Alb and Osteocalcin ng/ml.

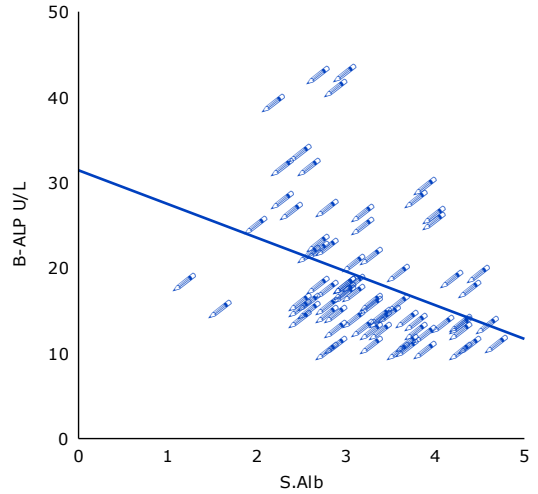

Fig.(12): Correlation between S. Alb and B-ALP U/L

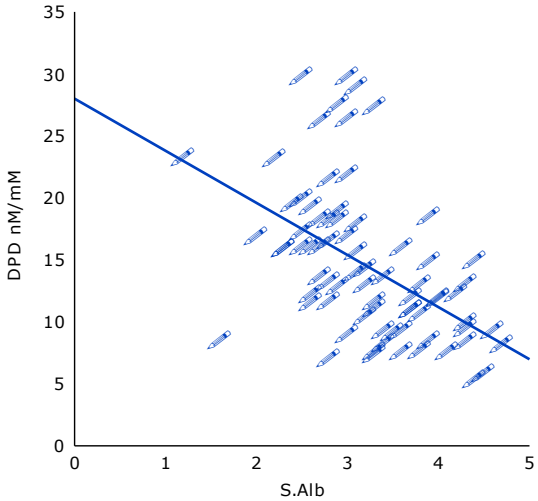

Fig.(13): Correlation between S. Alb and DPD nM/mM

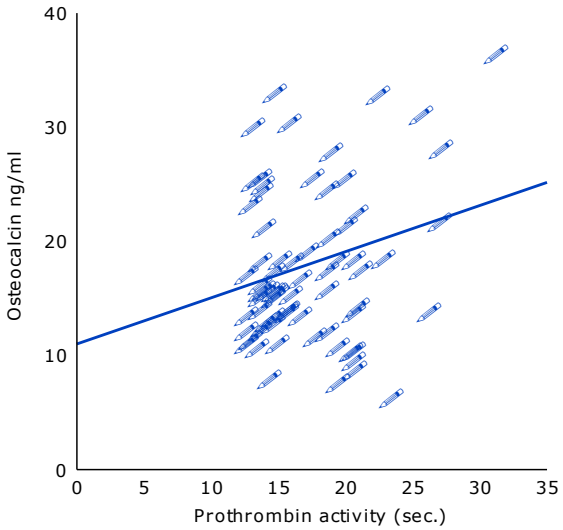

Fig.(14):Correlation between prothrombin activity and Osteocalcin ng/ml.

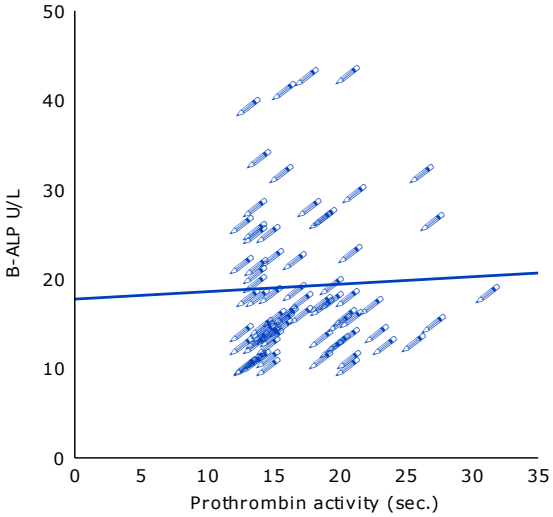

Fig.(15): Correlation between prothrombin activity and B-ALP U/L

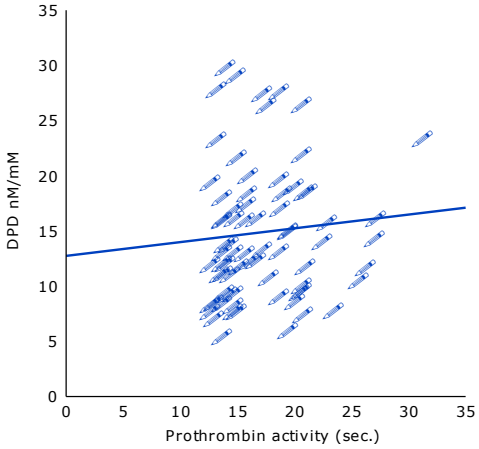

Fig.(16): Correlation between prothrombin activity and DPD nM/mM

Table (19): Comparison between metabolic liver disease groups regarding biochemical markers of bone turnover as regard the diagnosis.

