RESULTS

This study had been conducted on 42 patients with CHC viral infection. The different demographic and clinical data of the patients was collected and analyzed as follow:

I. Demographic data:

Demographic data in relation to the control group :

Table (3), and Fig. (4), shows the demographic data in the two studied groups, it was found that the age of patients was ranged from 23 – 56 years, with a mean of 41.64±8.71 years while in control group the age ranged from 21 – 56 years with a mean of 35.9±10.2 years, there was no significant difference between the two studied groups regarding age.

Thirty four patients (81%) were males, whereas 8 patients (19%) were females. In control group there was 10 male (66.7%) and 5 female (33.3%) there was no significant difference between the two studied groups regarding sex. (Table 3, Fig. 4)

Table (3): Comparison between patients and control regarding demographic data.

	Control gp.	**Patients gp.**
Age		
Range	23 - 56	21 - 56
Mean	35.9	41.64
S.D.	10.2	8.71
T	1.71	
p	0.076	
Sex		
Male	10 (66.7%)	34 (81.0%)
Female	5 (33.3%)	8 (19.0%)
X^2	1.28	
p	0.25	

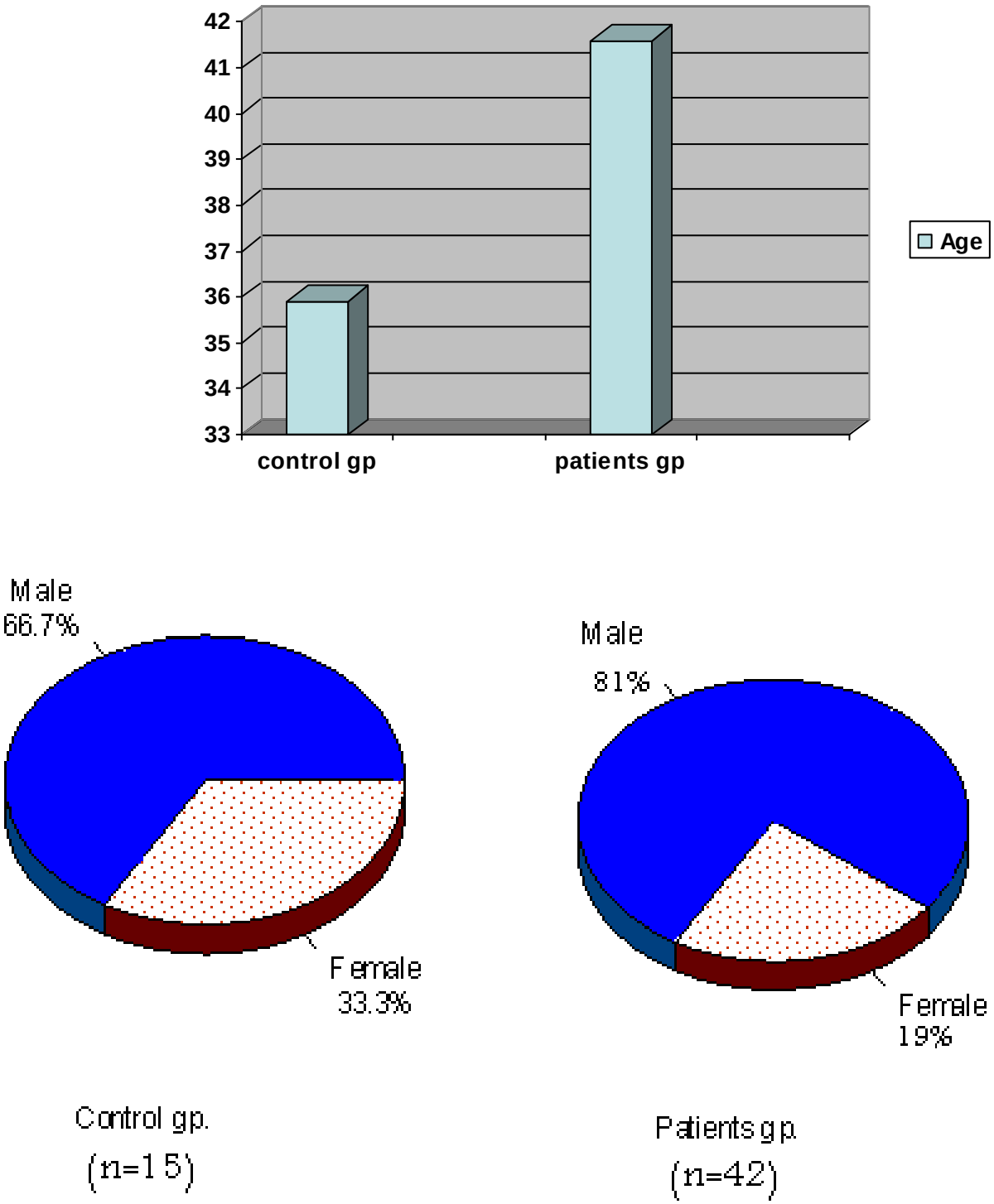


Fig. (4): Comparison between patients and control regarding demographic data.

Demographic data in relation to the plasma level of chemokine cxcl10 before starting antiviral therapy :

The result was as follow : 27 patient (64.2 %) were above 40 years with mean plasma CXCL10 : 864.1 PG/ml , whereas 15 patients (35.8%) were below 40 years with mean plasma CLCX10 : 654.4 PG/ml

Thirty four patients (80.9%) were males with mean plasma chemokine CXCL10 : 837 PG/ml whereas 8 patients (19.1%) were females with mean plasma chemokine CXCL10 : 762 PG/ml

Table (4) & table (5) : relation between demographic data & starting CXCL10.

Table (4) :

	No.	**Percent (%)**	**Starting CXCL10 PG/ml**
Age			
Above 40 years	27	64.2 %	864.1
Below 40 years	15	35.8 %	654.4
Z		4.03	
P		0.013*	
Sex			
Male	34	80.9 %	837
Female	8	19.1 %	762
Z		5.22	
p		0.004*	

Table (5) :

varient	No.	Mean cxcl10 PG/ml	SD	Min.	Max.	t	Sig.
Age							
Above 40	27	864.1	562.5	100	1940	0.98	0.196
Below 40	15	654.4	425.7	59	1136		
Sex							
Male	34	837	625.3	59	1929	1.09	0.101
female	8	662	452.6	179	1433		

