RESULTS

The present study was carried out on 15 infants and children, another 10 children severed as controls.

Each patient had underwent liver Biopsy and abdominal ultrasonograpay to detect the degree of hepatic fibrosis and disease activity. The patient were classified by three ways:

According to fibrosis stage (biopsy) into 3 groups:

Group I : (F0 , F1).

Group II: (F2).

Group III: (F3, F4).

According to disease Activity (biopsy) into 3 groups:

Group 1 : A0 → A8

Group 2 : A9 → A12

Group 3 : A13 → A18

According to grades of fibrosis (sonar) into 3 groups:

Group A : (G0 , G1).

Group B : (G2).

Group C : (G3 , G4).

Table (1) : Distribution of patients according to sex and clinical manifestations.

Variables	No	%
1-sex		
Male	8	53.3
Femal	7	46.7
2-Clinical manifestaions		
Splenomegaly	10	66.6
Jaundice	8	53.3
Hepatomegaly	11	73.3

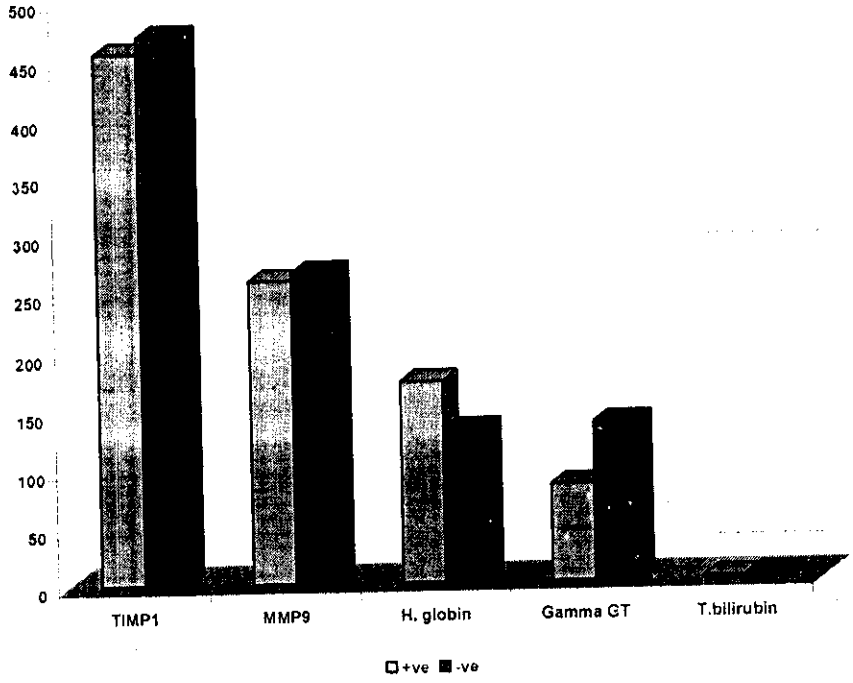
The table shows sex, clinical manifestations in patients. Hepatomegaly was the most frequent finding.

Table (2): Comparison of liver function tests and fibrosis markers between the studied groups:

St. group / Variables	Cases (n=15) $\bar{X} \pm$ SD	Controls (n=10) $\bar{X} \pm$ SD	t	p
TIMP1	458.7 ± 58.1	328 ± 33.7	7.1	<0.001
MMP9	267.5± 46.8	142.8 ± 41.3	7.03	<0.001
Total bilirubin	3.03 ± 3.9	0.6 ± 0.3	2.4	<0.05
GGT	97.7 ± 62.7	39 ± 5.2	3.61	<0.01
Haptoglobin	162.3 ± 76.8	292.2 ± 20.92	6.21	<0.001
ALT	105.7 ± 76.8	10 ± 4.27	3.15	<0.01
AST	126.2 ±44.9	13 ± 3.3	3.02	<0.01
PT	19.08 ± 7.75	12 ± 0.4	3.53	<0.01

The table shows mean values of liver function tests and fibrosis markers among studied groups which were significantly higher in patients than in controls except haptoglobin which was significantly lower in patients than controls..

Fig (1) means of fibrosis markers according to hepatomegaly



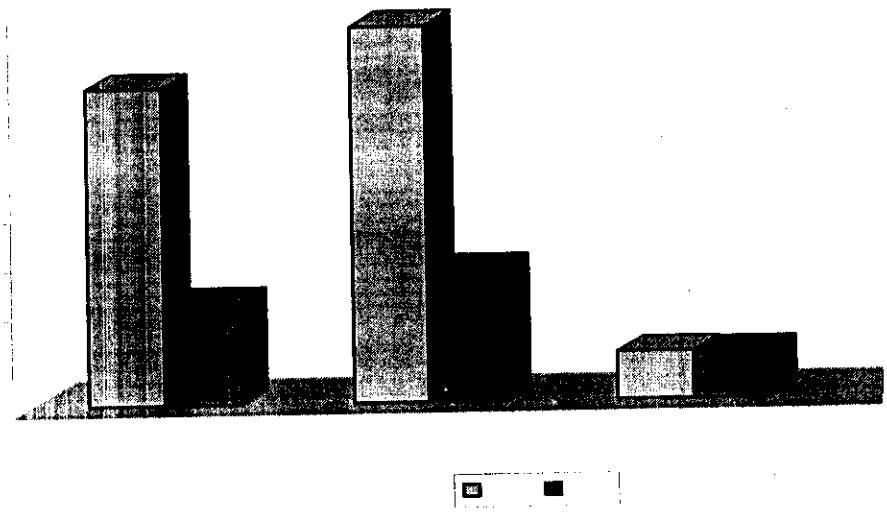


Table (4): Fibrosis markers and liver function tests among the patients group according to splenomegaly

splenomegaly / Variables	+ve (n=10) $\overline{X} \pm$ SD	-ve (n =5) $\overline{X} \pm$ SD	t	p
TMP1	483.7 ± 73.3	442.1 ± 42.1	1.26	> 0.05
MMP9	257.9 ± 32.6	262.8 ± 44.9	0.25	> 0.05
Haptoglobin	147.33 ± 80.4	172.3 ± 77.4	0.6	> 0.05
GGT	75.7 ± 27.6	112.3 ± 76.2	1.32	> 0.05
Total bilirubin	6.28 ± 4.48	0.85 ± 0.43	2.96	< 0.01
ALT	76 ± 36.6	125.4 ± 149.1	0.95	> 0.05
AST	92.5 ± 52.4	148.7 ± 183.4	0.87	> 0.05
PT	21.3 ± 9.7	17.6 ± 6.4	0.81	> 0.05

The table shows that. There were no significant difference in liver function tests, TIMP1, MMP9, GGT and haptoglabin in both groups. However, a significant difference was found in total bilirubin in patients with splenomegaly and patients without splenomegaly.