Variables	Wilson disease "n=13"	GSD "n=12"	t	p
Osteocalcin (ng/mL) Range Mean S.D.	 10.9-36.6 18.896 11.372	 10.8-18.4 14.59 2.51	2.98	0.02*
B-ALP (U/L) Range Mean S.D.	 10.5-34.9 17.050 7.234	 12.8-22.3 16.65 3.58	0.98	0.39
DPd (nM/mM) Range Mean S.D.	 5.6-23.5 12.203 5.337	 7.8-19.5 13.02 3.90	1.6	0.10

*Significance difference.

This table shows a statistical significant difference between children affected with Wilson disease (n=14) and those suffering from GSD (n=11) regarding the level of serum osteocalcin ($P<0.05$) as osteocalcin level was (18.896 ± 11.372 ng/ml) in Wilson disease and (14.59 ± 2.51 ng/ml) in GSD. Regarding the serum level of B.ALP and urinary level of DPD there was no significant difference between Wilson disease group and GSD group ($P>0.05$).

Table (20): Comparison between cirrhotic and the non cirrhotic patients in metabolic liver disease group regarding biochemical markers of bone turn over.

Variables	Wilson disease "n=14"		GSD "n=11"	
	Cirrhotic "n=9"	Non cirrhotic "n=5"	Cirrhotic "n=2"	Non cirrhotic "n=8"
Osteocalcin (ng/mL)				
Range	15.1-36.6	10.9-28.5	12.3-18.4	10.8-17.3
Mean	19.9	16.25	16.15	13.15
S.D.	12.11	9.58	3.01	2.04
t, p	**2.79, 0.012***		**1.98, 0.035***	
B-ALP (U/L)				
Range	13.9-34.9	10.5-29.5	15.3-22.3	12.8-21.3
Mean	18.050	15.65	17.65	14.52
S.D.	7.234	6.98	3.28	4.03
t, p	**3.12, 0.01***		**2.85, 0.021***	
DPd (nM/mM)				
Range	6.5-23.5	5.6-20.3	8.6-19.5	7.8-15.6
Mean	10.9	8.52	14.22	10.9
S.D.	4.36	5.8	2.90	3.25
t, p	**2.32, 0.031***		**4.05, 0.001***	

GSD: Glycogen storage disease.

The table shows that bone turn over markers was significantly higher in cirrhotic than in non cirrhotic patients in both Wilson disease group and the GSD group (P>0.001&>0.01).