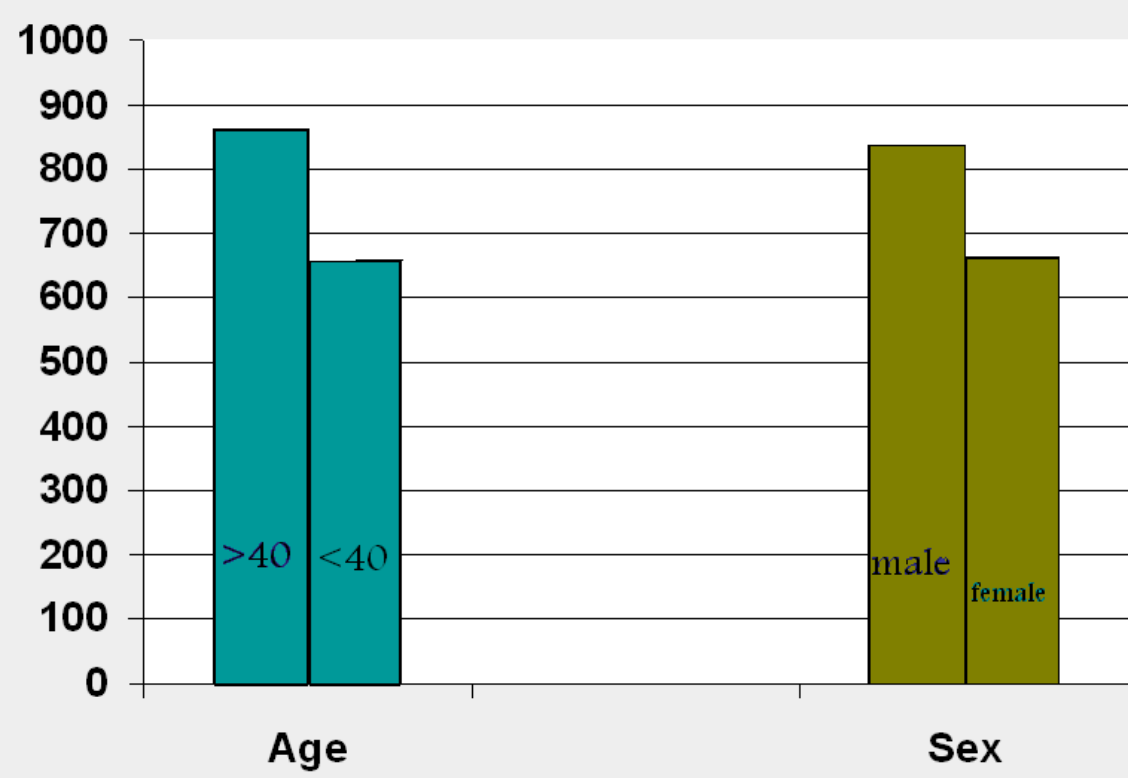


Fig. (5) Age & sex in relation to the level of CXCL10 before starting treatment .

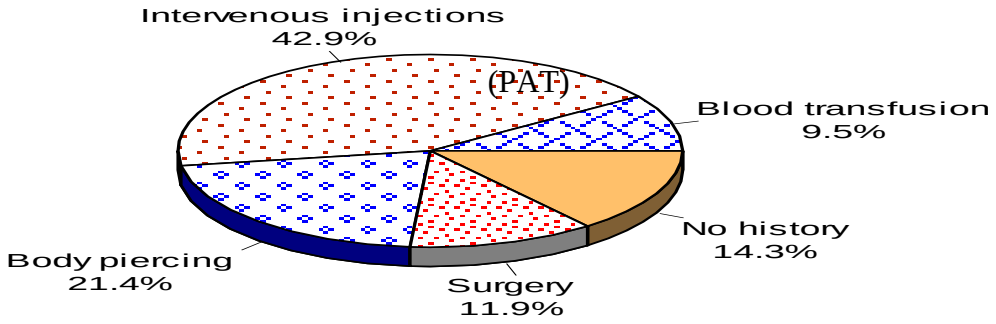
II. Clinical data:

- **Risk of exposure to HCV infection:**

Four patients (9.5%) had history of blood transfusion, 18 patients (42.9%) had history of intravenous drug injections for treatment of bilharziasis, 9 patients (21.4%) has history of body piercing, 5 patients (11.9%) had history of surgery, 6 patients (14.3%) had no history of exposure to HCV, while no one had history of abnormal sexual behavior. (Table 6 and Fig. 6).

Table (6) & Fig (6): Distribution of the studied patients regarding the risk of exposure to HCV infection.

Variable	Number of patients	Percent (%)
Risk of exposure to HCV infection:		
Blood transfusion	4	9.5%
Intervenous injections	18	42.9%
Body piercing	9	21.4%
Surgery	5	11.9%
No history	6	14.3%



- **Clinical findings and the relation of the predictor finding (BMI) to the baseline plasma level of CXCL10 :**

Sign and symptoms:

28 patients (66.7%) were asymptomatic and presented by accidental discovery of abnormally elevated liver enzymes with mean plasma level of cxcl10 554 PG/ml , while 6 patients (14.2%) had history of fatigue with mean plasma level of cxcl10 610 PG/ml and 8 patients (19.1%) had history of abdominal discomfort with mean plasma level of cxcl10 664 PG/ml.

On examination: 11 patients (26.2%) had normal weight (BMI = 20 - < 25 Kg/m^2) with mean plasma level of cxcl10 478.8 PG/ml, 12 patient (28.6 %) had over weight (BMI = 25 - < 30 Kg/ m^2) with mean plasma level of cxcl10 711.4 PG/ml , 17 patient (40.4 %) had obesity (BMI >30 Kg/ m^2) with mean plasma level of cxcl10 758.2 PG/ml , whereas 2 patients (4.8 %) had underweight (BMI < 20 Kg/ m^2) with mean plasma level of cxcl10 815.7 PG/ml , 5 patients (11.9%) had liver stigmata in the form of spider angiomata with mean plasma level of cxcl10 815.7 PG/ml , 32 patient (76.1 %) had normal sized liver with mean plasma level of cxcl10 838.7 PG/ml , 8 patients (19.1 %) had enlarged liver with mean plasma level of cxcl10 838.7 PG/ml whereas 2 patients (4.8 %) had small liver with mean plasma level of cxcl10 847 PG/ml and 40 patients (95.2%) had normal size of spleen with mean plasma level of cxcl10 724.5 PG/ml whereas 2 patients (4.8%) had mild spleenomegally with mean plasma level of cxcl10 1571 PG/ml . table (7)

