Table (3): Clinical characters of the studied groups.

	Control n= 30		CH n= 30		LC n= 30		HCC n= 30	
	No.	%	No.	%	No.	%	No.	%
Sex								
Male	18	60	20	66.7	19	63.3	22	73.3
Female	12	40	10	33.3	11	36.7	8	26.7
Age (year)								
Range	37 - 55		37 - 58		37 - 63		38 - 65	
Mean±SD	44.83±5.34		46.13±6.64		51.10±7.86		52.27±8.12	
Liver size								
Normal	30	100	2	6.6	0	0.0	3	10
Enlarged	0	0.0	28	93.4	23	76.7	21	70
Shrinked	0	0.0	0	0.0	7	23.3	6	20
Spleen								
Normal	0	100	9	30	2	6.6	4	13.3
Enlarged	0	0.0	21	70	28	93.4	26	86.7
Ascitis								
Negative	30	100	30	100	2	6.6	8	26.6
Positive	0	0.0	0	0.0	28	93.4	22	73.4

CH = Chronic hepatitis LC = Liver cirrhosis HCC = hepatcellular carcinoma

Table (4): Comparison between studied groups as regards liver function tests

	TB (mg/dL)		DB (mg/dL)		TP (gm/dL)		Alb (gm/dL)		AST (IU/L)		ALT (IU/L)		ALP (IU/L)	
	$\overline{X} \pm SD$	t	$\overline{X} \pm SD$	t	$\overline{X} \pm SD$	t	$\overline{X} \pm SD$	t	$\overline{X} \pm SD$	t	$\overline{X} \pm SD$	t	$\overline{X} \pm SD$	t
I Control (n=30)	0.69±0.15		0.12±0.07		7.38±0.38		4.23±0.31		30.0±4.09		30.37±4.82		74.23±8.82	
II CH (n=30)	2.13±1.66	4.47**	1.13±1.52	3.62**	6.89±0.81	3.03**	3.31±0.38	10.30**	102.4±37.6	10.47**	105.7±32.3	12.63**	124.6±30.8	8.61**
III LC (n=30)	2.86±1.23	9.63**	1.72±0.98	8.94**	6.99±1.07	4.34**	2.23±0.34	23.85**	94.0±26.14	9.11**	96.9±42.53	8.52**	124.9±38.8	6.98**
IV HCC (n=30)	2.20±1.11	7.37**	1.31±1.06	6.13**	6.38±0.73	6.48**	2.66±0.47	15.20**	123.3±64.5	7.91**	122.5±63.6	7.91**	175.4±85.9	6.41**
F	2.70		1.92		2.70		55.55**		2.20		2.20		7.81**	
P	> 0.05		> 0.05		>0.05		<0.001 All sig.		>0.05		>0.05		<0.001 (II=III<IV)	

TB = total bilirubin, DB = direct bilirubin, TP = total protein, Alb = Albumin, AST = Aspartate aminotransferase, ALT = Alanine aminotransferase, ALP = Alkaline phosphatase.
CH = Chronic hepatitis LC = Liver cirrhosis HCC = Hepatocellular carcinoma.
t = student t-test for comparison between each group and control group as regards parametric values.
F (ANOVA) for comparison between more than 2 groups (CH, LC and HCC groups) as regards parametric values.
P (probability) > 0.05 = Non-significant, P<0.05 = Significant (*) P<0.01 = Highly significant (**)

This table shows that all the liver function tests are highly significantly increased (**) except in total protein and albumin, there is high significant decrease in the three groups (CH, LC and HCC) in comparison with the control group.
There are no significant changes between patient groups except for albumin which is highly significantly decreased in the three groups and alkaline phosphatase which is highly significantly increased in HCC group in comparison with CH and LC groups.

Table (6): Comparison between studied groups as regards α-fetoprotein (AFP) (ng/ml)

	Control n= 30	CH n= 30	LC n= 30	HCC n= 30
Mean ± SD	3.20±1.920.1	8.69±5.37	26.52±29.11	784.61±914.71
Range	0.10- 6.8	2.10 - 21.90	2.5 - 117.0	3.3 - 3000
Median	2.80	7.80	15.90	376.0
Mann-Whitney		4.65	5.98	6.13
P		<0.001**	<0.001**	<0.001**
Kruskal-Wallis		36.36		
P		<0.001**		
Mann-Whitney		(CH=LC) < HCC		

CH = Chronic hepatitis LC = Liver cirrhosis HCC = hepatcellular carcinoma

Mann-Whitney test for comparison between two groups (each group and control group) as regards non-parametric variables.