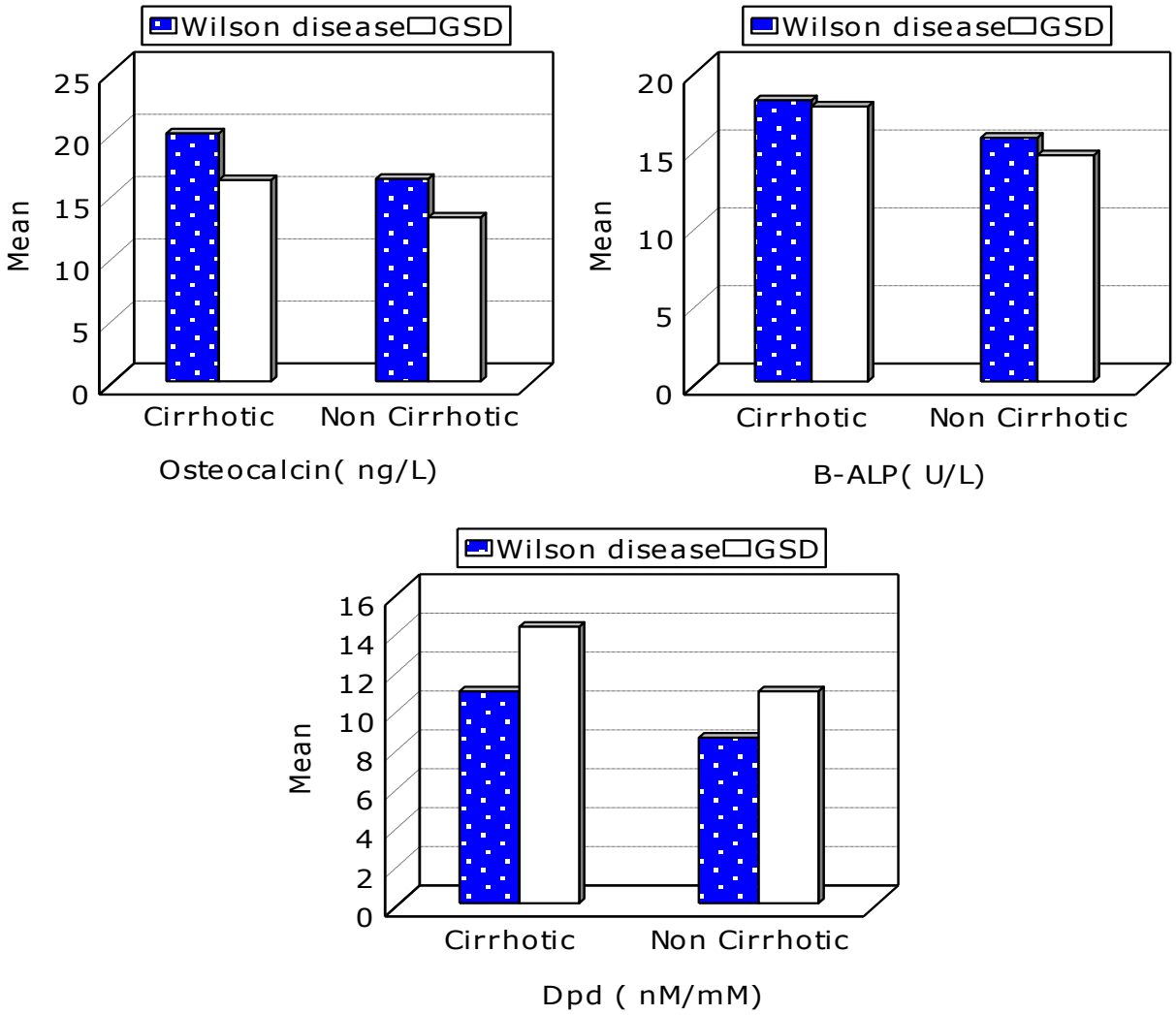

Fig.(17): Comparison between cirrhotic and the non cirrhotic patients in metabolic liver disease group regarding biochemical markers of bone turn over .

Table (21): Comparison between autoimmune hepatitis (AIH) type I and AIH type II groups regarding Biochemical markers of bone turnover.

Variables	Type I "n=15"	Type II "n=10"	t	P
Osteocalcin(ng/mL) Range Mean S.D.	 7.76-25.6 19.41 6.80	 6.44-48.4 16.61 10.67	2.33	0.03*
B-ALP(U/L) Range Mean S.D.	 13.1-42.46 43.69 11.589	 10.5-32.9 21.21 11.76	9.52	0.001**
DPd (nM/mM) Range Mean S.D.	 7.6-50 16.27 9.91	 6.1-19.2 12.83 4.81	3.2	0.02*

*Significance difference ** High significance difference.

This table illustrates a comparison between type I and type II AIH in relation to the changes in bone turnover markers; where osteocalcin, B-ALP and DPd was higher in type I AIH (n=15) (19.41 ± 6.80ng/ml & 43.69±11.589U/L and 16.27 ± 9.91nM/mM respectively) than in type II AIH (n=7) (16.41 ± 6.80ng/ml &21.21±11.76 U/L and 12.83 ± 4.81nM/mM). Also this table shows high significant difference between type I and type II AIH regarding the three bone turnover markers ($p<0.05$&$P<0.0001$).

Table (22): Comparison between cirrhotic and the non cirrhotic patients in auto immune hepatitis group regarding biochemical markers of bone turn over.

Variables	Type I "n=15"		Type II "n=10"	
	Cirrhotic "n=9"	Non cirrhotic "n=6"	Cirrhotic "n=4"	Non cirrhotic "n=6"
Osteocalcin(ng/mL)				
Range	9.35-48.4	6.76-42.65	9.95-25.6	6.44-23.1
Mean	20.36	17.26	18.89	15.40
S.D.	11.5	9.85	5.85	6.80
t, p	**3.02, 0.006***		**2.78, 0.021***	
B-ALP(U/L)				
Range	13.8-42.46	13.1-28.1	14.2-32.9	10.5-30.5
Mean	42.10	40.12	21.23	18.20
S.D.	11.89	8.51	12.39	10.68
t, p	**3.52, 0.002***		**5.26, 0.0001***	
DPd (nM/mM)				
Range	9.5-50.0	7.6-42.6	7.9-19.2	6.1-17.2
Mean	17.39	15.25	13.92	10.65
S.D.	9.05	8.65	4.14	5.03
t, p	**3.03, 0.013***		**2.65, 0.035***	

The table shows that bone turn over markers was significantly higher in cirrhotic than in non cirrhotic patients in both auto immune hepatitis type I group and the auto immune hepatitis type II group (P>0.001&>0.01).

