Table (1): Study of age differences between all studied groups

Studied variables	F0 (no. 9) Mean ± SD	F1 (no. 13) Mean ± SD	F2 (no. 9) Mean ± SD	F3 (no. 13) Mean ± SD	F4 (no. 2) Mean ± SD	Test of Significance	P-value	Post Hoc test
Age	30.4 ± 9.5	35.4 ± 11.6	42.1 ± 4.2	38.5 ± 8.1	37 ± 7.1	**ANOVA test 2.1**	**> 0.05**	

There is no statistical significant difference between studied groups as regards age

Table (2) study of the sex difference between all groups

Gender	*METAVIR score*										Test of significance	P–value
	F0 (no. 9) No	%	F1 (no. 13) No	%	F2 (no. 9) No	%	F3 (no. 13) No	%	F4 (no. 2) No	%		
Female	3	33.3	3	23.1	4	44.4	2	15.4	0	0.0	**X^2 test: 3.36**	**> 0.05**
Male	6	66.7	10	76.9	5	55.6	11	84.6	2	100.0		
Total	**9**	**100.0**	**13**	**100.0**	**9**	**100.0**	**13**	**100.0**	**2**	**100.0**		

There is no statistical significant difference between studied groups as regarding gender

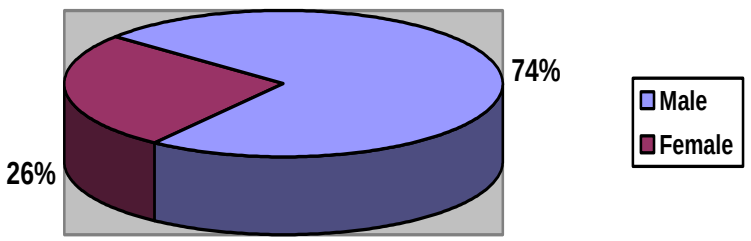

Fig (1): Male to female ratio in the studied cases

Table (3): Association between liver in ultrasound and METAVIR stage:

Liver in US	*METAVIR score*										Test of significance	P-value
	F0 (no. 9)		F1 (no. 13)		F2 (no. 9)		F3 (no. 13)		F4 (no. 2)			
	No	%	No	%	No	%	No	%	No	%		
- Normal	2	22.2	3	23.0	2	22.2	5	38.5	0	0.0	X^2 test: 15.9	< 0.05*
- Bright hepatomegally	3	33.3	5	38.5	7	77.8	1	7.7	0	0.0		
- Coarse liver	4	44.4	5	38.5	0	0.0	7	53.8	2	100.0		
Total	**9**	**100.0**	**13**	**100.0**	**9**	**100.0**	**13**	**100.0**	**2**	**100.0**		

There is a statistical significant difference between 5 stages (F4 100%) as regards liver appearance in U/S

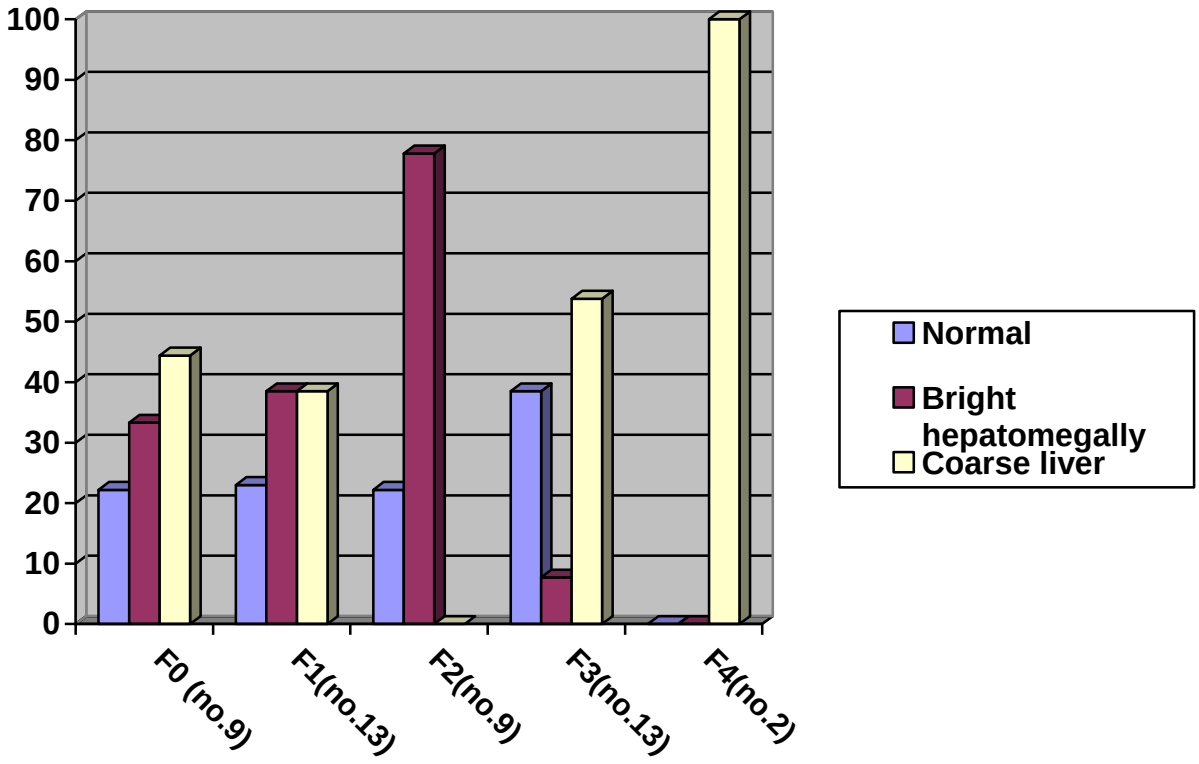

Fig (2): Liver appearance in ultrasound in different METAVIR stages.