Fig (3) means of fibrosis markers according to splenomegaly

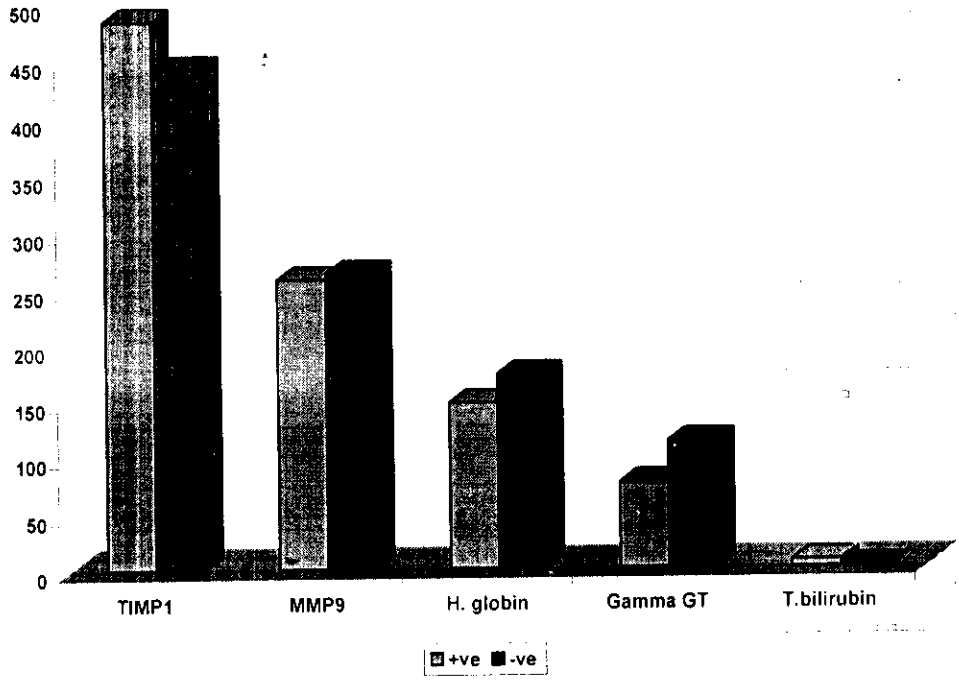


Fig (4): Means of liver function tests according to splenomegaly

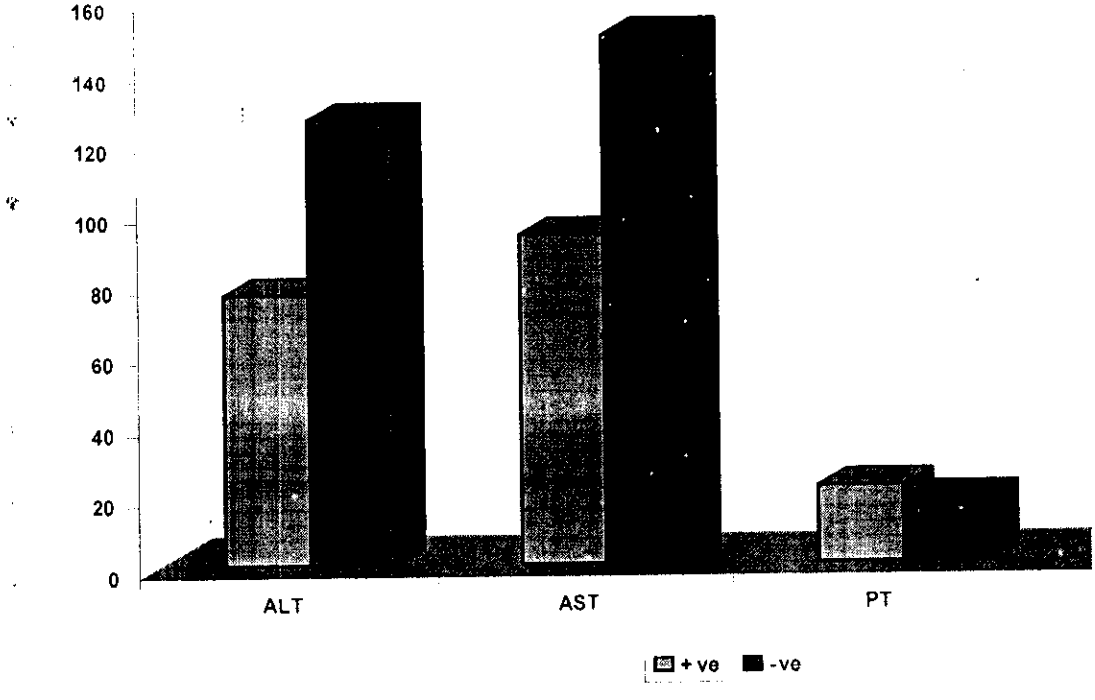


Table (5): Fibrosis markers and liver function tests among the patients group according to Jaundice.

Variables \ Jaundice	+ve (n=8) $\overline{X} \pm SD$	-ve (n=7) $\overline{X} \pm SD$	r	p
TIMP1	522.3 ± 53.9	425.6 ± 40.6	2.92	< 0.01
MMP9	268.6 ±28.4	257.9 ± 43.3	0.55	> 0.05
Haptoglobin	100.3 ± 42.3	184.9 ± 74.9	2.74	< 0.01
GGT	77.9 ± 35.4	104.9 ± 20.1	0.98	> 0.05
Total bilirubin	9.13 ± 1.07	0.81 ± 0.4	15.23	< 0.001
ALT	76.3 ± 32.9	116.4 ± 136.2	0.91	> 0.05
AST	102.8 ± 62.8	134.7 ± 167.1	0.54	> 0.05
PT	24.8 ± 10.3	17.01 ± 5.9	1.42	> 0.05

The table shows that there were no significant difference in liver function tests and fibrosis markers in both groups except total bilirubin which had a significant difference in patients with Jaundice and patients without Jaundice.

Fig (5) Means of fibrosis markers according to Jaundice

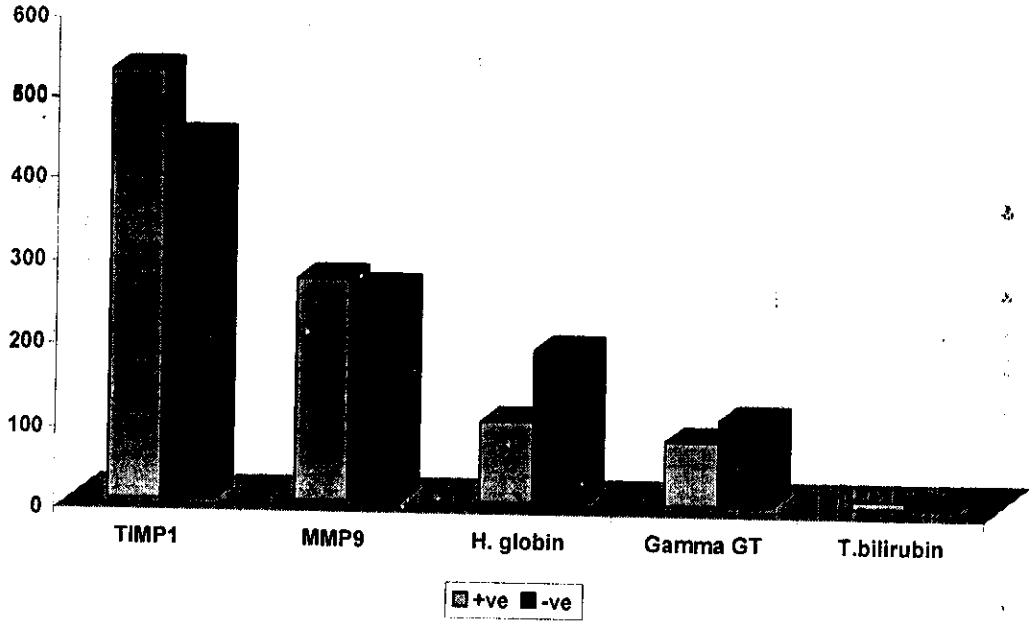


Fig (6): Means of liver function tests according to Jaundice

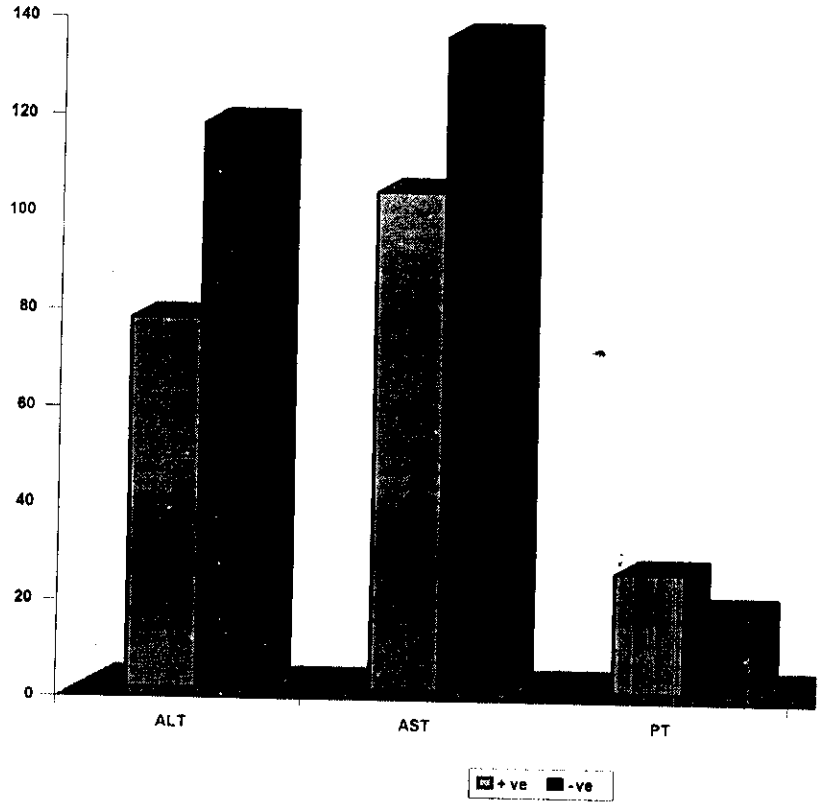


Table (6): Correlation coefficient (r) between grade of fibrosis (ulrasonography) and fibrosis markers

Grade fibrosis (sonar) / Fibrosis Markers	r	p
TIMP1	0.7319	< 0.01
MMP9	0.5316	< 0.05
Haptoglobin	- 0.81967	< 0.001
GGT	0.26604	> 0.05
Total bilirubin	0.6787	< 0.01

The table shows a significant correlation between TIMP1, MMP9, total bilirubin and haptoglobin and grade of fibrosis (sonar) but no significant correlation between GGT and grade of fibrosis (Sonar).