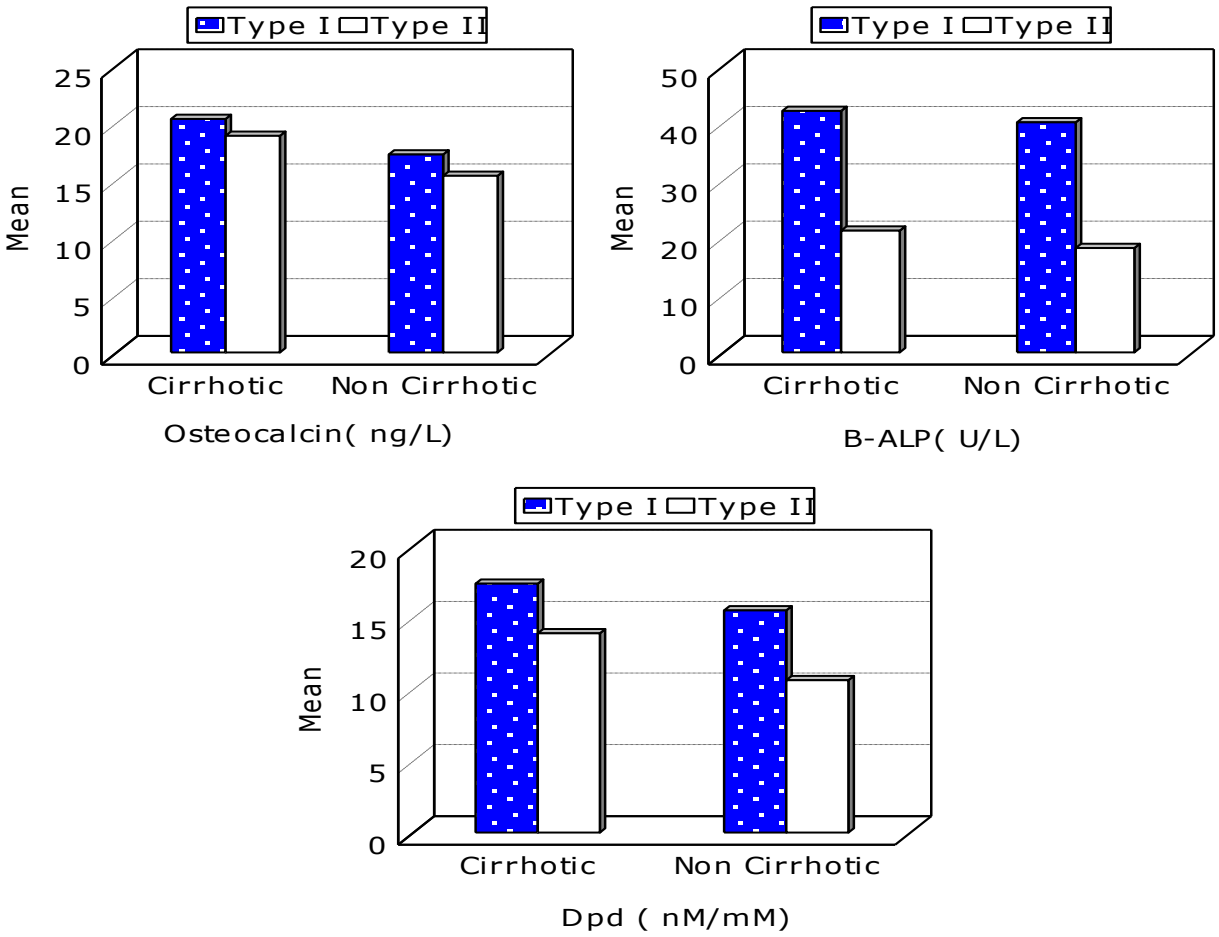

Fig.(18):Comparison between cirrhotic and the non cirrhotic patients in auto immune hepatitis group regarding biochemical markers of bone turn over .

Table (23): Comparison between HBV and HCV regarding biochemical markers of bone turnover.

Variables	HBV "n=9"	HCV "n=16"	t	p
Osteocalcin (ng/mL)				
Range	9.7-18.5	8.16-43.2		
Mean	13.69	22.88	4.25	0.001**
S.D.	3.38	9.22		
B-ALP (U/L)				
Range	10.6-28.8	9.6-43.1		
Mean	20.78	16.20	2.25	0.02*
S.D.	8.03	8.63		
DPd (nM/mM)				
Range	8.5-19.7	7.1-50		
Mean	11.58	16.39	1.98	0.04*
S.D.	4.12	9.96		

* Significance difference ** High significance difference

This table shows statistical significant difference between patients infected with HCV and other group of patients suffering from HBV infection regarding the level of osteocalcin, B-ALP and DPd. With higher levels in HCV group.

Table (24): Comparison between cirrhotic and the non cirrhotic patients in viral hepatitis group regarding biochemical markers of bone turn over.

Variables	HBV "n=9"		HCV "n=16"	
	Cirrhotic "n=8"	Non cirrhotic "n=1"	Cirrhotic "n=9"	Non cirrhotic "n=7"
Osteocalcin (ng/mL) Range Mean S.D.	 9.7-19.3 13.69 3.18	 9.7-18.0 11.25 2.85	 9.12-43.2 23.9 9.25	 8.16-42.0 21.33 9.48
t, p	**2.25, 0.01***		**2.52, 0.02***	
B-ALP (U/L) Range Mean S.D.	 17.2-28.8 19.78 8.03	 10.6-25.9 16.8 7.0	 11.3-43.1 20.8 8.26	 9.6-40.3 17.52 7.23
t, p	**2.58, 0.02***		**2.98, 0.001***	
DPd (nM/mM) Range Mean S.D.	 8.5-17.9 11.88 4.02	 8.5-16.5 9.9 3.25	 8.9-50 16.48 8.11	 7.1-48.2 14.89 8.76
t, p	**1.74, 0.02***		**1.26, 0.03***	

The table shows that serum level of osteocalcin and B-ALP was significantly higher in cirrhotic than in non cirrhotic patients in both HCV group and HBV group (P>0.001&>0.01), also there was significant difference between the cirrhotic and the non cirrhotic patients in both HCV and HBV groups regarding the urinary level of DPd.