Kruskal-Wallis test for comparison between more than 2 groups (CH, LC and HCC) studied groups as regards non-parametric values and if significant followed by Mann-Whitney test to compare between each 2 groups.

P>0.05 = Non-significant P<0.05 = Significant (*) P<0.001 = Highly significant (**)

Serum AFP is highly significantly increased in the three groups (CH, LC & HCC) in comparison with the control group and also highly significantly increased in HCC group in comparison with CH and LC groups.

Table (8): Comparison between studied groups as regards circulating intercellular adhesion molecule-1 (cICAM-1) (ng/ml)

	Control n= 30	CH n= 30	LC n= 30	HCC n= 30
Mean ± SD	232.07±76.171	489.5±226.42	781.27±443.24	999.42±687.80
Range	07 - 305	105-920	115-2120	187-3130
Median	242.5	449.0	745.0	910.0
Mann-Whitney		5.01	5.28	5.75
P		<0.001**	<0.001**	<0.001**
Kruskal-Wallis		15.79		
P		<0.001**		
Mann-Whtieny		(LC=HCC)>CH		

CH = Chronic hepatitis LC = Liver cirrhosis HCC = hepatcellular carcinoma

Mann-Whitney test for comparison between two groups (each group and control group) as regards non-parametric variables.

Kruskal-Wallis test for comparison between more than 2 groups (CH, LC and HCC) studied groups as regards non-parametric values and if significant followed by Mann-Whitney test to compare between each 2 groups.

P>0.05 = Non-significant P<0.05 = Significant (*) P<0.001 = Highly significant (**)

cICAM-1 is highly significantly increased in the three groups (CH, LC & HCC) in comparison with the control group and also highly significantly increased in LC and HCC groups in comparison with CH group. There is no significant change between LC and HCC groups.

Table (10): Spearman rank correlation between AFP, PIIIP, cICAM-1 & MMP-9 and other variables in control group.

	AFP (ng/ml)	PIIIP (μg/L)	cICAM-1 (ng/ml)	MMP-9 (ng/ml)
AFP	1.000			
PIIIP	–0.191	1.000		
cICAM-1	–0.311	0.272	1.000	
MMP-9	–0.057	0.094	0.103	1.000
Age	0.028	–0.114	–0.014	–0.336
T. bilirubin	0.148	–0.047	0.329	0.120
D. bilirubin	0.353	0.062	0.339	0.069
Albumin	–0.140	–0.210	–0.070	–0.343
Total protein	–0.081	–0.307	–0.0750	–0.136
SGOT (AST)	–0.053	0.140	0.070	–0.082
SGPT (ALT)	0.317	–0.320	–0.280	–0.106
Al. P.	0.260	0.182	0.084	–0.290

Positive correlation = > 0.355 Negative correlation = < -0.355

There is no significant correlation.

Table (13): Spearman rank correlation between AFP, PIIIP, cICAM-1 & MMP-9 and other variables in hepatocellular carcinoma group (HCC)

	AFP (ng/ml)	PIIIP (μg/L)	cICAM-1 (ng/ml)	MMP-9 (ng/ml)
AFP	1.000			
PIIIP	0.017	1.000		
cICAM-1	0.003	-0.058	1.00	
MMP-9	0.006	0.067	0.013	1.000
Age	0.270	0.012	0.022	0.111
T. bilirubin	0.391*	0.249	–0.001	0.376*
D. bilirubin	0.420*	0.267	–0.061	0.401*
Albumin	–0.247	0.044	0.151	–0.280
Total protein	0.076	–0.280	0.215	–0.175
SGOT (AST)	0.115	0.231	0.145	0.209
SGPT (ALT)	0.228	0.135	0.086	0.278
Al. P.	0.084	0.056	0.420*	0.533*
No. of tumour	0.045	–0.006	0.238	0.340
Size of tumour	0.033	0.135	0.500*	0.287
Grading of tumour	–0.051	0.218	–0.047	0.494*

Positive correlation = > 0.355 Negative correlation = < -0.355

There are positive correlations between :

- Alpha fetoprotein and total bilirubin and direct bilirubin.
- Circulating intercellular adhesion molecule-1 and alkaline phosphatase and size of the tumor.
- Plasma matrix metalloproteinase-9 and total bilirubin, direct bilirubin, alkaline phosphatase and grading of tumours.