Fig (7) correlation coeff. between TIMP1 and fibrosis grade (sonar)

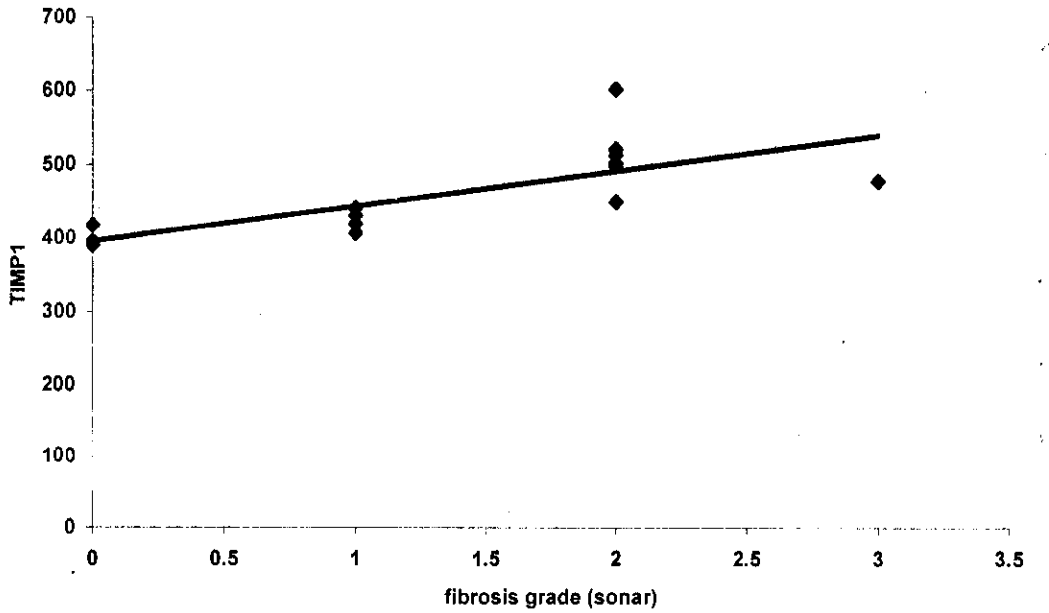


Fig (8) Correlation coeff. between MMP9 and fibrosis grade (sonar)

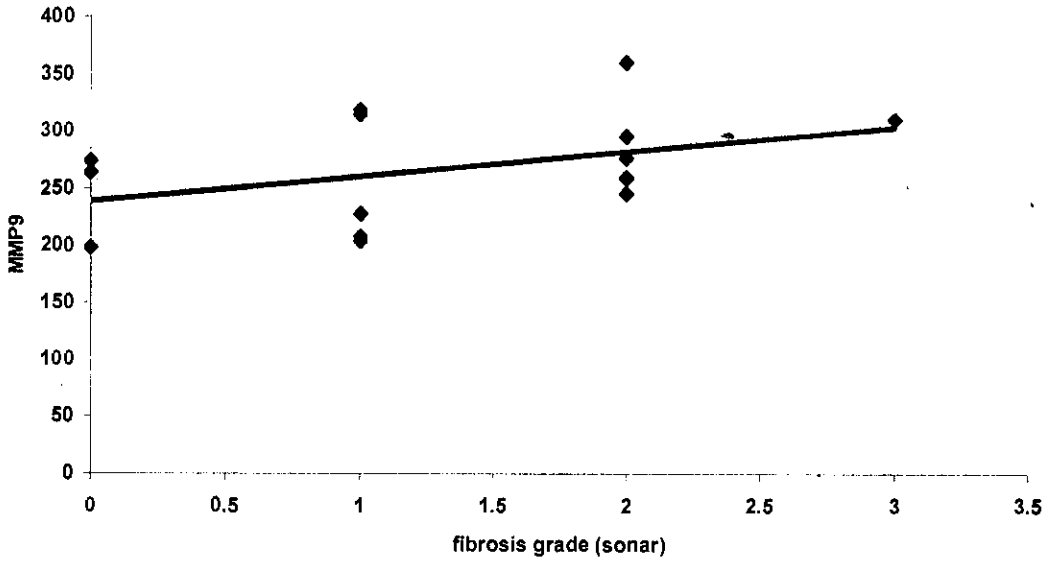


Fig (9): Correlation coeff. between haptoglobin and fibrosis grade (sonar)

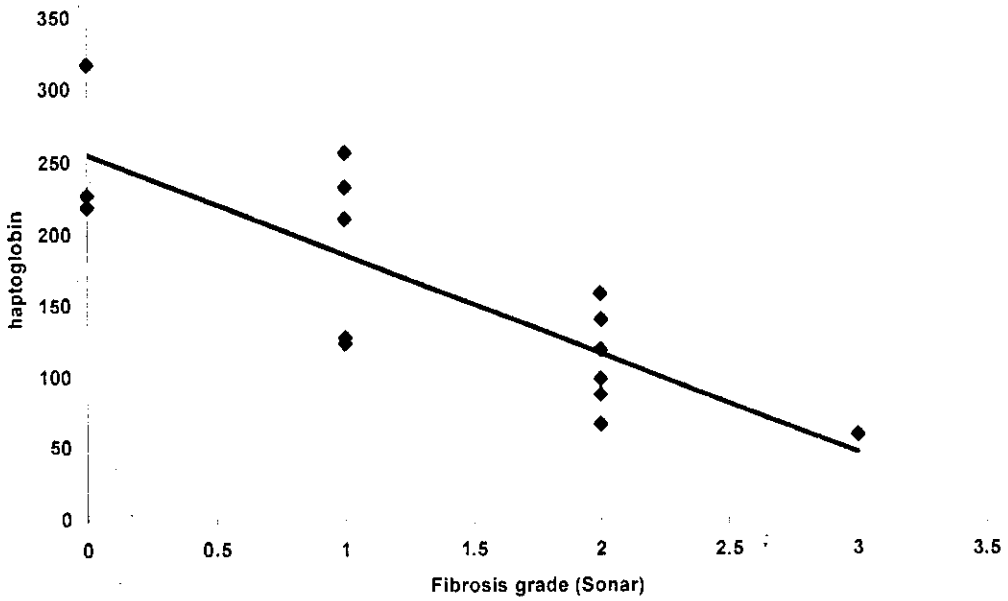


Fig (10): Correlation coeff. between Total bilirubin and fibrosis grade (sonar)

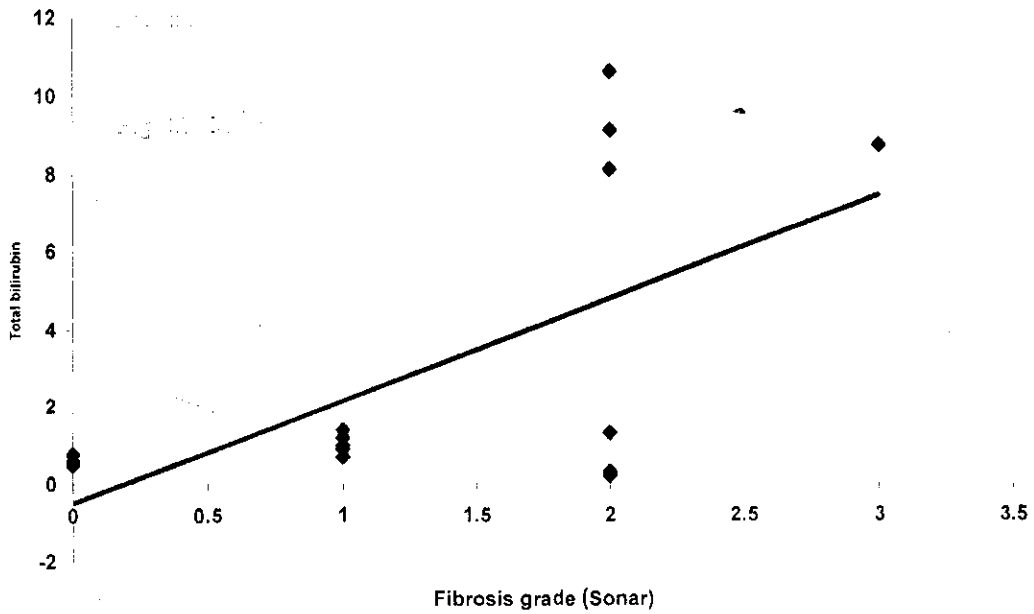


Table (7): Correlation coefficient (r) between fibrosis stage (biopsy) and fibrosis markers

fibrosis stags (biopsy). / Fibrosis markers	r	p
TIMP1	0.8088	< 0.001
MMP9	0.67459	< 0.01
Haptoglobin	-0.52788	< 0.05
GGT	0.33602	> 0.05
Total bilirubin	0.5405	< 0.05

The table shows a significant correlation between (TIMP1, MMP9, total bilirubin and haptoglobin) and fibrosis stage (biopsy) but no significant correlation between GGT and fibrosis stage (biopsy).