Table (4): Association between hepato-splenomegaly and METAVIR stages:

Abdominal examination	*METAVIR score*					Test of significance	P–value
	F0 (no. 9) No %	F1 (no. 13) No %	F2 (no. 9) No %	F3 (no. 13) No %	F4 (no. 2) No %		
NAD	9 100.0	9 69.2	4 44.4	10 76.9	0 0.0	X^2 test: 18.3	< 0.05*
Hepatomegally	0 0.0	4 30.8	3 33.3	3 23.1	1 50.0		
Splenomegally	0 0.0	0 0.0	2 22.2	0 0.0	1 50.0		
Total	**9 100.0**	**13 100.0**	**9 100.0**	**13 100.0**	**2 100.0**		

There is statistical significant difference between 5 stages of METAVIR stages (50% - hepatomegaly and splenomegaly in f4)

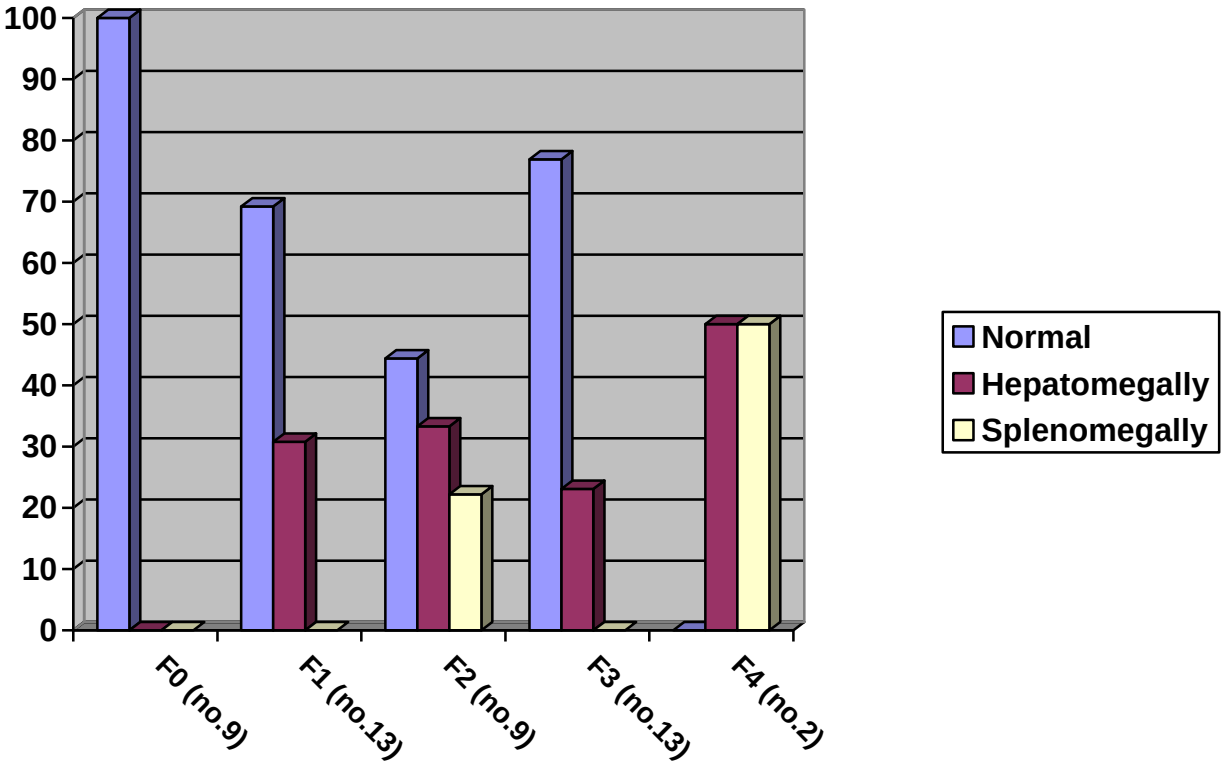

Fig (3): Association between organomegaly and METAVIR stages.

Table (5): Difference in laboratory findings between METAVIR activity grades:

Studied variables	A1 (no. 33) Mean ± SD	A2 (no. 12) Mean ± SD	A3 (no. 1) Mean ± SD	Test of Significance	P-value	Post Hoc test
Hb	13.64 ± 1.3	13.8 ± 1.8	12.6 ± 0	**ANOVA test 0.31**	**> 0.05**	
Platelets	6614.2 ± 2094.6	5510 ± 1201.3	4700 ± 0.0	**ANOVA test 1.61**	**> 0.05**	
WBCs	222 ± 52.4	182.9 ± 40.7	189 ± 0	**ANOVA test 2.63**	**> 0.05**	
Albumin	4.2 ± 0.51	4.15 ± 0.31	2.9 ± 0.0	**ANOVA test 3.78**	**< 0.05***	**P1=> 0.05 P2=.< 0.05* P3= < 0.05***
Prothrombin time	13.13 ± 1.17	13.04 ± 0.79	14 ± 0.0	**ANOVA test 0.35**	**> 0.05**	
Prothrombin conc	87.2 ± 12.13	86.5 ± 7.5	80 ± 0.0	**ANOVA test 0.21**	**> 0.05**	
ALT	80.9 ± 72	65.6 ± 25.7	24 ± 0.0	**Kruskal Wallis test 1.5**	**> 0.05**	
AST	54.2 ± 42.15	77.5 ± 75.7	32 ± 0.0	**Kruskal Wallis test 2.9**	**> 0.05**	
Total bilirubin	0.77 ± 0.26	0.79 ± 0.22	0.7 ± 0	**ANOVA test 0.08**	**> 0.05**	
Direct bilirubin	0.23 ± 0.14	0.24 ± 0.12	0.1 ± 0	**Kruskal Wallis test 1.87**	**> 0.05**	

This table is showing statistical significant difference between METAVIR grades regarding albumin (between A2 and A3 & between A1 and A3) and no statistical significant difference as regards other laboratory data.

Table (6) Differences in studied non invasive markers between METAVIR activity grades:

Studied variables	A1 (no. 33) Mean ± SD	A2 (no. 12) Mean ± SD	A3 (no. 1) Mean ± SD	Test of Significance	P-value	Post Hoc test
TIMP-1	187.07 ± 37.8	200.9 ± 44.9	130.3 ± 0.0	**ANOVA test 1.66**	**> 0.05**	
MMP-1	4.3 ± 3.85	4.6 ± 4.7	2.14 ± 0	**Kruskal Wallis test 0.25**	**> 0.05**	
MMP-2	384.9 ± 181.4	477.02 ± 136.4	475.3 ± 0	**Kruskal Wallis test 3.52**	**> 0.05**	
HA	59 ± 86.16	116.8 ± 122.07	50.93 ± 0.0	**Kruskal Wallis test 5.17**	**> 0.05**	

Studied variables	A1 (no. 33) Mean ± SD	A2 (no. 12) Mean ± SD	A3 (no. 1) Mean ± SD	Test of Significance	P-value	Post Hoc test
API	2.21 ± 1.9	3.92 ± 1.3	4 ± 0.0	**Kruskal Wallis test 7.75**	**< 0.05***	**P1> 0.05 P2< 0.05* P3> 0.05**
APRI	0.69 ± 0.54	1.23 ± 0.89	0.94 ± 0.0	**Kruskal Wallis test 8.5**	**< 0.05***	**P1 < 0.05* P2 > 0.05 P3 > 0.05**

P1 between A1 and A2 P2 between A1 and A3 P3 between A2 and A3

N.B. Tamhamne post hoc test is done for variables tested with Kruskal wallis test while LSD post hoc test is done for variables tesed with ANOVA test.