Table (15): Comparison between HCC grades as regards procollagen III peptide (PIIIP) (μg/L)

	Grade I n = 8	Grade II n = 13	Grade III n = 9
Mean ± SD	21.71 ± 16.86	26.77 ± 20.43	30.60 ± 19.09
Range	8.50 - 49.00	7.50 - 62.20	9.30 - 73.20
Median	14.50	18.70	28.30
Kruskal-Wallis	1.43		
P	> 0.05		

Kruskal-Wallis test for comparison between more than 2 groups as regards non-parametric variables.

There is no significant changes in PIIIP level as regards HCC grades.

Table (18): Comparison between cases in HCC group with a background of CH or LC as regards AFP, PIIIP, cICAM-1, MMP-9

Variable	CH n = 7	LC n = 23	Comparison	
	Mean ±SD	Mean ±SD	Mann-Whitney	P
AFP (ng/ml)				
Mean±SD	711.20±788.26	840.75±1021.16		
Range	3.30-2300.0	3.5-3000.0	0.31	>0.05
Median	443.0	93.60		
PIIIP (µg/L)				
Mean±SD	26.73±18.80	26.45±19.35		
Range	7.70-59.10	7.50-73.20	0.06	>0.05
Median	16.10	18.70		
cICAM-1 (ng/ml)				
Mean±SD	380.21±718.49	1155.31±639.14		
Range	270.0-2180.0	187.60-3130.0	1.51	>0.05
Median	955.0	682.0		
MMP-9 (ng/ml)				
Mean±SD	138.62±110.69	268.31±248.85		
Range	13.90-364.0	20.95-937.00	1.34	>0.05
Median	89.80	166.70		

Mann-Whitney test for comparison between two groups (CH and LC cases in HCC group) as regards nonparametric variables.

There is no significant change in AFP, PIIIP, cICAM-1 and MMP-9 levels in HCC group as regards a background of CH and LC.

Table (20): Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of AFP in diagnosis of HCC at different cut-off levels (HCC vs. CH & LC).

Level (ng/ml)	Sensitivity %	Specificity %	PPV %	NPV %	Accuracy %
3.3	100.0	10.0	35.7	100.0	40.0
3.9	93.3	13.3	35.0	80.0	40.0
6.1	90.0	28.3	61.4	85.0	48.9
10.3	86.7	41.7	42.6	86.2	56.7
21.4	83.3	78.3	65.8	90.4	80.0
24	80.0	86.7	75.0	89.7	84.4
29	76.7	90.0	79.3	88.5	85.5
68*	70.0	96.7	91.3	86.6	87.8
373	53.3	100.0	100.0	81.1	84.4

* The cut-off level which maximizes the sum of sensitivity and specificity

68 ng/ml was chosen as the optimum cut-off value, so in the diagnosis of HCC from CH & LC, the sensitivity was 70% and the specificity was 96.7%. The positive predictive value, the negative predictive value and the accuracy were 91.3%, 86.6% and 87.8%, respectively.