Fig (11): Correlation coeff. between TIMP1 and fibrosis stage (biopsy)

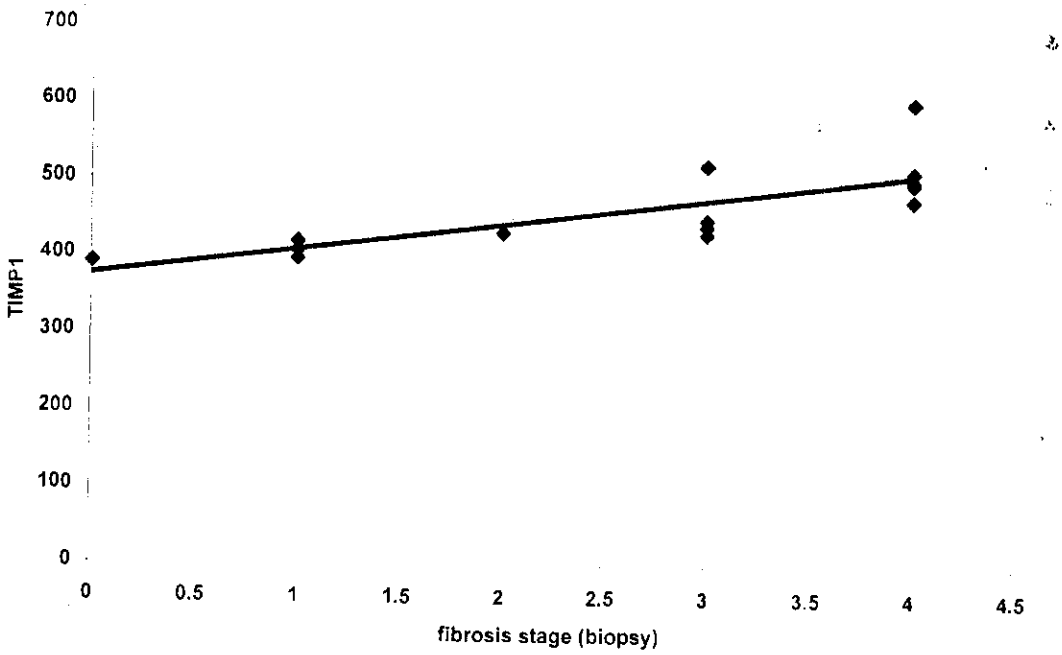


Fig (12): Correlation coeff. between haptoglobin and fibrosis stage (biopsy)

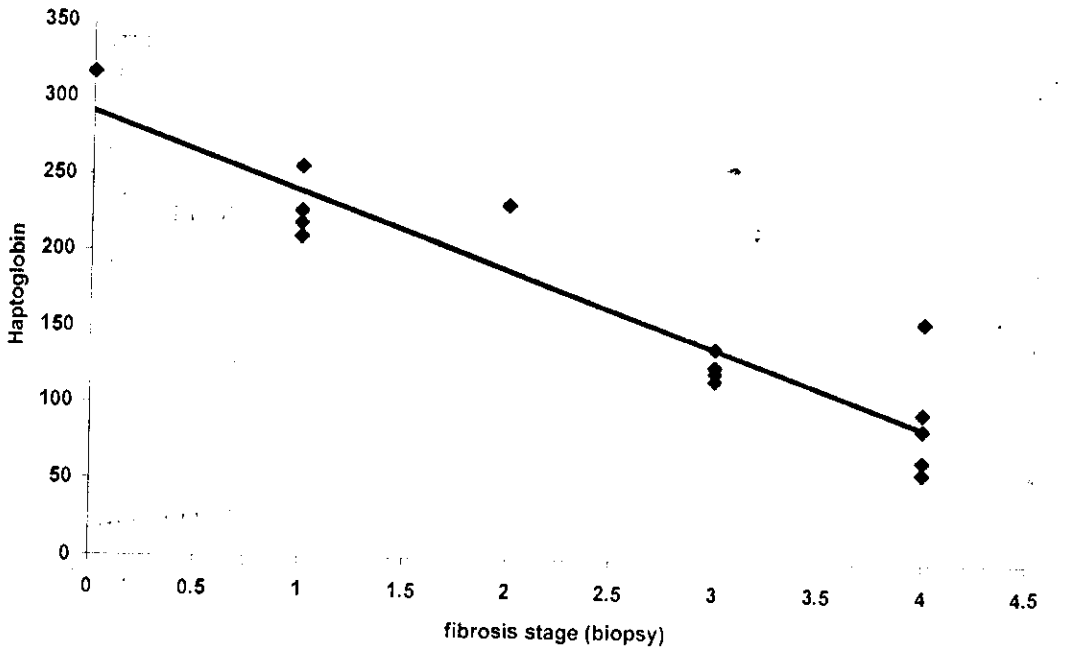


Fig (13): Correlation coeff. between total bilirubin and fibrosis stage (biopsy)

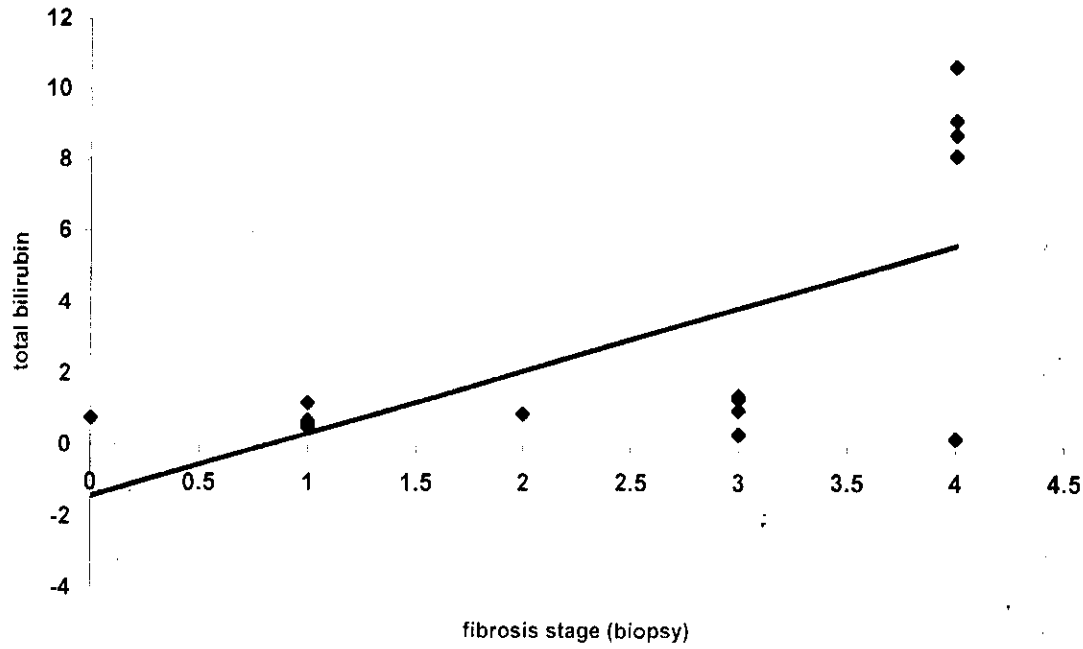


Fig (14): correlation coeff. between MMP9 and fibrosis stage (biopsy)

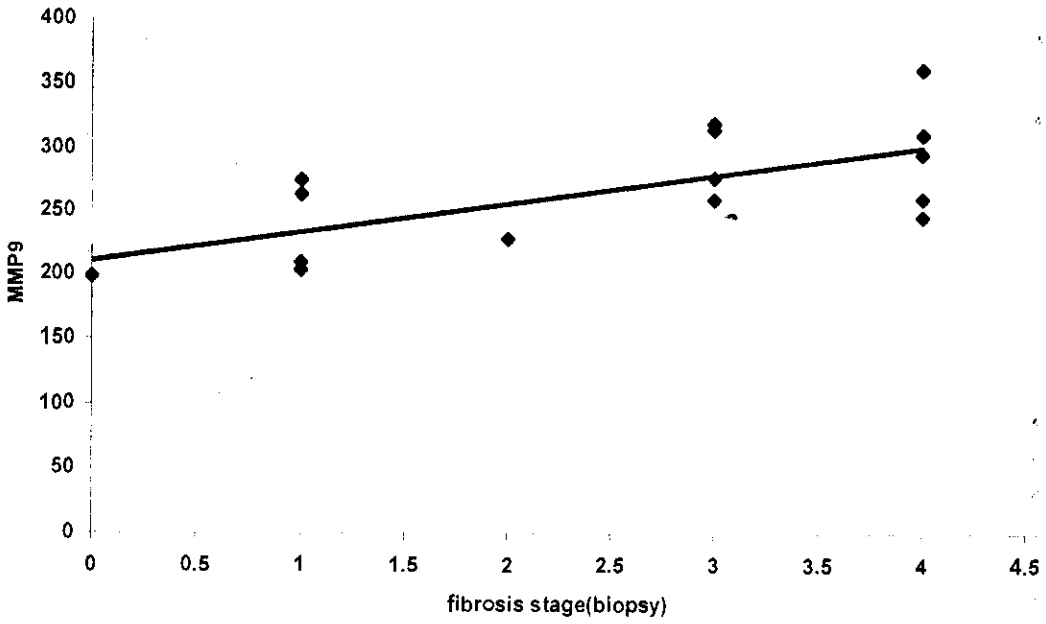


Table (8): Correlation coefficient (r) between Disease activity (biopsy) and fibrosis Markers.

disease activity (biopsy) / fibrosis Markers	r	p
TIMP1	0.5325	< 0.05
MMP9	0.75573	< 0.01
Haptoglobin	-0.74896	< 0.01
GGT	0.0045	> 0.05
Total bilirubin	0.74896	< 0.01

The table shows a significant correlation between (TIMP1, MMP9, haptoglobin and total bilirubin) and disease activity (biopsy) but no significant correlation between GGT and disease activity (biopsy).