This table showing statistical significant difference between METAVIR activity grade regarding API (between A1and A3) and APRI (between A1 and A2) but there is no statistical significant difference between other studied variables

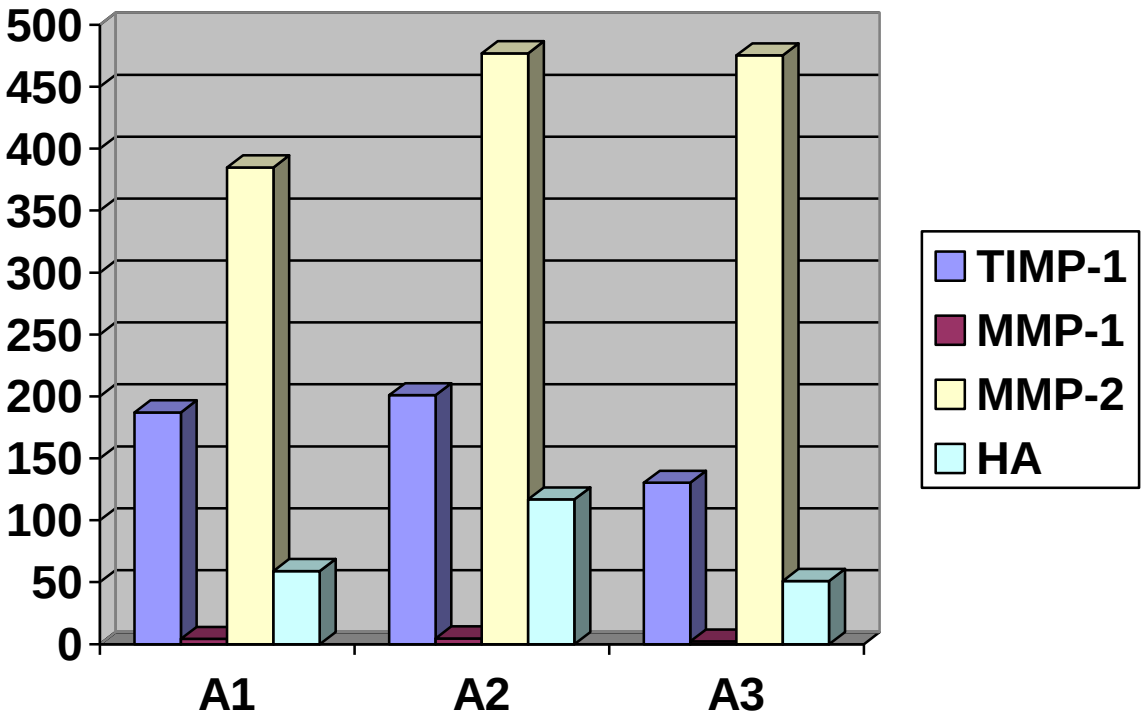

Fig (4): Difference between studied non invasive markers in different METAVIR activity grades.

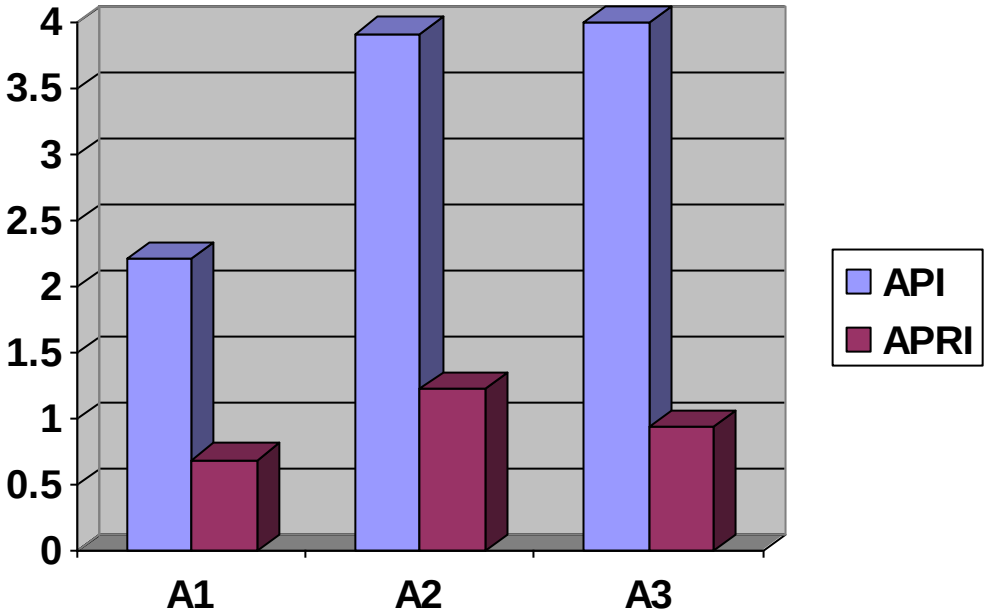

Fig (5): API and APRI in different METAVIR activity grades.

Table (7): Relation between the disease duration in months and METAVIR stages:

Studied variables	F0 (no. 9) Mean ± SD	F1 (no. 13) Mean ± SD	F2 (no. 9) Mean ± SD	F3 (no. 13) Mean ± SD	F4 (no. 2) Mean ± SD	Test of Significance	P-value	Post Hoc test
Duration of disease in months	19 ± 9.7	43 ± 39.7	9.2 ± 9.4	32.3 ± 16.5	19 ± 24.04	**Kruskal Wallis test 11.65**	**<0.05***	**P1> 0.05 P2> 0.05 P3> 0.05 P4> 0.05 P5> 0.05 P6> 0.05 P7> 0.05 P8< 0.01** P9> 0.05 P10> 0.05**

This table is showing that, there is highly statistical significant difference between F2 and F3 as regards disease duration.