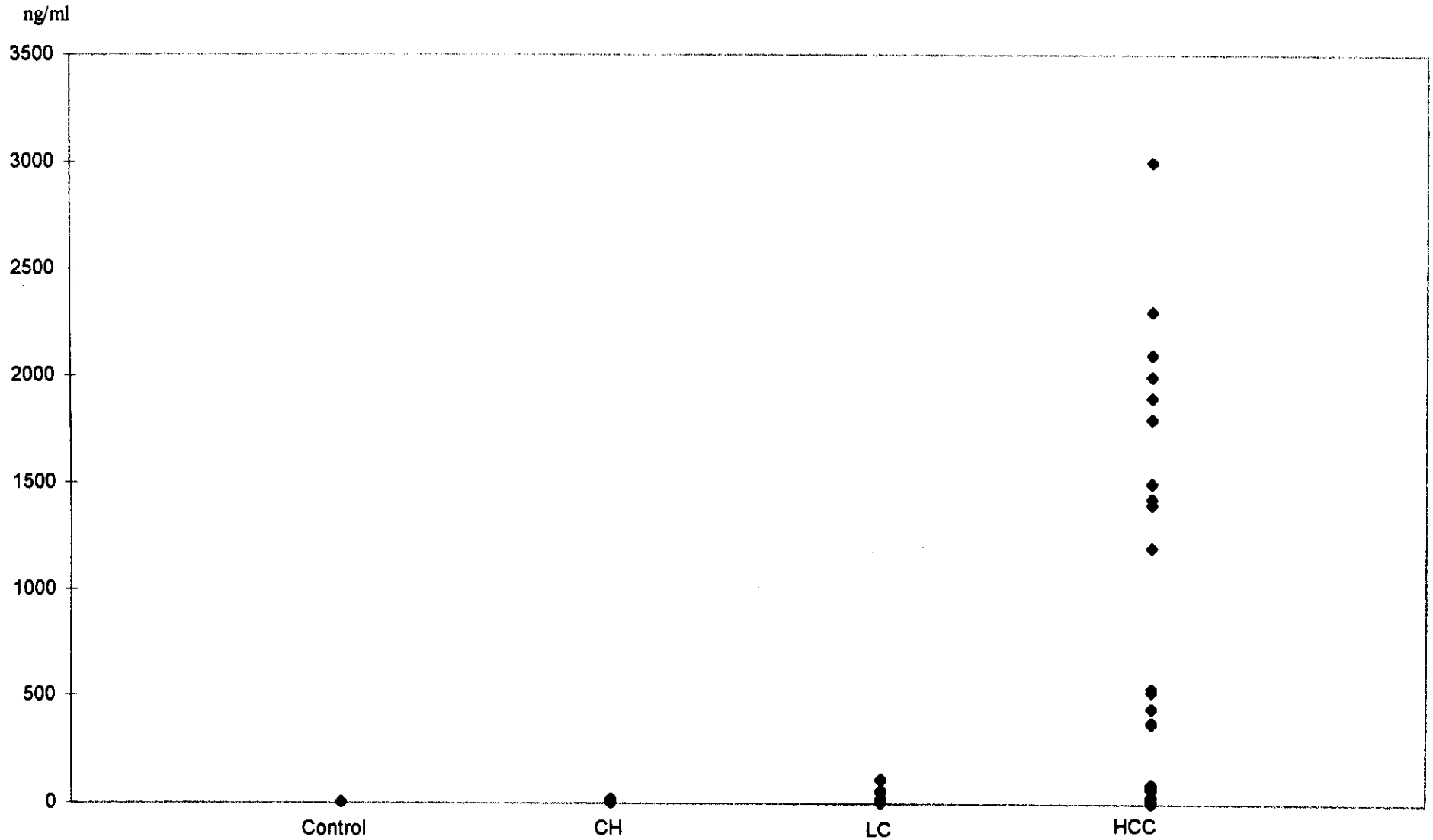

Figure (3): Shows the results of α-fetoprotein (AFP) in the studied groups

CH Chronic hepatitis
LC Liver cirrhosis
HCC Hepatocellular carcinoma