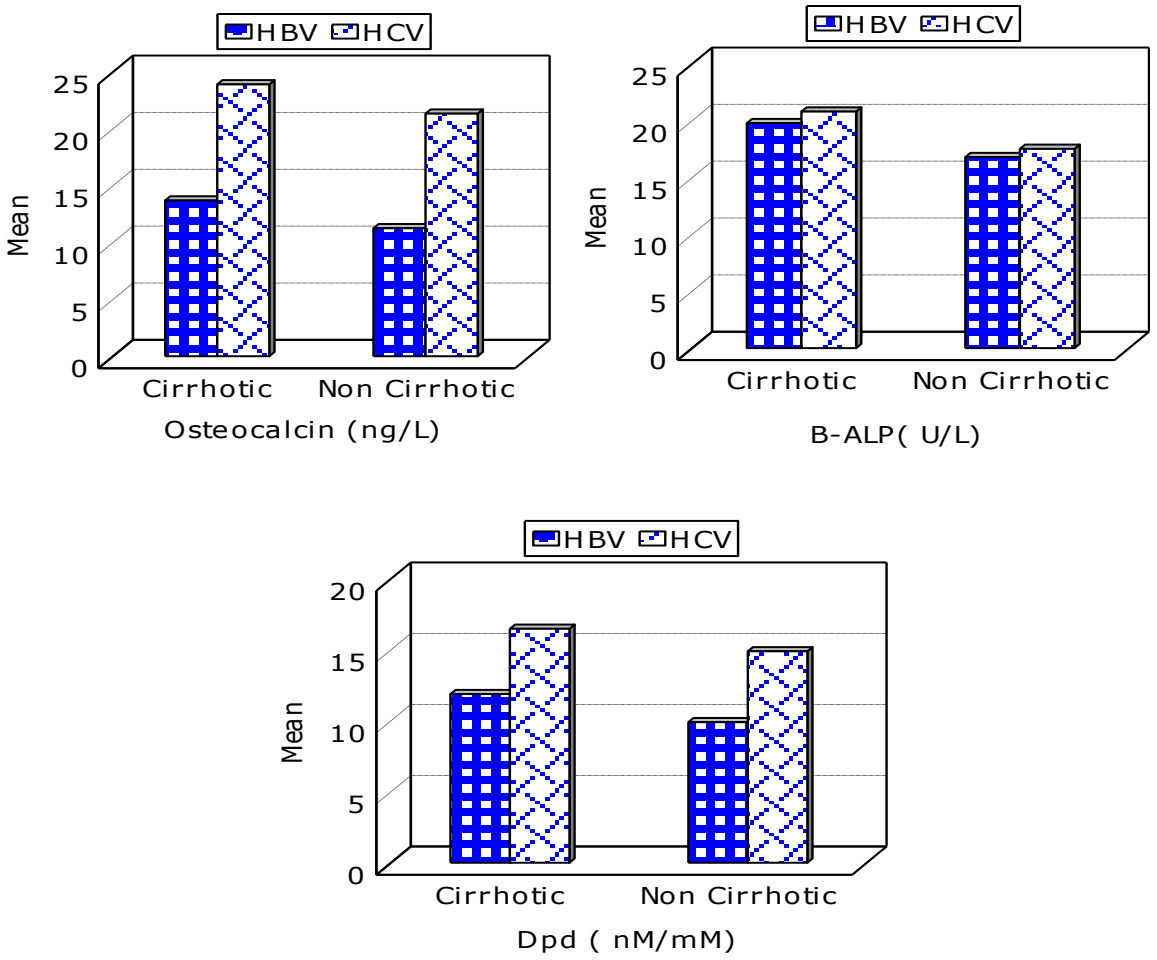

Fig.(19):Comparison between cirrhotic and the non cirrhotic patients in hepatitis group regarding biochemical markers of bone turn over .

Table (25): comparison between patients receiving corticosteroids and those did not regarding bone turnover markers.

Variables	Patients treated with corticosteroids "n=25"	Patients not treated With corticosteroids "n=50"
Osteocalcin (ng/mL) Range Mean S.D.	 10.8-36.6 18.28 9.04	 8.16-43.2 20.81 9.04
T **P**	**0.95** **0.39**	
B-ALP(U/L) Range Mean S.D.	 9.6-43.1 29.34 8.34	 10.5-42.46 32.60 6.67
T **P**	**1.7** **0.10**	
DPd(nM/mM) Range Mean S.D.	 8.1-50 18.06 8.82	 4.2-23 11.36 4.53
T **P**	**3.12** **0.02****	

** High significance difference

This table shows no significant difference between these two groups regarding the level of serum osteocalcin and B-ALP (P=0.39 & P=0.10). Meanwhile there was a high significance difference between both groups regarding the urinary level of DPd, as it was (18.06±8.82nM/mM) in the group of patients receiving corticosteroid treatment and (11.63±4.53nM/mM) in the other group of patients did not receive corticosteroids (P<0.002).