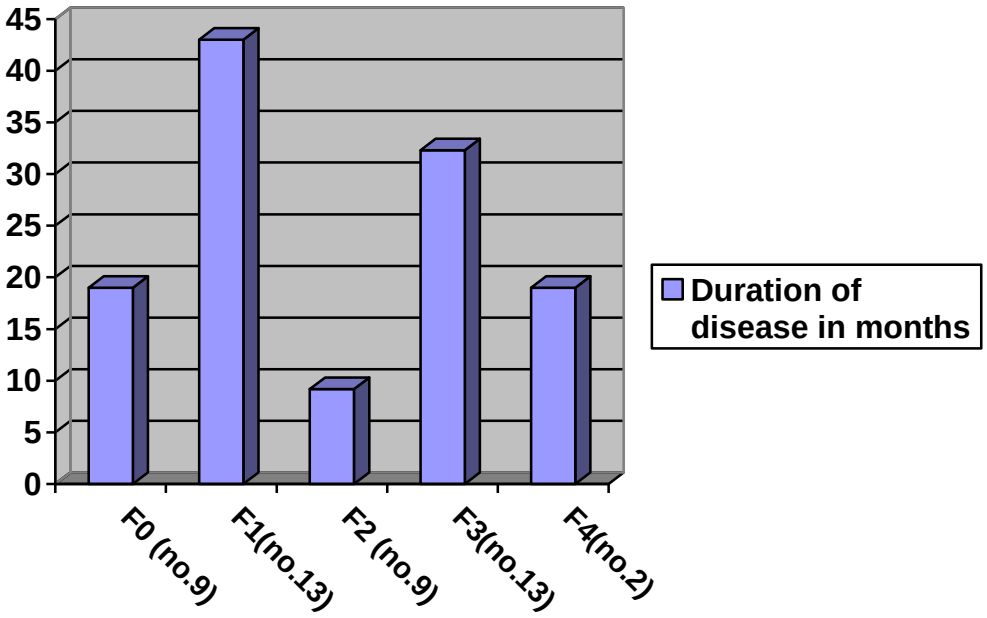

Fig (6): Relation between the Means of disease duration in months and METAVIR stages.

This table showing that:

1. There is highly statistical significant difference between all METAVIR stages as regarding MMP-2 (between F0 and F1 & between F0 and F3), as regards API (between F1 and F4) and as regarding APRI between all METVAIR stages (p value < 0.01).
2. There is statistical significant difference between all METAVIR stages as regards API and HA.

Table (10): Study of Spearman's correlation between METAVIR stage and studied variables:

METAVIR Stage	r	p- value
Age	**0.3**	**< 0.05***
Hb	**0.12**	**> 0.05**
Platelets	**- 0.18**	**> 0.05**
WBCs	**- 0.44**	**< 0.01****
Albumin	**0.12**	**> 0.05**
Prothrombin time	**0.18**	**> 0.05**
Prothrombin conc	**- 0.06**	**> 0.05**
ALT	**0.09**	**> 0.05**
AST	**0.33**	**< 0.05***
ALP	**- 0.16**	**> 0.05**
Total bilirubin	**0.23**	**> 0.05**
Direct bilirubin	**0.36**	**< 0.05***
HAI score	**0.97**	**< 0.01****
Tissue inhibitor of Metalloproteinase	**0.36**	**< 0.05***
Metalloproteinase -1	**0.008**	**> 0.05**
Metalloproteinase -2	**0.61**	**< 0.01****
Hyaluronic acid	**0.38**	**< 0.01****
API	**0.47**	**< 0.01****
APRI	**0.53**	**< 0.01****
Duration of disease in months	**- 0.01**	**> 0.05**
Spleen in US	**0.22**	**> 0.05**

This table is showing that:

1. Positive correlation between METAVIR stages and age, AST, direct bilirubin, TIMP-1**.**
2. Strong positive correlation between METAVIR stages and MMP-2, HA, API, APRI.
3. Strong negative correlation between METAVIR stages and WBCs.
4. **No correlation with other variables.**

Table (11): Study of Spearman's correlation between METAVIR activity and studied variables:

METAVIR activity	r	p- value
Age	**0.29**	**< 0.05***
Hb	**0.12**	**> 0.05**
Platelets	**- 0.21**	**> 0.05**
WBCs	**- 0.5**	**< 0.01****
Albumin	**0.003**	**> 0.05**
Prothrombin time	**0.13**	**> 0.05**
Prothrombin conc	**- 0.04**	**> 0.05**
ALT	**0.18**	**> 0.05**
AST	**0.35**	**> 0.05**
ALP	**- 0.23**	**> 0.05**
Total bilirubin	**0.15**	**> 0.05**
Direct bilirubin	**0.43**	**< 0.01****
HAI score	**0.98**	**< 0.01****
Tissue inhibitor of Metalloproteinase	**0.03**	**> 0.05**
Metalloproteinase -1	**- 0.03**	**> 0.05**
Metalloproteinase -2	**0.63**	**< 0.01****
Hyaluronic acid	**0.52**	**< 0.01****
API	**0.47**	**< 0.01****
APRI	**0.54**	**< 0.01****
Duration of disease in months	**- 0.01**	**> 0.05**
Spleen in US	**0.22**	**> 0.05**

This table is showing:

1. Positive correlation between METAVIR activity grades and age.
2. Strong positive correlation between METAVIR activity grades and direct bilirubin,
3. MMP-2, HA, API, APRI.
4. Strong negative correlation between METAVIR activity grades and WBCs.
5. No correlation with other variables.

Table (12): Study Pearson's correlation between TIMP-1 and studied variables:

Tissue inhibitor of metalloproteinase-1	r	p- value
Age	**0.17**	**> 0.05**
Hb	**- 0.08**	**> 0.05**
Platelets	**0.23**	**> 0.05**
WBCs	**- 0.06**	**> 0.05**
Albumin	**- 0.02**	**> 0.05**
Prothrombin time	**0.04**	**> 0.05**
Prothrombin conc	**0.13**	**> 0.05**
ALT	**0.07**	**> 0.05**
AST	**0.27**	**> 0.05**
ALP	**- 0.04**	**> 0.05**
Total bilirubin	**0.008**	**> 0.05**
Direct bilirubin	**0.11**	**> 0.05**
Metalloproteinase 1	**0.36**	**< 0.05***
Metalloproteinase 2	**0.34**	**< 0.05***
Hyaluronic acid	**0.22**	**> 0.05**
API	**0.18**	**> 0.05**
APRI	**0.22**	**> 0.05**
Duration of disease in months	**0.05**	**> 0.05**
Spleen in US	**0.09**	**> 0.05**

This table is showing that, there was:

1. Positive correlation between TIMP-1 and MMP-2.
2. Positive correlation between TIMP-1 and MMP-1.
3. No correlation between TIMP-1 and other variables.