Fig (15) : Correlation coeff. between haptoglobin and disease activity (biopsy)

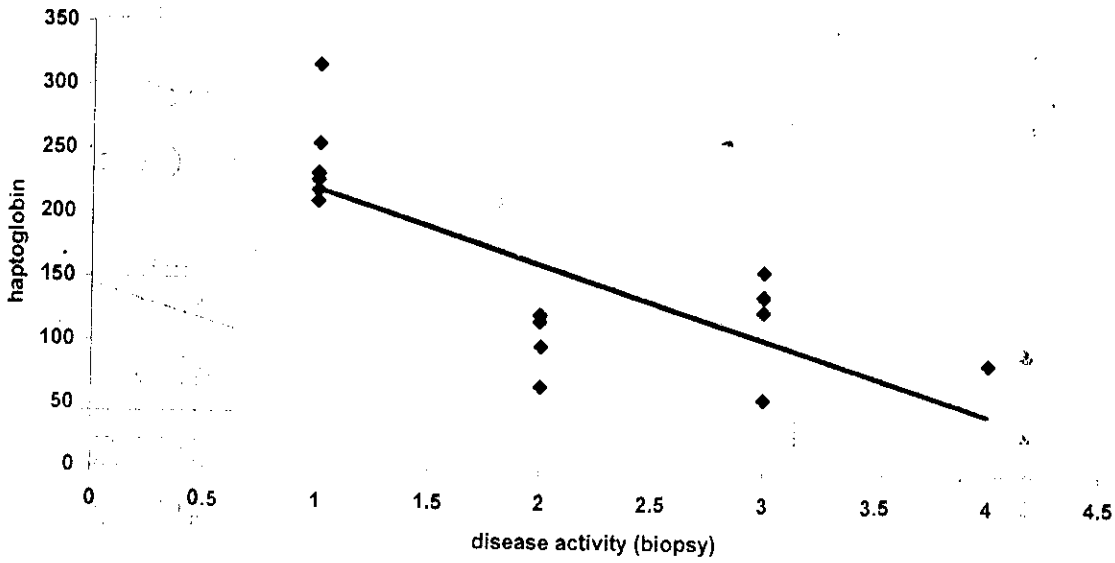


Fig (16): Correlation coeff. between TIMP1 and disease activity (biopsy)

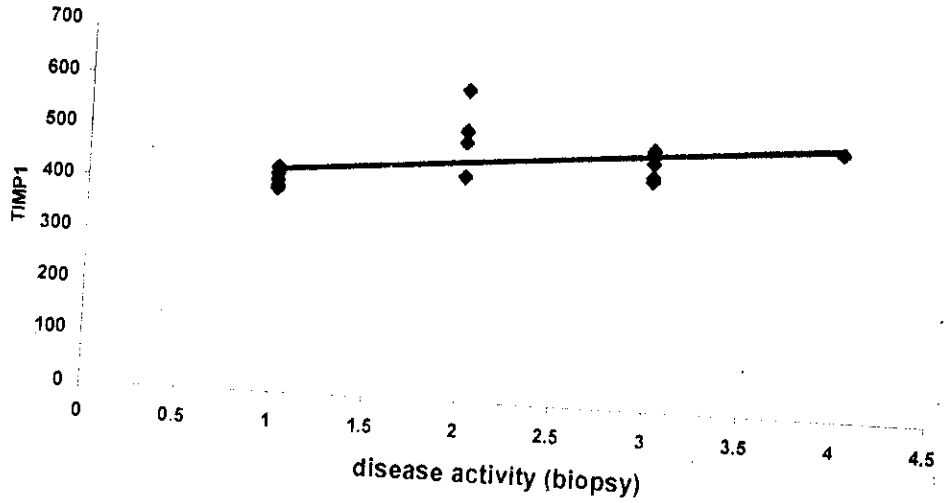


Fig (17): Correlation coeff. between MMP9 and disease activity (biopsy)

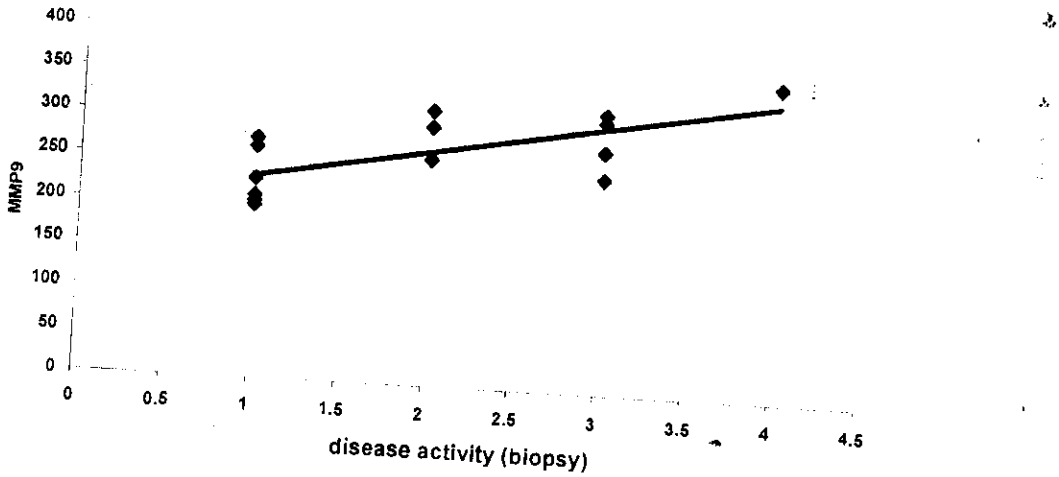


Fig (18): Correlation coeff. between Total bilirubin and disease activity (biopsy)

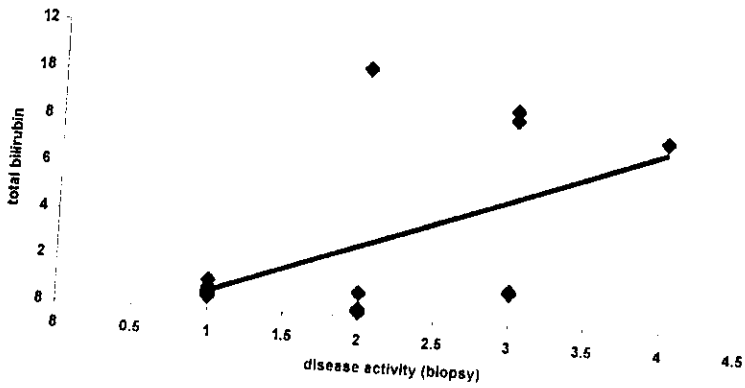


Table (9): Correlation coefficient (r) between TIMPI and (liver function tests and other fibrosis markers)

Variables \ TIMP1	r	p
ALT	- 0.0187	> 0.05
AST	- 0.00469	> 0.05
PT	0.57897	< 0.01
Total bilirubin	0.69967	< 0.01
GGT	0.19266	> 0.05
Haptoglobin	-0.72039	< 0.01
MMP9	0.53212	<0.05

The table shows a significant correlation between TIMP1 and other fibrosis markers except GGT. However, no significant correlation found between TIMP1 and liver function tests except PT which had significant correlation with TIMP1.

Fig (19) correlation coeff. between TIMP1 and PT

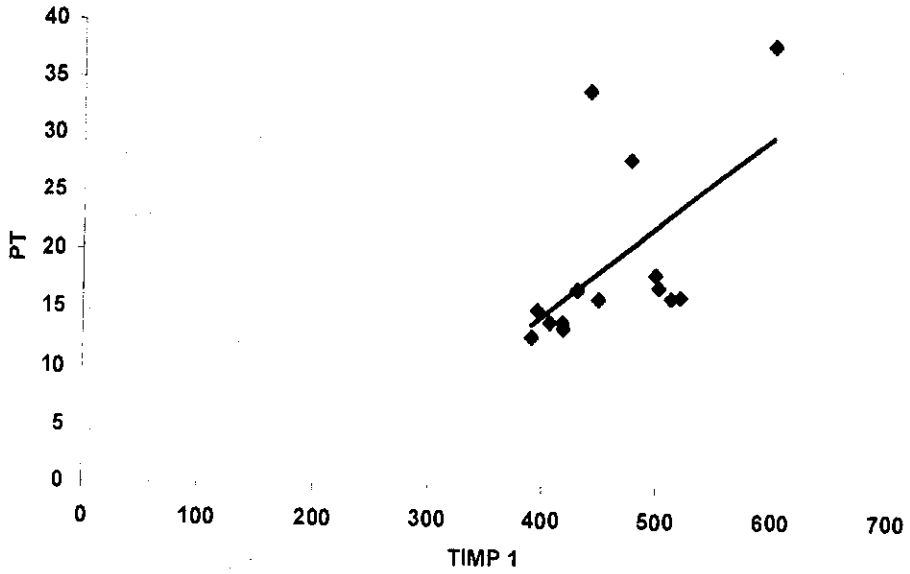


Fig (20): Correlation coeff. between TIMP1 and total bilirubin

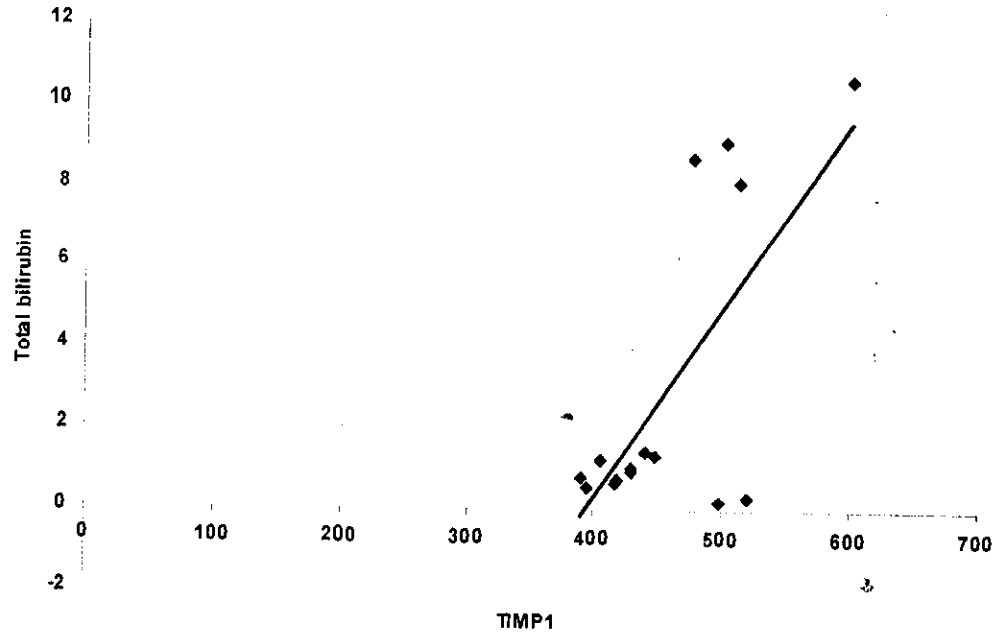


Table (10): Correlation coefficient (r) between MMP9 and (liver function tests and other fibrosis markers)