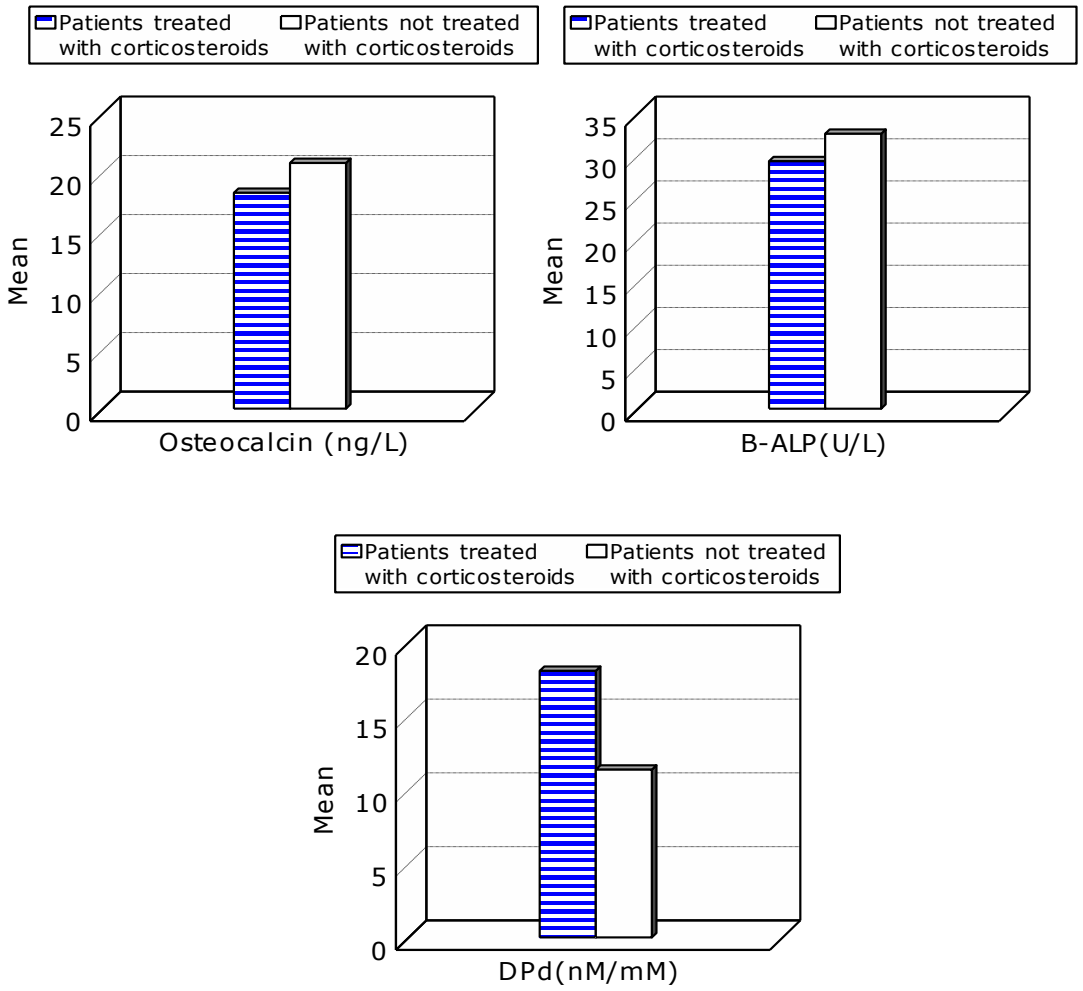

Fig. (20): Comparison between patients receiving corticosteroids and those did not regarding bone turnover markers.

Table (26): Distribution of the selected cases from the diseased groups regarding BMD changes as diagnosed by DXA.

Variables	Group I "n=3"		Group II "n=3"		Group III "n=3"	
	No.	%	No.	%	No.	%
+ve osteoporosis	1	33.3	2	66.7	3	100.0
-ve osteoporosis	2	66.7	1	33.3	0	0.0

BMD: Bone mineral density.

DXA: Dual x-Ray absorptiometry

This table shows the distribution of the children selected from the three diseased groups regarding the changes in BMD (bone mineral density) which was assessed by dual x-Ray absorptiometry (DXA). Only 1 case (33.3%) out of the three cases of the metabolic liver disease group has osteoporotic changes and 2 cases from the three cases of AIH group (66.7%) have changes in BMD denoting osteoporotic changes. While the 3 cases selected from the viral hepatitis group all have osteoporosis which is evident by changes in BMD.