Table (13): Study of Pearson's correlation between MMP-1 and studied variables:

Metalloprotienase-1	R	p- value
Age	**0.22**	**> 0.05**
Hb	**0.2**	**> 0.05**
Platelets	**0.23**	**> 0.05**
WBCs	**0.21**	**> 0.05**
Albumin	**- 0.21**	**> 0.05**
Prothrombin time	**- 0.03**	**> 0.05**
Prothrombin conc	**0.08**	**> 0.05**
ALT	**- 0.14**	**> 0.05**
AST	**- 0.006**	**> 0.05**
ALP	**0.15**	**> 0.05**
Total bilirubin	**- 0.35**	**> 0.05**
Direct bilirubin	**- 0.28**	**> 0.05**
Metalloproteinase -2	**0.25**	**> 0.05**
Hyaluronic acid	**- 0.04**	**> 0.05**
API	**- 0.09**	**> 0.05**
APRI	**- 0.009**	**> 0.05**
Duration of disease in months	**0.45**	**< 0.01****
Spleen in US	**- 0.07**	**> 0.05**

This table is showing that, there was:

1. Strong positive correlation between MMP-1 and duration of disease.
2. No correlation with other variables.

Table (14): Study of Pearson's correlation between MMP-2 and studied variables:

Metalloprotienase-2	R	p- value
Age	**0.06**	**> 0.05**
Hb	**0.26**	**> 0.05**
Platelets	**- 0.09**	**> 0.05**
WBCs	**- 0.14**	**> 0.05**
Albumin	**0.03**	**> 0.05**
Prothrombin time	**0.26**	**> 0.05**
Prothrombin conc	**- 0.1**	**> 0.05**
ALT	**- 0.01**	**> 0.05**
AST	**0.26**	**> 0.05**
ALP	**0.33**	**> 0.05**
Total bilirubin	**0.15**	**> 0.05**
Direct bilirubin	**0.24**	**> 0.05**
Hyaluronic acid	**- 0.5**	**< 0.05***
API	**0.11**	**> 0.05**
APRI	**0.32**	**< 0.05***
Duration of disease in months	**0.11**	**> 0.05**
Spleen in US	**- 0.5**	**< 0.05***

This table is showing that, there was:

1. Negative correlation between MMP-2 and HA, spleen size in ultrasound.
2. Positive correlation between MMP-2 and APRI.

Table (15): Study Pearson's correlation between Hyaluronic acid and studied variables:

Hyaluronic acid	R	p- value
Age	**0.01**	**> 0.05**
Hb	**0.17**	**> 0.05**
Platelets	**- 0.14**	**> 0.05**
WBCs	**- 0.03**	**> 0.05**
Albumin	**0.12**	**> 0.05**
Prothrombin time	**0.37**	**< 0.05***
Prothrombin conc	**0.38**	**< 0.05***
ALT	**0.04**	**> 0.05**
AST	**0.39**	**< 0.05***
ALP	**0.02**	**> 0.05**
Total bilirubin	**0.4**	**< 0.05***
Direct bilirubin	**0.41**	**< 0.05***
Duration of disease in months	**0.18**	**> 0.05**
Spleen in US	**0.04**	**> 0.05**

This table showing that, there was:
1. Positive correlation between HA and PT.
2. Positive correlation between HA and AST.
3. Positive correlation between HA and bilirubin.
4. No correlation with other variables.

Table (16): Study of Pearson's correlation between API and studied variables:

API	R	p- value
Age	**0.59**	**< 0.01****
Hb	**- 0.18**	**> 0.05**
Platelets	**0.01**	**> 0.05**
WBCs	**- 0.85**	**< 0.01****
Albumin	**0.21**	**> 0.05**
Prothrombin time	**0.15**	**> 0.05**
Prothrombin conc	**- 0.19**	**> 0.05**
ALT	**0.19**	**> 0.05**
AST	**0.06**	**> 0.05**
ALP	**0.05**	**> 0.05**
Total bilirubin	**- 0.28**	**> 0.05**
Direct bilirubin	**- 0.2**	**> 0.05**
Hyaluronic acid	**0.03**	**> 0.05**
APRI	**0.38**	**< 0.01****
Duration of disease in months	**0.02**	**> 0.05**
Spleen in US	**0.48**	**< 0.01****

This table revealed that, there was:

1. Strong negative correlation between API and white cell count.
2. Strong positive correlation between API and APRI.
3. Strong positive correlation between API and APRI.

Table (17): Study of Pearson's correlation between APRI and studied variables:

APRI	R	p- value
Age	**0.02**	**> 0.05**
Hb	**- 0.21**	**> 0.05**
Platelets	**- 0.35**	**< 0.05***
WBCs	**- 0.45**	**< 0.01****
Albumin	**0.1**	**> 0.05**
Prothrombin time	**0.2**	**> 0.05**
Prothrombin conc	**- 0.12**	**> 0.05**
ALT	**0.47**	**< 0.01****
AST	**0.74**	**< 0.01****
ALP	**- 0.11**	**> 0.05**
Total bilirubin	**0.21**	**> 0.05**
Direct bilirubin	**0.31**	**> 0.05**
Hyaluronic acid	**0.26**	**> 0.05**
Duration of disease in months	**- 0.06**	**> 0.05**
Spleen in US	**0.42**	**< 0.01****

This table is showing the following:

1. There was negative correlation between APRI and platelet count.
2. There was strong negative correlation between APRI and white cell count.
3. There was strong positive correlation between APRI and liver enzymes (AST – ALT).
4. There was strong positive correlation between APRI and spleen size in ultrasound.

Table (18): Stepwise linear regression between METAVIR score and significant variables with correlation:

Studied variables	METAVIR score	
	R square = 0.51	
	β0= - 0.06	
	B	p-value
Age	0.06	> 0.05
WBCs	- 0.18	> 0.05
AST	- 0.17	> 0.05
Direct bilirubin	0.15	> 0.05
Tissue inhibitor of Metalloprotienase	0.26	> 0.05
Metalloprotienase -1	0.05	> 0.05
Metalloprotienase -2	0.004	< 0.01**
Hyaluronic acid	0.08	> 0.05
API	0.19	> 0.05
APRI	0.59	< 0.05*

This table revealed that:
(MMP-2 was an independent marker in diagnosis of progressive fibrosis, while the other studied markers were dependent in diagnosis of progressive fibrosis).