Variables \ MMP9	r	p
ALT	0.2715	> 0.05
AST	0.1866	> 0.05
PT	0.3524	> 0.05
Total biliruben	0.2996	> 0.05
GGT	0.2584	> 0.05
Haptoglobin	- 0.7725	< 0.01
TIMP	0.53212	< 0.05

The table shows non significant corrolation between MMP9 and liver function tests. Also, there were no significant correlation between MMP9 and fibrosis Markers except Haptoglobin and TIMP1 which had significant correlation with MMP9.

Fig (21): Correlation coeff. between MMP9 and haptoglobin

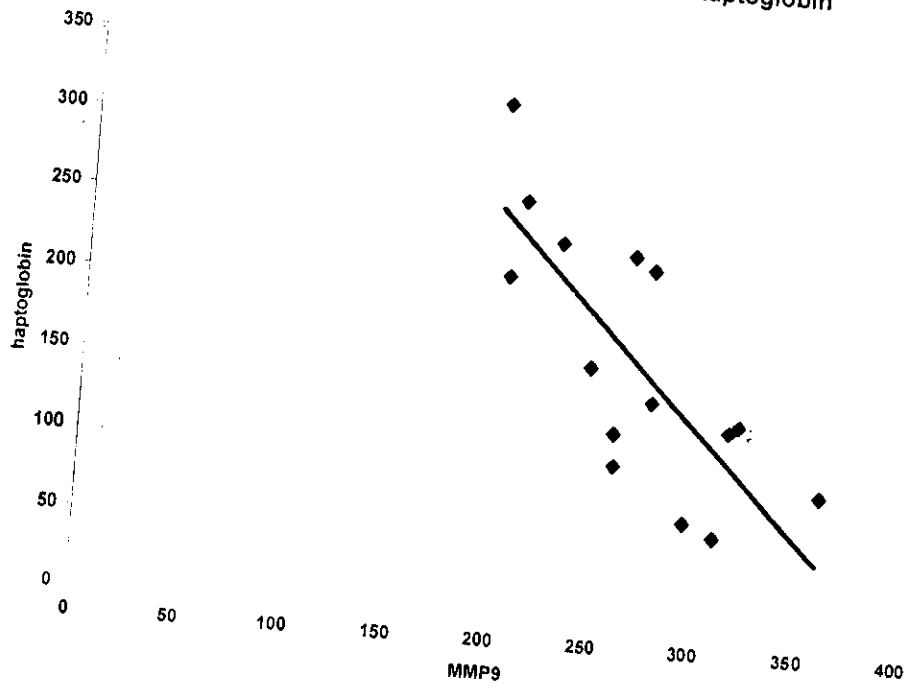


Fig (22): Correlation coeff. between TIMP1 and MMP9

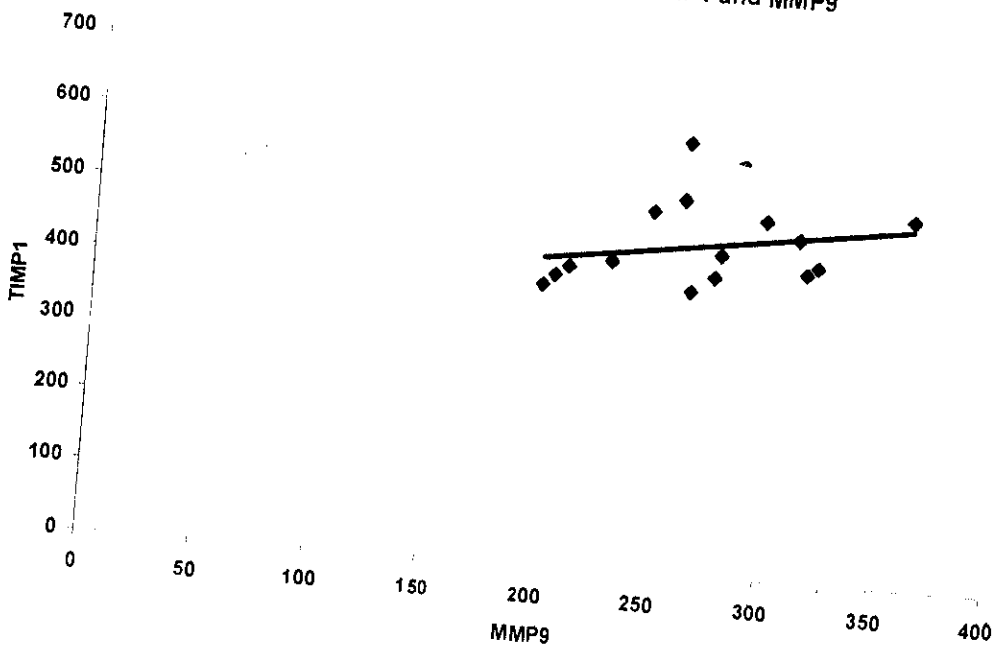


Table (11): Comparison between mean values of fibrosis markers in different grades of fibrosis (Sonar):

Grades of fibrosis (sonar) / Fibrosis Markers	Group A (n=6) $\bar{X} \pm SD$	Group B (n=6) $\bar{X} \pm SD$	Group C (n=3) $\bar{X} \pm SD$	f	p
TIMP1	400.06 ± 14.3	424.7 ± 13.05	507.9±47.25	13.59	<0.001
MMP9	244.9 ± 40.96	254.6 ± 57.3	272.01±23.05	0.56	>0.05
Total bilirubin	0.63 ± 0.14	1.04 ± 0.27	5.47 ± 4.6	3.67	<0.05
GGT	74.7 ± 20.1	89.3 ± 24.4	113.5 ± 89.6	0.43	>0.05
Haptoglobin	254.3 ± 54.4	189.6 ± 61.2	103.4 ± 37.01	11.01	<0.001

The table shows no significant difference was found between different grades of fibrosis (sonar) in MMP9 and GGT. However, a significant difference was found in TIMP1, total bilirubin and haptoglobin.

Table (12): comparison between mean values of fibrosis markers in different grades of disease activity (biopsy)

grades of disease activity (biopsy) / Fibrosis Markers	Group 1 (n=6) $\bar{X} \pm SD$	Group 2 (n=4) $\bar{X} \pm SD$	Group 3 (n=5) $\bar{X} \pm SD$	f	p
TIMP1	409.3 ± 15.1	511.95 ±70.1	475.4±31.6	8.26	<0.001
MMP9	229.2 ±32.2	281.78 ±27.5	282.02 ±31.7	5.24	<0.05
Total bilirubin	0.78 ±0.25	3.03 ±5.06	5.72 ±4.01	2.83	>0.05
GGT	78.6 ±21.6	143.95±109.08	83.5 ± 36.3	1.63	>0.05
Haptoglobin	243.5 ±39.2	101.3 ± 25.9	73.8 ±40.6	24.4	<0.001

The table shows that no significant difference was found between different grades of disease activity (biopsy) in total bilirubin and GGT. However, significant difference was found in TIMP1, MMP9 and haptoglobin.

Table (13): comparison between mean values of fibrosis markers in different fibrosis stages (biopsy):

fibrosis stages (biopsy) / Fibrosis Markers	Group I (n=5) $\bar{X} \pm$ SD	Group II (n=4) $\bar{X} \pm$ SD	Group III(n=6) $\bar{X} \pm$ SD	f	p
TIMP1	405.2 ± 12.6	453.5±37.9	517.4 ±47.99	12.18	<0.001
MMP9	229.4 ±36.04	279.1±38.3	273.9 ±27.3	3.2	>0.05
Total bilirubin.	0.76 ±0.27	0.98 ± 0.43	7.34 ±4.1	12.3	<0.001
GGT	71.68±15.01	97.8 ±22.6	123.5±106.45	0.83	>0.05
Haptoglobin	245.6 ±43.4	147.8±47.7	93.4 ±39.5	15.65	<0.001

The table shows that no significant difference was found between different fibrosis stages (biopsy) in MMP9 and GGT. However, a significant difference was found in TIMP1, total bilirubin and haptoglobin.