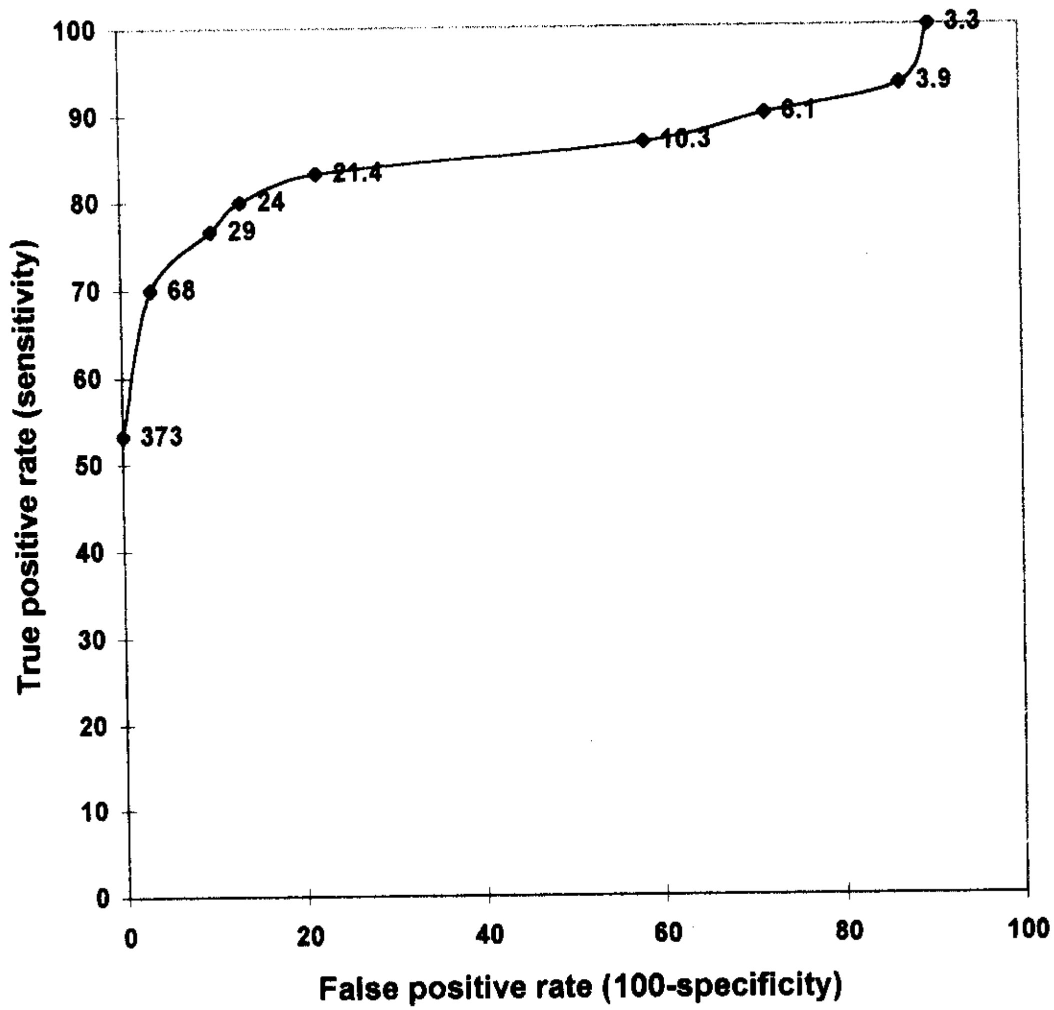

Figure (7): Receiver operator characteristic (ROC) curve for α-fetoprotein (HCC vs Ch & LC)

... as the optimum cut off value of AFP in the diagnosis of HCC from CH and LC patients