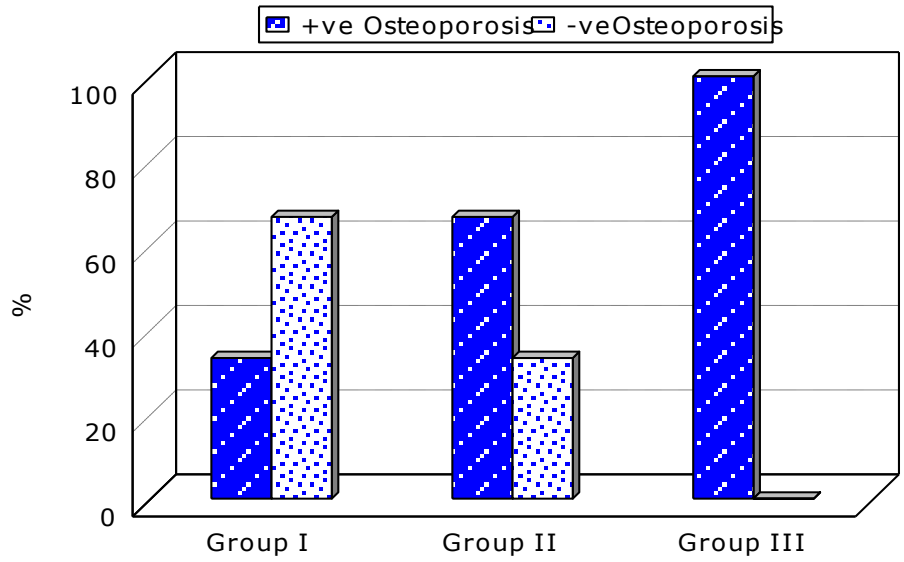

Fig.(21): Distribution of the selected cases form the diseased groups regarding BMD changes as diagnosed by DXA.

Table (27): Distribution of cases having +ve and –ve osteoporotic changes regarding bone turnover markers.

Variables	+ve Osteoporosis "n=6"	-ve Osteoporosis "n=3"
Osteocalcin (mg/L)		
Range	11.53-18.91	9.7-13.86
Mean	16.45	11.587
S.D.	2.70	2.107
T	**3.21**	
P	**0.003****	
B-ALP (U/L)		
Range	12.5-27.3	14.3-25.3
Mean	19.1	18.400
S.D.	6.35	6.011
T	**1.21**	
p	**0.10**	
DPd (nM/mM)		
Range	13.5-19.8	7.1-11.9
Mean	16.533	9.600
S.D.	2.49	2.406
T	**4.65**	
p	**0.001****	

** High significance difference.

This table demonstrates a high significance difference between the cases having +ve osteoporosis (n=6) and those having no osteoporotic changes (n=3) as diagnosed by DXA regarding the levels of bone turn over markers ($p<0.05$)