Table (13): comparison between mean values of fibrosis markers in different fibrosis stages (biopsy):

fibrosis stages (biopsy) / Fibrosis Markers	Group I (n=5) $\bar{X} \pm SD$	Group II (n=4) $\bar{X} \pm SD$	Group III(n=6) $\bar{X} \pm SD$	f	p
TIMP1	405.2 ± 12.6	453.5±37.9	517.4 ±47.99	12.18	<0.001
MMP9	229.4 ±36.04	279.1±38.3	273.9 ±27.3	3.2	>0.05
Total bilirubin.	0.76 ±0.27	0.98 ± 0.43	7.34 ±4.1	12.3	<0.001
GGT	71.68±15.01	97.8 ±22.6	123.5±106.45	0.83	>0.05
Haptoglobin	245.6 ±43.4	147.8±47.7	93.4 ±39.5	15.65	<0.001

The table shows that no significant difference was found between different fibrosis stages (biopsy) in MMP9 and GGT. However, a significant difference was found in TIMP1, total bilirubin and haptoglobin.

Fig (23): Means of TIMP1 according to grades of fibrosis(sonar), fibrosis stages (biopsy) and grades of disease activity(biopsy)

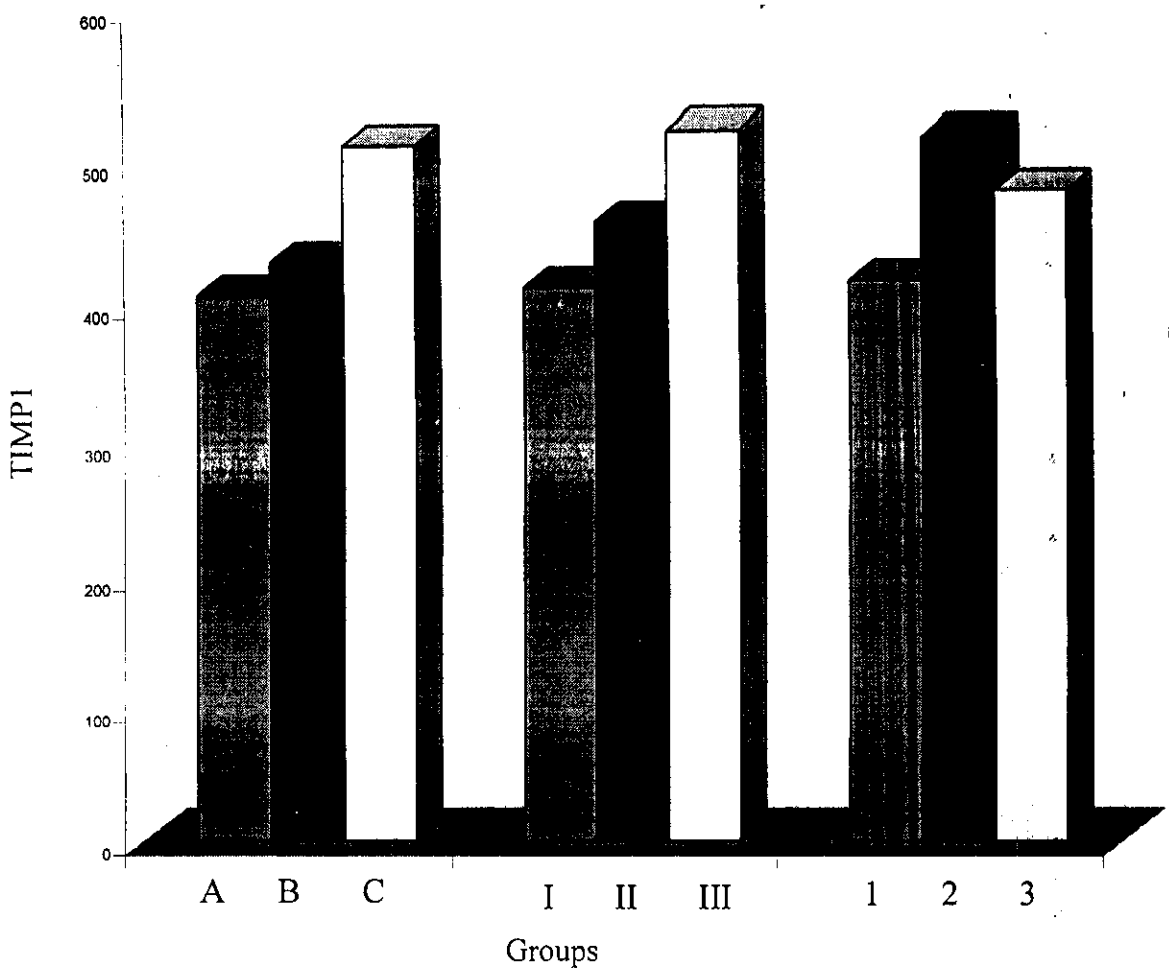


Fig (24): Means of MMP9 according to grades of fibrosis(sonar), fibrosis stages (biopsy) and grades of disease activity (biopsy)

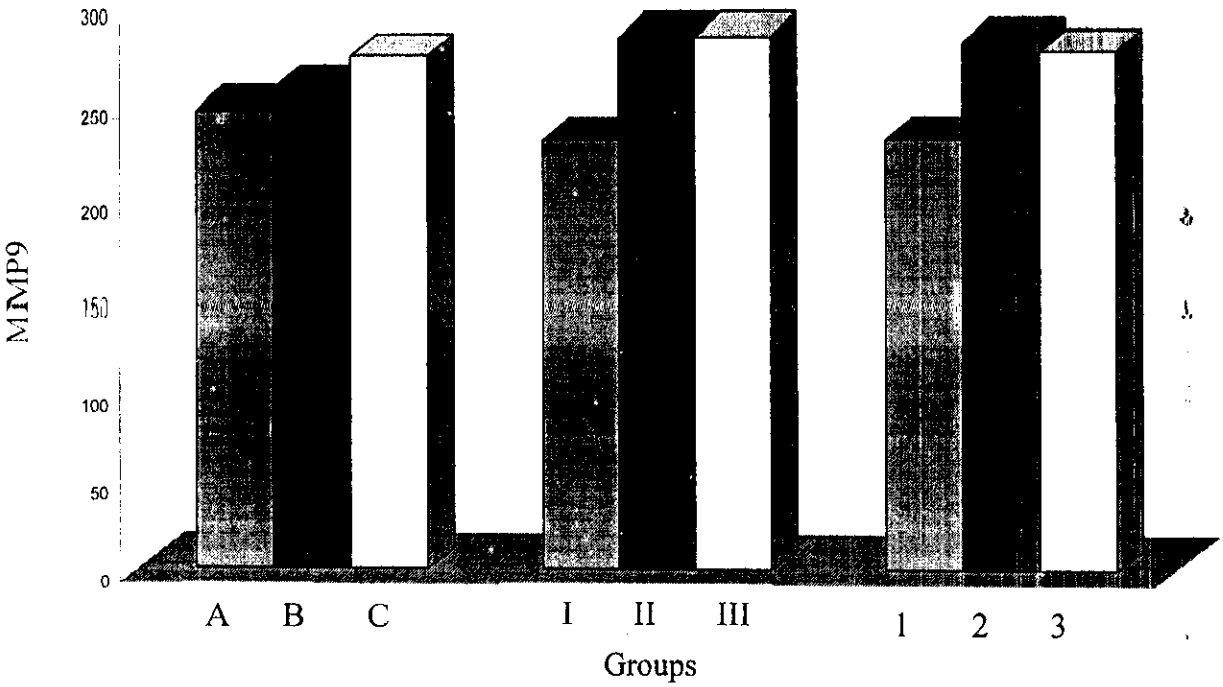


Fig (25): Means of total bilirubin according to grades of fibrosis(sonar), fibrosis stages (biopsy) and grades of disease activity (biopsy)