Table (7): Clinical data of the studied patients group :

Variable	Number of patients	Percent (%)
Symptoms		
-Asymptomatic (elevated liver enzymes)	28	66.7%
-Fatigue	6	14.2%
-Abdominal discomfort	8	19.1%
BMI (Kg \ m2\surface area)		
-Normal **(20-25)**	11	26.2%
-Overweight **(25-30)**	12	28.6%
-Obese (more than 30)	17	40.4 %
-Underweight (less than 20)	2	4.8%
Stigmata of liver disease	5	11.9%
Size of the liver		
-Normal	32	76.1%
-Increased	8	19.1%
-Decreased	2	4.8%
Size of the spleen		
-Normal	40	95.2%
-Enlarged	2	4.8%

Relation between BMI and the baseline plasma level of CXCL10 :

Table (8) show the relation between the BMI and the plasma level of CXCL10 , it was found that there was a significant relation between plasma CXCL10 before treatment and BMI

BMI	No.	Mean cxcl10 PG/ml	SD	Min.	Max.	F	Sig.
Normal	11	478.8	136.8	117	864	12.2	0.035*
Overweight	12	711.4	226.5	179	1940		
Obese	17	758.2	327.6	59	1929		
Underweight	2	815.7	452.6	248	1239		

III-Laboratory data and there relation to the baseline plasma level of chemokine CXCL10 :

a) Liver enzymes (ALT and AST)

Alanine transaminase (ALT) were normal in 26 patients (61.9%), while 9 patients (21.4%) were elevated twice, while the other 7 cases (16.7%) were elevated triple or more (Table 5, Fig. 7).

Aspartate transaminase (AST) were normal in 25 patients (59.5%), wile 12 patients (28.6%) were elevated twice, while the other 5 cases (11.9%) were elevated triple or more (Table 9, Fig. 8).

Table (9): Distribution of the studied patients regarding increase in ALT & AST

Variable	Normal	%	Elevated twice	%	Elevated > 3 times	%	Total No.	%
ALT	26	61.9	9	21.4	7	16.7	42	100
AST	25	59.5	12	28.6	5	11.9	42	100

- **Relation between the plasma CXCL10 levels and liver enzymes:**

The results of plasma levels of CXCL10 in patients studied were compared with the liver enzymes plasma levels and the result were:

Table (10): Relation between levels of ALT & AST and levels of CXCL10 before starting antiviral therapy:

ALT		**N**	**Mean**	**S.D.**	**Min.**	**Max.**	**F**	**Sig.**
CXCL10 before starting treatment	Normal	26	601.1	442.0	59.0	1940.0	0.997	0.378
	Elevated twice	9	830.1	583.6	234.0	1662.0		
	Elevated 3 or more	7	809.7	548.3	434.0	1929.0		
AST		**N**	**Mean**	**S.D.**	**Min.**	**Max.**	**F**	**Sig.**
CXCL10 before starting treatment	Normal	25	629.5	439.7	100.0	1940.0	0.657	0.524
	Elevated twice	12	709.5	546.9	59.0	1662.0		
	Elevated 3 or more	5	903.2	640.7	434.0	1929.0		

Table (10) show the relation between change in ALT and AST and the plasma level of CXCL10 in patient with CHC, it was found that there was no significant relation between CXCL10 before treatment and ALT and AST levels.