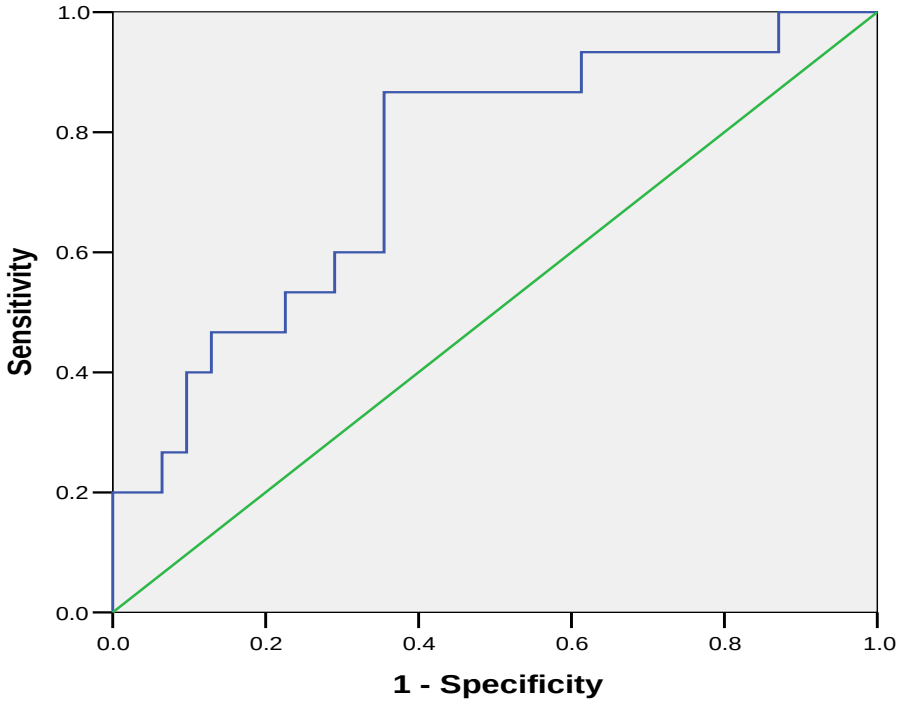

Fig (7): ROC curve testing the ability of TIMP-1 to diagnose significant fibrosis

Table (19): Sensitivity, specificity, area under ROC and accuracy of TIMP-1 in diagnosis of progressive fibrosis:

Studied variables	Sensitivity	Specificity	AUC	Accuracy	P- value	CI
Tissue inhibitor of Metalloprotienase Cut level 193.51	86.7 %	64.5 %	0.75	75.5 %	< 0.01**	0.59 – 0.9

Table (20): PPV and NPV of TIMP-1 for diagnosis of significant fibrosis:

TIMP as a screening tool	Clinical diagnosis		Total
	Significant fibrosis	Non significant fibrosis	
Positive	13	11	24
Negative	2	20	22
Total	15	31	46

-Positive predictive value of TIMP-1= 54.2 %.
-Negative predictive value of TIMP-1= 90.9 %.

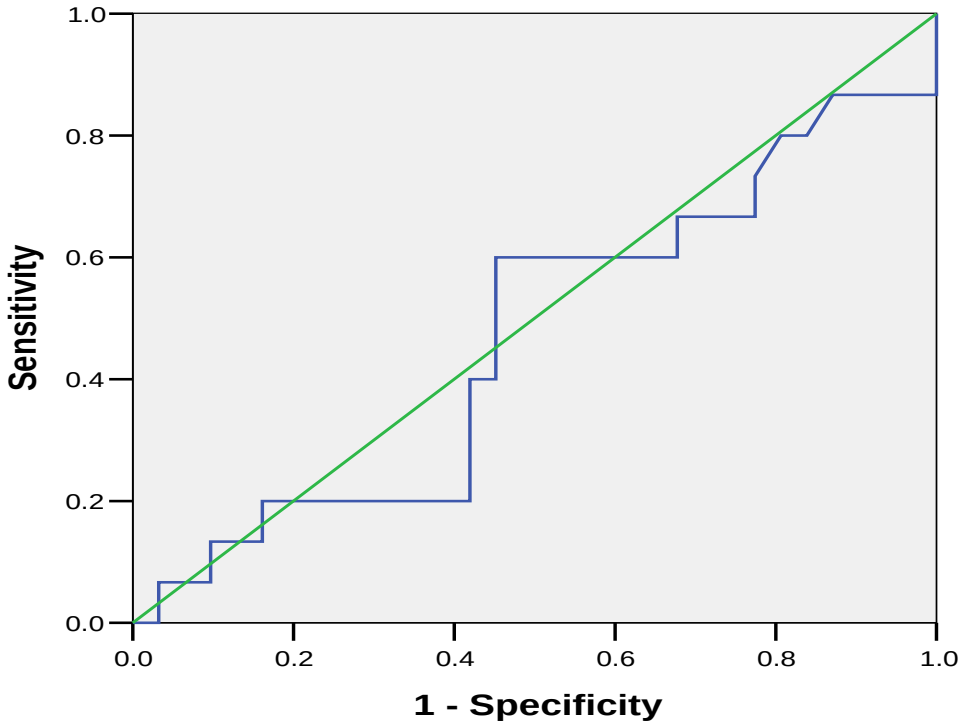

Fig (8): ROC curve testing the ability of MMP-1 to diagnose significant fibrosis

Table (21): Sensitivity, specificity, area under ROC and accuracy of MMP-1 in diagnosis of progressive fibrosis:

Studied variables	Sensitivity	Specificity	AUC	Accuracy	P- value	CI
Metalloprotienase 1 Cut level 2.41	60.0 %	54.8 %	0.47	47.2 %	> 0.05	0.28 – 0.65

Table (22): PPV and NPV of MMP-1 for diagnosis of significant fibrosis:

MMP-1 as a screening tool	Clinical diagnosis		Total
	Significant fibrosis	Non significant fibrosis	
Positive	8	14	22
Negative	7	17	24
Total	15	31	46

-Positive predictive value of MMP-1= 36.4 %.
-Negative predictive value of MMP-1= 70.8 %.