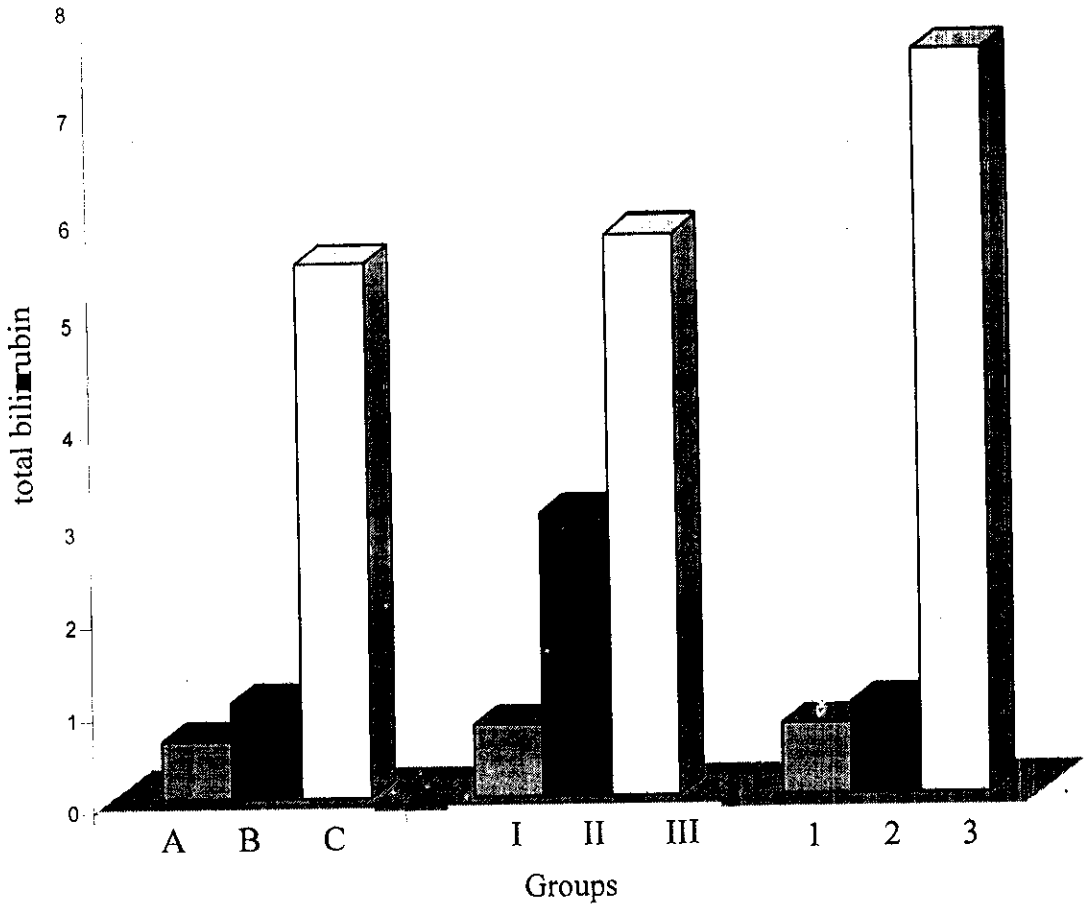


Fig (26): Means of GGT according to grades of fibrosis (sonar), fibrosis stages (biopsy) and grades of disease activity (biopsy)

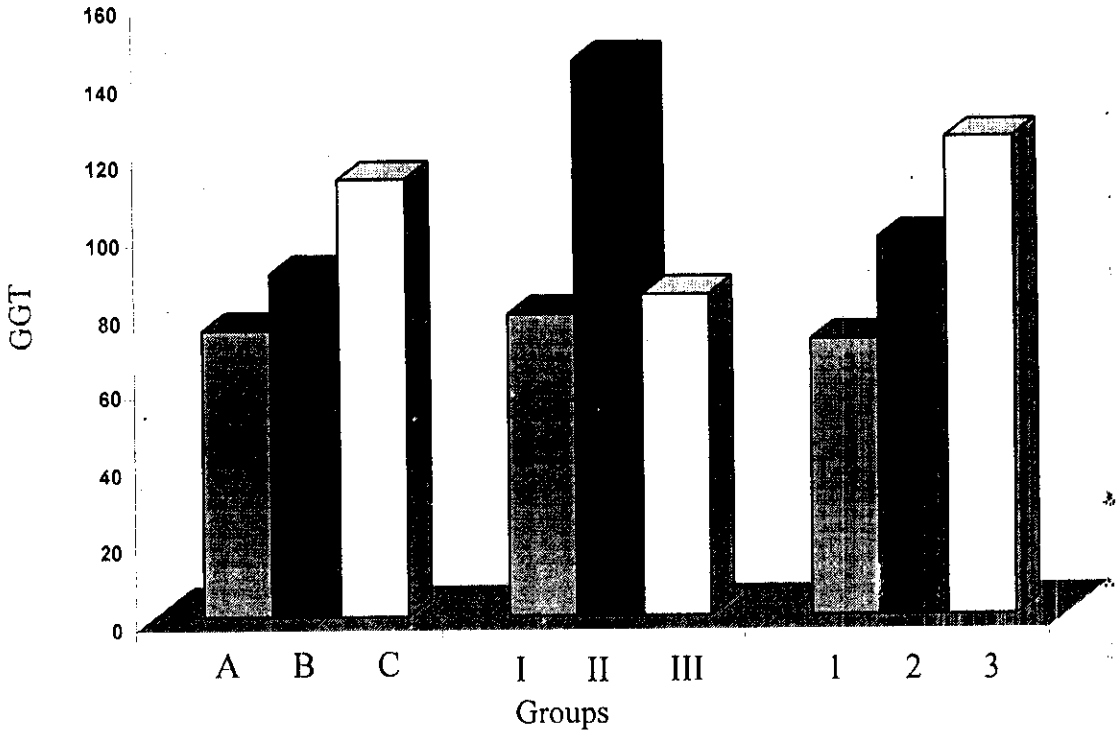


Fig (27): Means of Haptoglobin according to grades of fibrosis (sonar) fibrosis stages (biopsy) and grades of disease activity (biopsy)

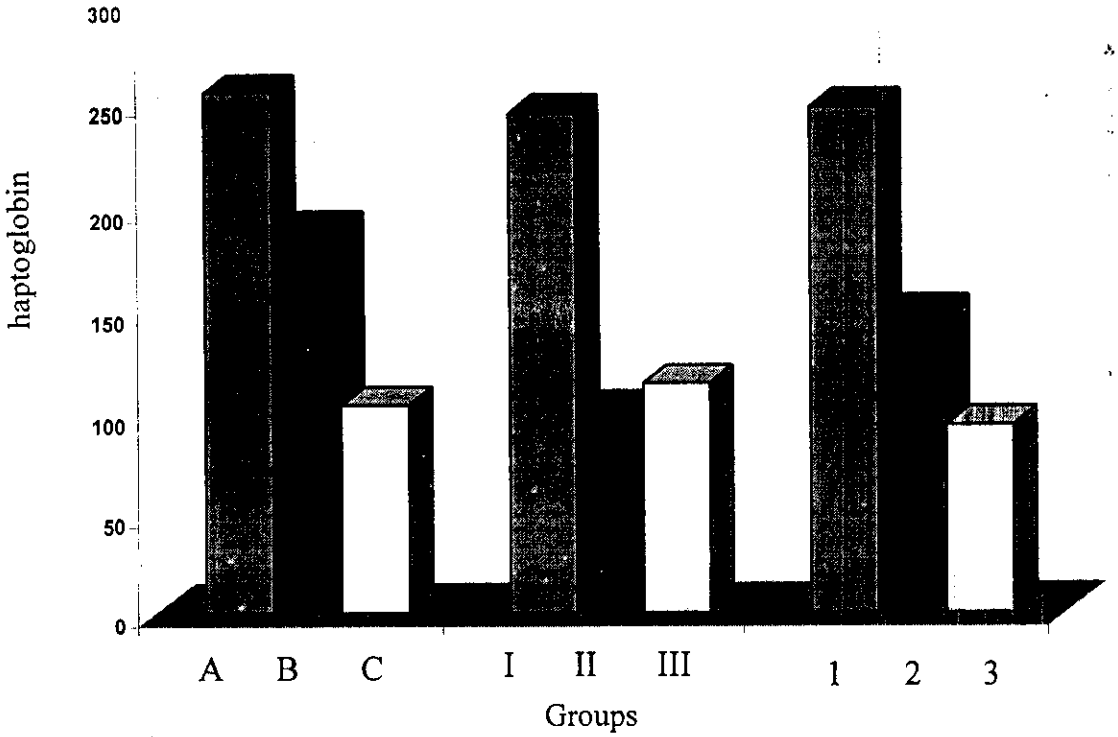


Table (14): Stepwise multi regression analysis :

Variables	Value	Regression coefficient	p
TIMP1	512	0.2345	< 0.01
MMP9	309	0.2091	< 0.01
Haptoglobin	219	0.0112	< 0.05
Total bilirubin	6	0.0139	< 0.05

In our study stepwise multiregression analysis shows that the most sensitive predictors for extensive stage of fibrosis (stage more than two) were found to be TIMP1 (more than 512), MMP9 (more than 309), haptoglobin (less than 219) and total bilirubin (more than 6).

Table (15): Sensitivity, specificity and cut off fibrosis markers, in diagnosis of fibrosis stage (F0, F1 , F2 versus F3 , F4)

Variable markers	Sensitivity (S)	Specificity (SP)	Cut off
TTMP1	92.9%	90%	516.8
MMP9	85.7%	80%	314.3
Haptoglobin	74.3%	70%	239.1
Bilirubin	71.4%	75%	6.93

The table shows that 516.8 , 314.3 , 239.1 and 6.93 were found to be the optimum cut off value of TIMP1, MMP9, haptoglobin and total bilirubin respectively in discrimination of mild fibrosis from extensive fibrosis (F0, F1, F2 VS F3 , F4).

Table (16): Diagnostic accuracy % of ultrasonography and fibrosis markers for the evaluation of fibrosis stage (biopsy).

Variables	Group I	Group II	Group III
TIMP1	88.9	92.3	90.7
MMP9	86.1	94.7	85.5
ultrasonography	53.3	87.6	69.4
Haptoglobin	76.5	72.4	78.8
Total bilirubin	74.1	78.9	82.3

The table shows that the diagnostic accuracy of TIMP1 and MMP9 was higher than Ultrasonography in group I, II, III, while diagnostic accuracy of ultrasonography was higher than haptoglobin and total bilirubin in group II. However, the diagnostic accuracy of haptoglobin and total bilirubin was higher than ultrasonography in group I,III