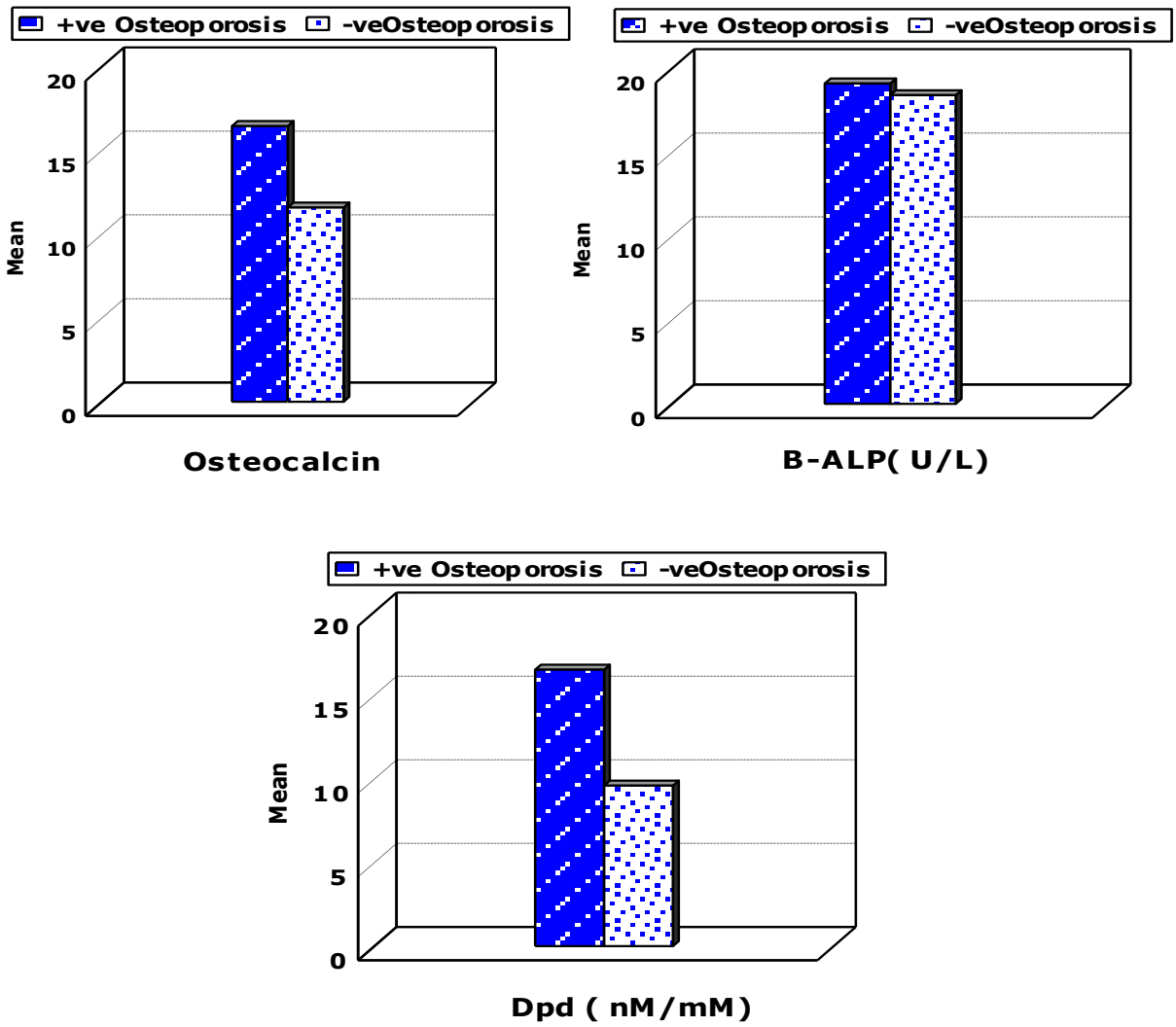

Fig.(22): Distribution of cases having +ve and -ve osteoporotic changes regarding bone turnover markers.

RESULTS

From the data illustrated in the previous tables and figures; the results of this study was summarized in the following points:

*The four studied groups were matched regarding the age and sex with no statistical significant difference between them ***(tables 1& 2).***

*The most frequent clinical presentation in the diseased groups was hepatosplenomegaly and the highest percent of this presentation was in group I (metabolic liver disease group) ***(table 3)***.

*Regarding the nutritional assessment of the diseased groups which was done by measuring the body mass index (BMI); our results showed that most of the cases within the average for age and sex. No cases found to fall above the 95^{th} centile or below the 5^{th} centile ***(table 4)***.

*Regarding the liver function tests; it was worst in group II (AIH group) .The highest level of S.bilirubin (total, direct) & AST & ALT & T-ALP & PT and the lowest level of PC was found in group II ***(table 5)***.

*Ultrasonographic findings reveals that hepatosplenomegaly was mostly affecting group I (metabolic liver disease group) .Meanwhile liver cirrhosis as diagnosed by liver biopsy was highest in group III (virus hepatitis group) ***(tables 6&7 and figure 1)***.

*To diagnose hepatic osteodystrophy bone turnover markers was measured and the results were the following:

- There was marked increase in the level of bone turn over markers (serum osteocalcin & B-ALP and urine level of DPd) in the three diseased groups with high significant difference between them and the control group***(table 8)***.

- In spite of the increased levels of bone turn over markers in the three diseased groups there was no statistical significant difference between them regarding the level of serum osteocalcin and serum level of B-ALP; meanwhile there was statistical significant increased level of urine level of DPd in group II more than in groups I and III .In the same time in each group there was high significant difference between group of patients had liver cirrhosis and those did not ***(table 9- table 17)*** and ***(figure 3- figure10)***.
- Regarding the relation between the deterioration of liver functions and the increased levels of bone turn over markers; there was statistical significant difference between the decreased level of serum albumin and the decreased prothrombin activity in one hand and the increased levels of bone turn over markers (osteocalcin, B-ALP and DPd) with negative correlation. Meanwhile there was positive moderate correlation with statistical significant difference between the level of T-ALP and B-ALP ***(table18)*** and ***(figure 11- figure 16)***.
- In group I (metabolic liver disease) there was no statistical significant difference between patients had Wilson disease and the other group suffering from GSD regarding increased serum level of osteocalcin, B-ALP and DPd. Meanwhile in each group there was high significant difference between patients had liver cirrhosis and those did not regarding all markers of bone turn over ***(tables 19&20)*** and ***(figure 17)***.
- In group II (auto immune hepatitis group) there was high statistical significant difference between groups of patients was having AIH type I and those had AIH type II with higher levels of bone turn over markers in AIH type I group***(tables 21&22)*** and ***(figure 18)***.

- In group III (virus hepatitis group) there was high statistical significant difference between group of patients infected with HCV and those infected with HBV regarding the level of serum osteocalcin, B-ALP and urine DPd. .Meanwhile in each group there was statistical significant difference between patients had liver cirrhosis and those did not regarding the level of osteocalcin, B-ALP and DPd ***(tables 23&24)*** and ***(figure19)*** .
- Regarding the drug effect on bone turn over in chronic liver disease patients; there was no statistical significant difference between patients treated with corticosteroids and those did not regarding the level of serum osteocalcin and B-ALP .Meanwhile the urinary level of DPd was significantly higher in group of patients treated with corticosteroids than the other group of patients not receiving steroid therapy ***(table 25)*** and ***(figure 20)***.
- For the confirmation of the presence of hepatic osteodystrophy dual x-ray absorptiometry (DXA) was done only for 9 cases 3 from each group of the three diseased groups ; there was positive osteoporotic changes in only one case in group I & 2 cases in group II and the 3 cases selected from group III . When bone turn over markers of the cases had positive osteoporotic changes as diagnosed by DXA compared with those had no radiological osteoporotic changes there was statistical significant difference between both groups regarding the level of osteocalcin and DPd and no statistical significant difference with nearly equal levels of B-ALP between both groups***(tables 26&27)*** and ***(figures 21&22)***.