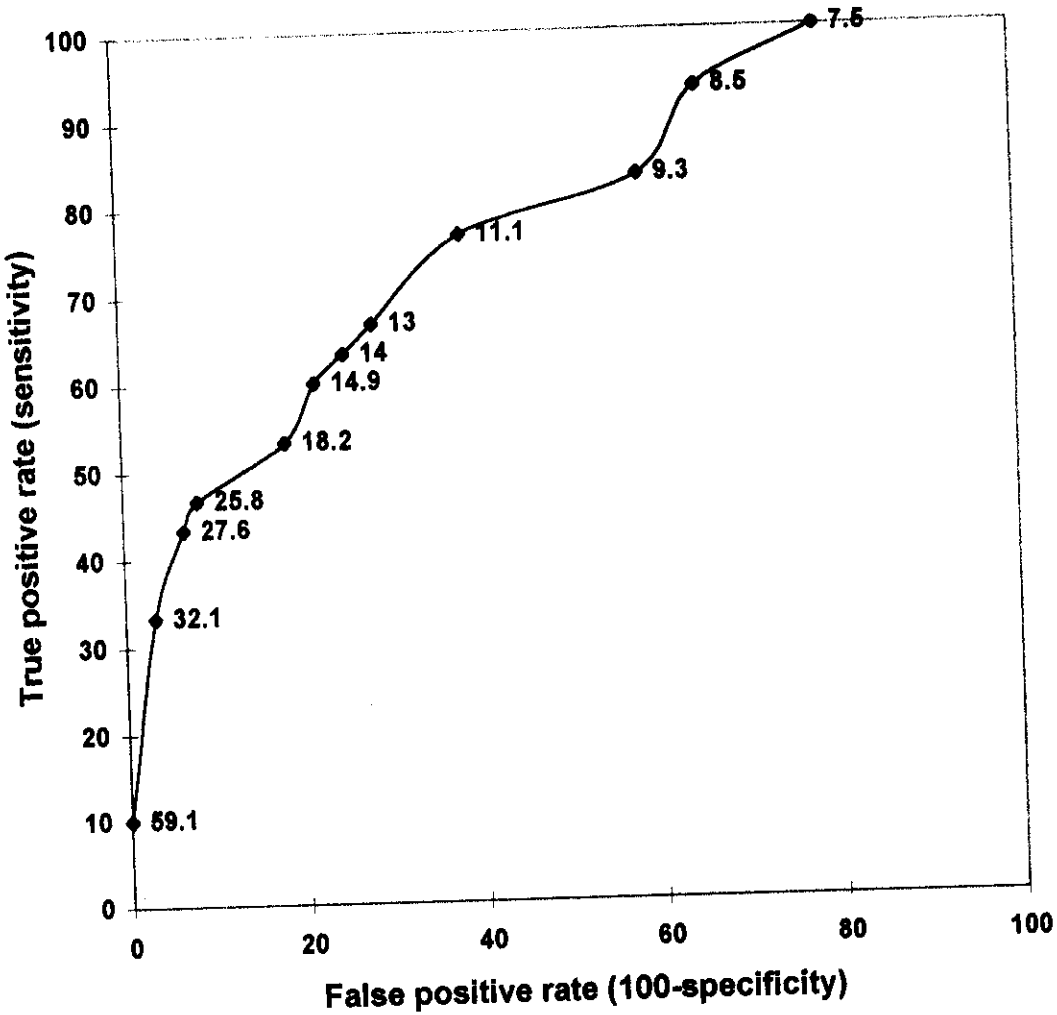

Figure (8): Receiver operator characteristic (ROC) curve for PIIIP (HCC vs CH & LC)

25.8 ug/L was chosen as the optimum cut-off value of PIIIP in the diagnosis of HCC from CH and LC patients.