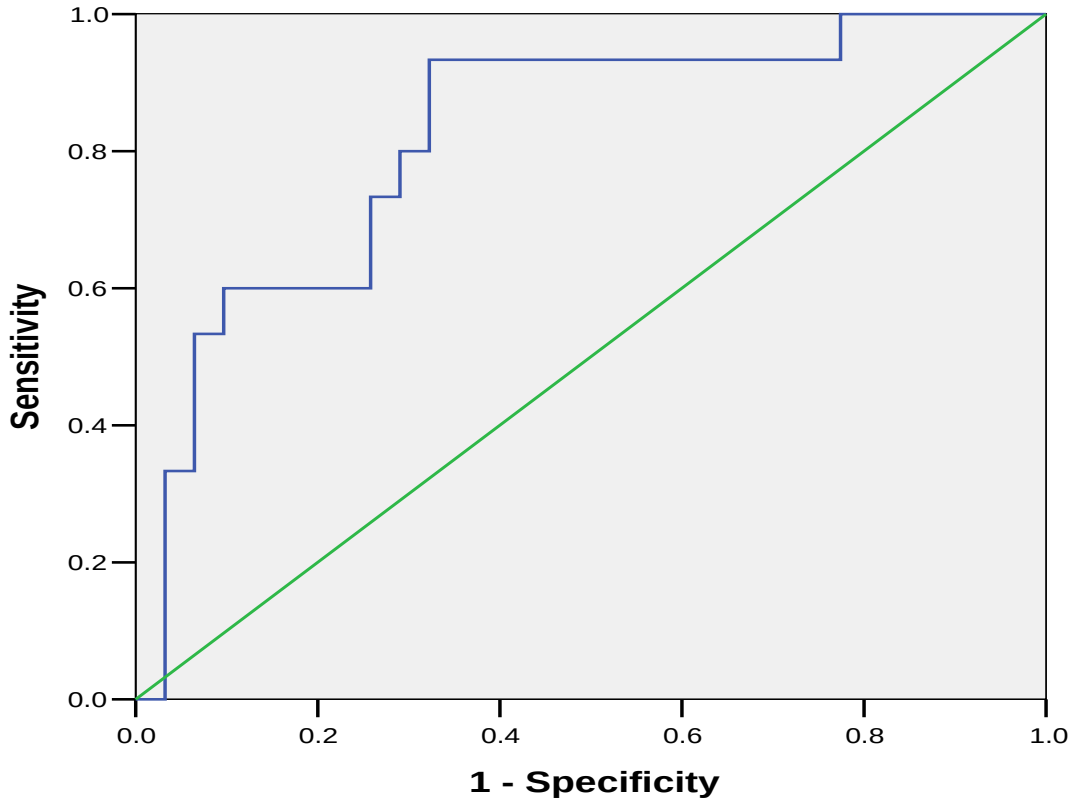

Fig (9): ROC curve testing the ability of MMP-2 to diagnose of significant fibrosis

Table (23): Sensitivity, specificity, area under ROC and accuracy of MMP-2 in diagnosis of progressive fibrosis:

Studied variables	Sensitivity	Specificity	AUC	Accuracy	P- value	CI
Metalloprotienase 2 Cut level 384.5	93.3 %	67.7 %	0.82	81.9 %	< 0.01**	0.69 – 0.95

Table (24): PPV and NPV of MMP-2 for diagnosis of significant fibrosis:

MMP-2 as a screening tool	Clinical diagnosis		Total
	Significant fibrosis	Non significant fibrosis	
Positive	14	10	24
Negative	1	21	22
Total	15	31	46

-Positive predictive value of MMP-2= 58.3 %.
-Negative predictive value of MMP-2= 95.4 %.

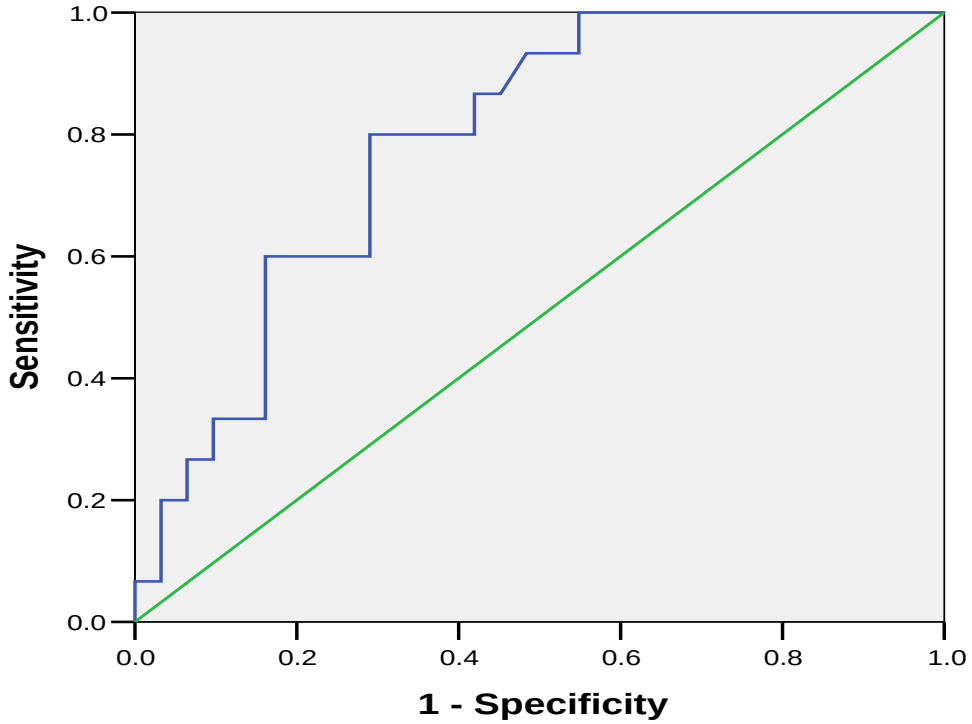

Fig (10): ROC curve testing the ability of Hyalouronic acid to diagnose significant fibrosis

Table (25): Sensitivity, specificity, area under ROC and accuracy value of Hyaluronic acid in diagnosis of progressive fibrosis:

Studied variables	Sensitivity	Specificity	AUC	Accuracy	P- value	CI
Hyaluronic acid Cut level 26.41	80.0 %	71.0 %	0.79	80.1 %	< 0.01**	0.66 – 0.92

Table (26): PPV and NPV of HA for diagnosis significant fibrosis:

HA as a screening tool	Clinical diagnosis		Total
	Significant fibrosis	Non significant fibrosis	
Positive	12	9	21
Negative	3	22	25
Total	15	31	46

-Positive predictive value of HA= 57.1 %.
-Negative predictive value of HA= 88.0 %

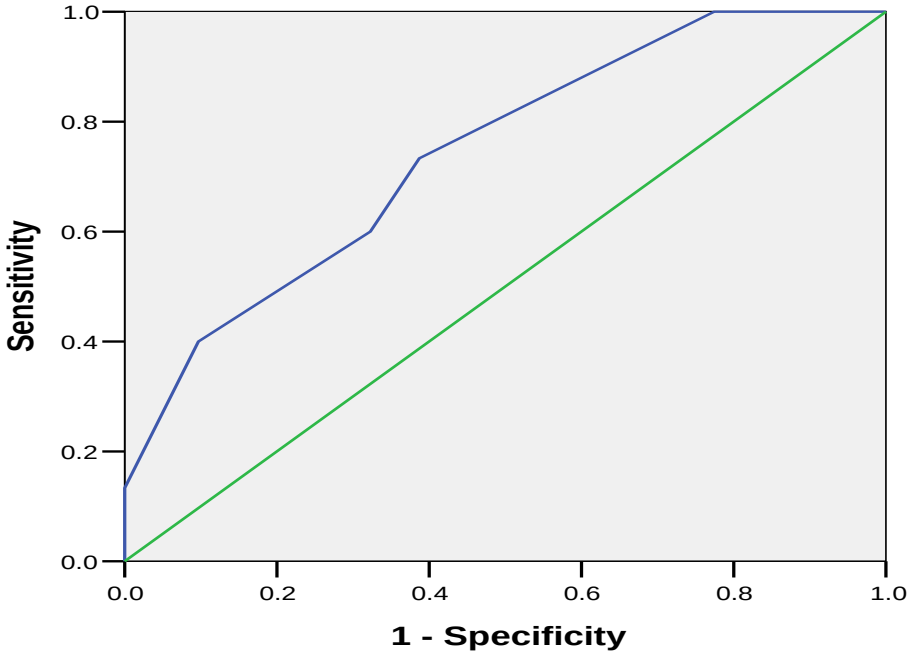

Fig (11): ROC curve testing the ability of API to diagnose significant fibrosis.

Table (27): Sensitivity, specificity, area under ROC and accuracy of API in diagnosis of significant fibrosis:

Studied variables	Sensitivity	Specificity	AUC	Accuracy	P- value	CI
API Cut level 2.5	73.3 %	61.3 %	0.74	73.8 %	< 0.01**	0.59 – 0.89

Table (28): PPV and NPV of API for diagnosis of significant fibrosis:

API as a screening tool	Clinical diagnosis		Total
	Significant fibrosis	Non significant fibrosis	
Positive	11	12	23
Negative	4	19	23
Total	15	31	46

-Positive predictive value of API= 47.8 %.
-Negative predictive value of API= 82.6 %.

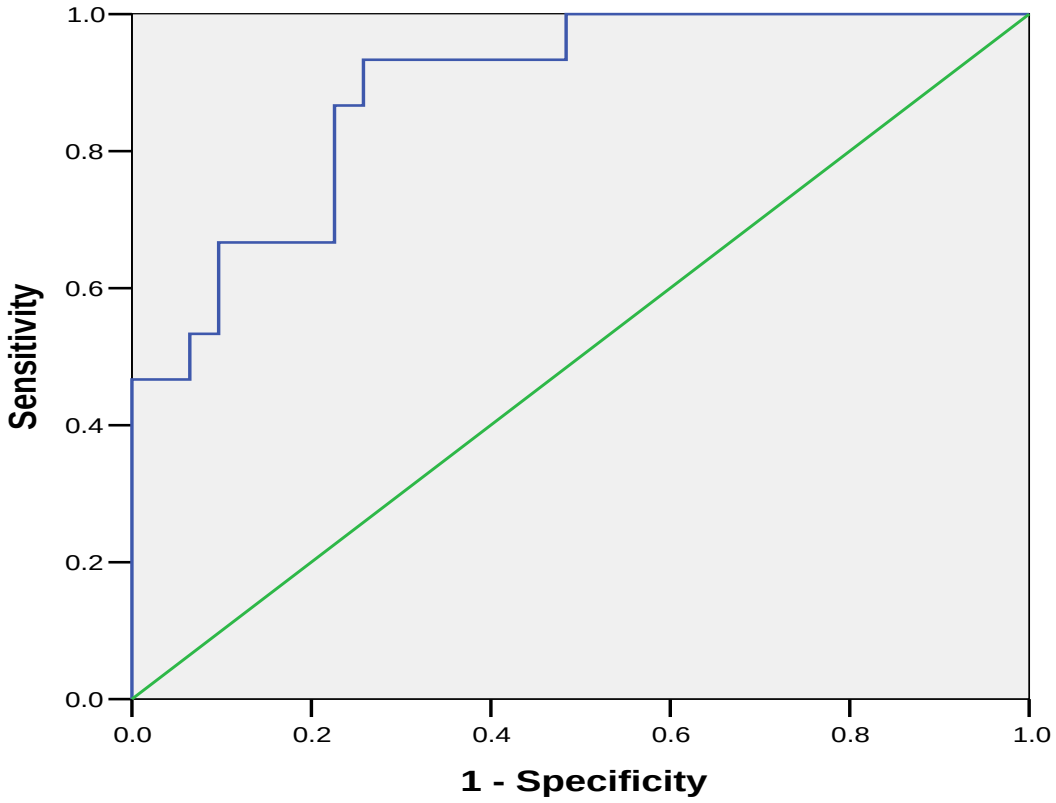

Fig (12): ROC curve testing the ability of APRI to diagnose significant fibrosis.

Table (29): Sensitivity, specificity, area under ROC curve and accuracy of APRI in diagnosis of significant fibrosis:

Studied variables	Sensitivity	Specificity	AUC	Accuracy	P- value	CI
APRI Cut level 0.63	93.3 %	74.2 %	0.89	89.6 %	< 0.01**	0.79 – 0.98

Table (30): PPV and NPV of APRI for diagnosis of significant fibrosis:

APRI as a screening tool	Clinical diagnosis		Total
	Significant fibrosis	Non significant fibrosis	
Positive	14	8	22
Negative	1	23	24
Total	15	31	46

-Positive predictive value of APRI= 63.6 %.
-Negative predictive value of APRI= 95.8 %.