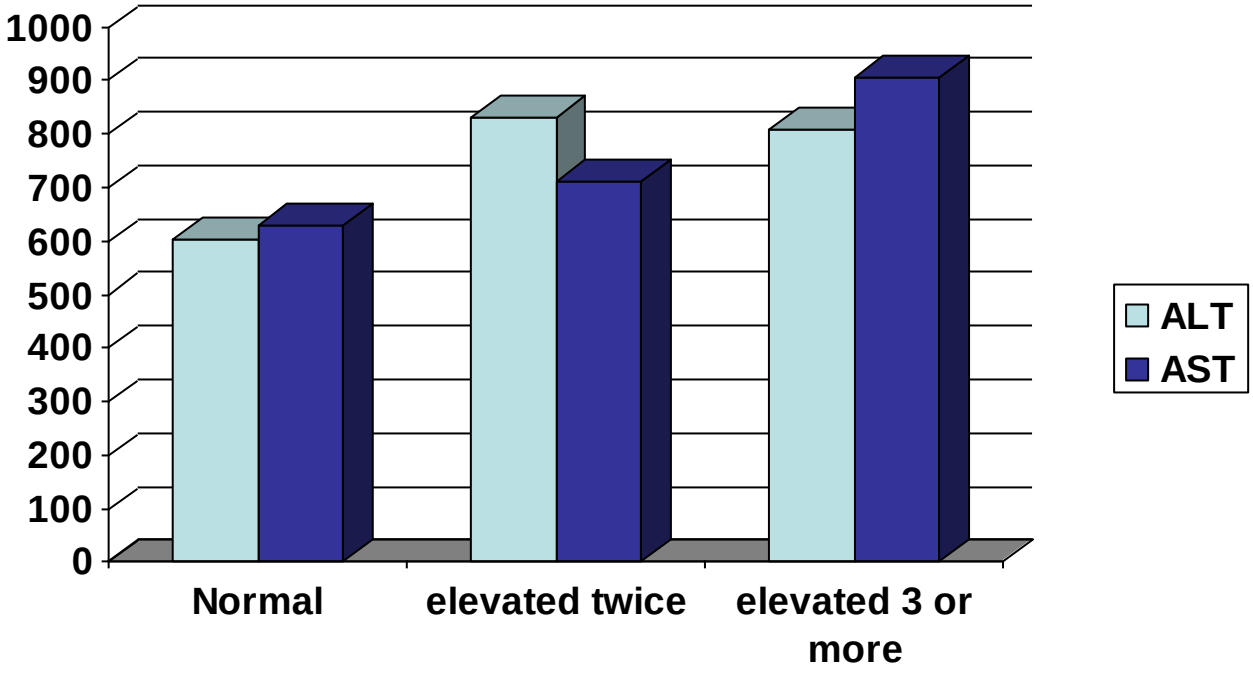


Fig. (7) : relation between levels of ALT&AST and levels of CXCL10 before starting antiviral therapy

b) Viral load and its relation to baseline plasma levels of CXCL10 :

PCR for HCV-RNA quantitative test: 9 patients (21.4%) had viral load more than 800,000 IU/ml with mean plasma level of cxcl10 1137 PG/ml and 33 patients (78.6%) had viral load less than 800,000 IU/ml with mean plasma level of cxcl10 531 PG/ml (Figure 8).

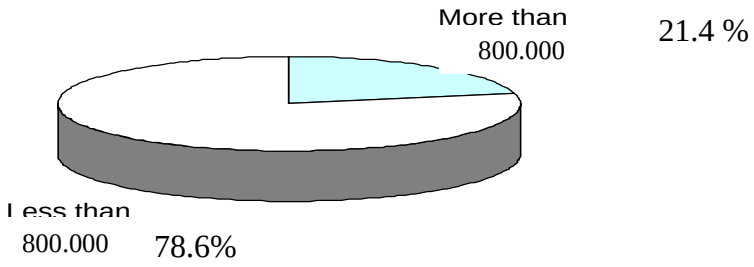


Fig. (8): Viral load in the studied patients group.