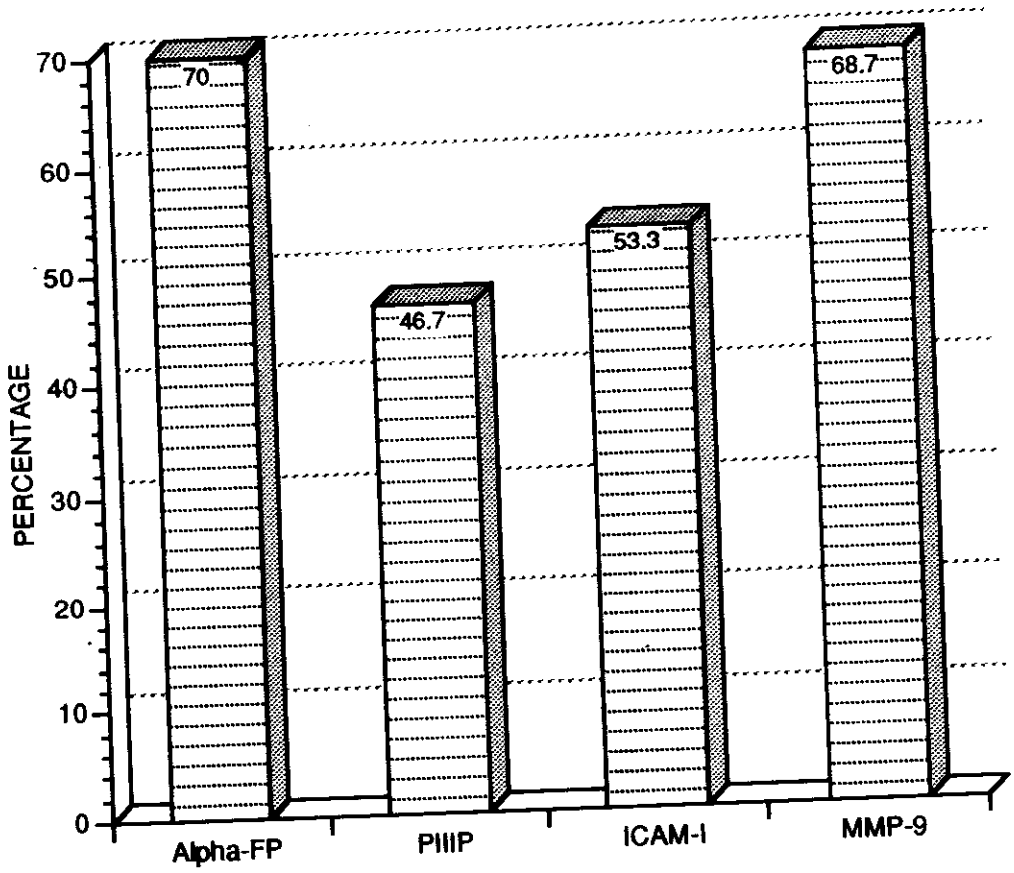

Figure (12): Sensitivity of AFP, PIIIP, cICAM-1 and MMP-9 in cases of HCC Vs. CH & LC groups at their cut-off values

AFP is the most sensitive marker (70%) followed by plasma MMP-9 (68.7%), cICAM-1 (53.3%) and PIIIP (46.7%) respectively.

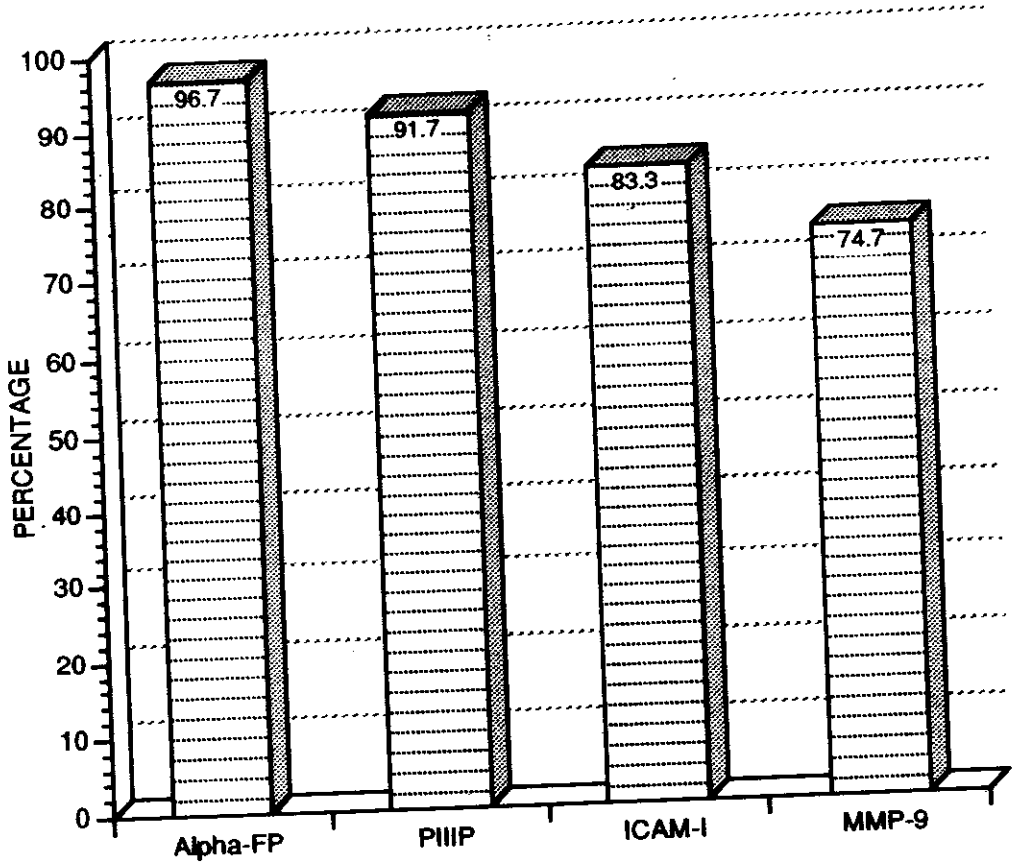

Figure (13): Specificity of AFP, PIIIP, cICAM-1 and MMP-9 in cases of HCC Vs. CH & LC groups at their cut-off values

AFP is the most specific marker (96.7%) followed by PIIIP (91.7%), cICAM-1 (83.3%) and plasma MMP-9 (74.7%) respectively.