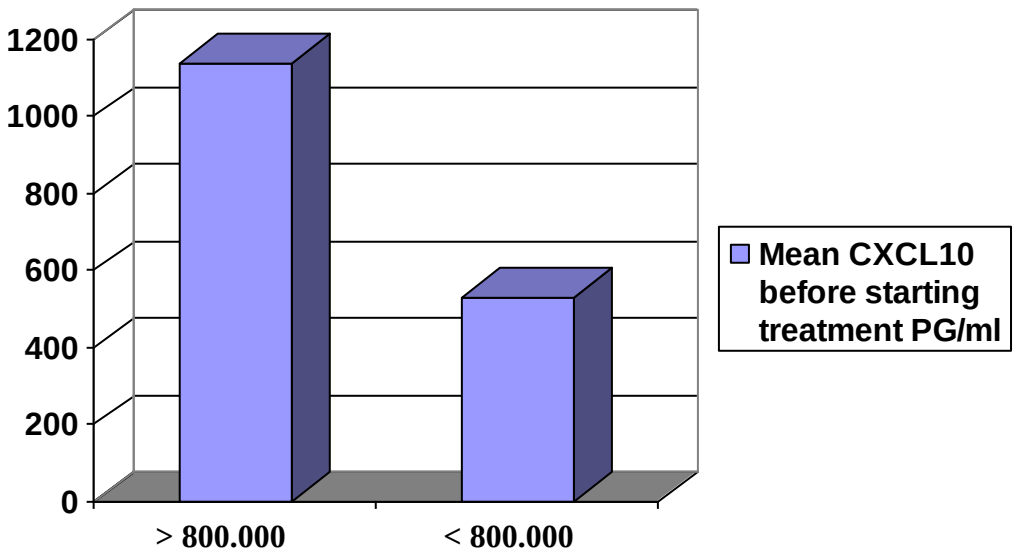


Fig (9) the relation between viral load and plasma cxcl10 before starting treatment . it was found that the elevation of cxcl10 more than 2 folds in patients with viral load > 800,000 IU/ml .

IV-Ultrasonographic data & there relation to the plasma level of CXCL10 before starting treatment

It was found that 16 patients (38.1%) had a normal liver with mean plasma level of cxcl10 643.6 PG/ml , 8 patients (19.1%) had a mild enlarged fatty liver with mean plasma level of cxcl10 838.7 PG/ml , 14 patients (33.3%) had fine periportal fibrosis with mean plasma level of cxcl10 769 PG/ml , 3 patients (7.1%) had early cirrhotic changes with mean plasma level of cxcl10 847 PG/ml and 1 patient (2.4%) had coarse pattern with shrunked liver with mean plasma level of cxcl10 847 PG/ml. Two patients (4.8%) had mild spleenomegally with mean plasma level of cxcl10 1571 PG/ml whereas the rest of patients had normal spleen with mean plasma CXCL10 854.5 PG/ml . **Table (11) .**

Table (11): Ultrasonographic finding of the studied patients.

Variable	Number of patients	Percent (%)	Mean CXCL10 PG/ml
Liver :			
-Normal ultrasonography	16	38.1%	643
-Fatty liver	8	19.1%	838.7
-Peripheral periportal fibrosis	14	33.3%	769
-Early cirrhotic changes	3	7.1%	847
-Coarse pattern with shrunked liver	1	2.4%	847
Spleen :			
-Mild splenomegaly	2	4.8%	1571
- Normal spleen	40	95.2%	854.5

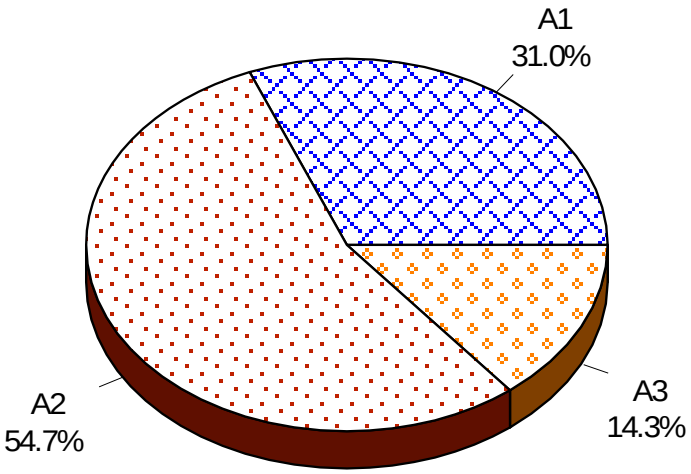
V. Histopathological data and there relation to the plasma level of CXCL10 before starting treatment :

The histopathological diagnosis of 42 liver biopsy specimens from these patients with CHC viral infection according to "METAVIR score" were: ranging from A1 to A3 & from F1 to F3 and non of them had A4 or F4 . the result were :

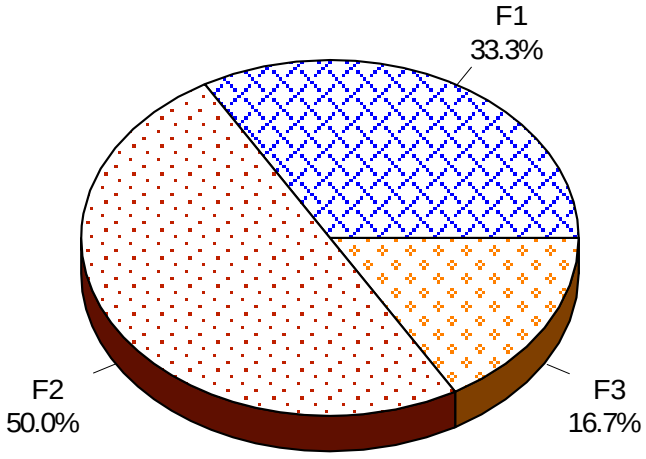
Necroinflammatory changes: 13 patients (31.0%) had A1, 23 patients (54.7%) had A2 and 6 patients (14.3%) had A3; and fibrosis stage were: 14 patients (33.3%) had F1, 21 patients (50%) had F2 and 7 patients (16.7%) had F3 (Table 8 and Fig. 11).

Table (12): Histopathological data of the studied patients.

Variable	Number of patients	Percent (%)
Necroinflammatory changes		
A1	13	31.0
A2	23	54.7
A3	6	14.3
Fibrosis score		
F1	14	33.3
F2	21	50.0
F3	7	16.7



Necroinflammatory changes



Fibrosis score

Fig.(10): Necroinflammatory changes and fibrosis score.

Plasma CXCL10 levels was studied in relation to the histopathological stages in CHC patients:

Among 42 patients studied, it was found that, the plasma CXCL10 levels were higher among patients with higher necroinflammatory stages and fibrosis scores, on liver biopsy.

Table (13): Relation between CXCL10 plasma level and necroinflammtory stages & fibrosis score.

Necro-inflammatory stage	**N**	**CXCL10 (mean) PG/ml**	**S.D.**	**Min.**	**Max.**	**F**	**Sig.**
A1	13	437.5	318.7	59.0	1136.0	3.514	0.040*
A2	23	739.0	502.7	100.0	1940.0		
A3	6	1013.5	434.0	434.0	1929.0		
Fibrosis score	**N**	**CXCL10 (mean) PG/ml**	**S.D.**	**Min.**	**Max.**	**F**	**Sig.**
F1	14	827.1	602.9	175.0	1940.0	1.354	0.270
F2	21	562.9	432.7	59.0	1481.0		
F3	7	766.6	360.9	372.0	1433.0		

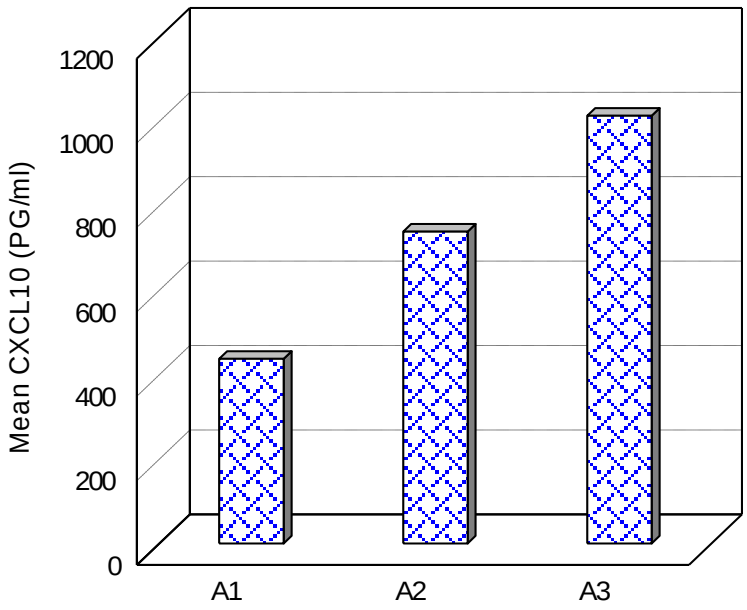


Fig. (11): Plasma CXCL10 before starting treatment in relation to necroinflammatory stages.

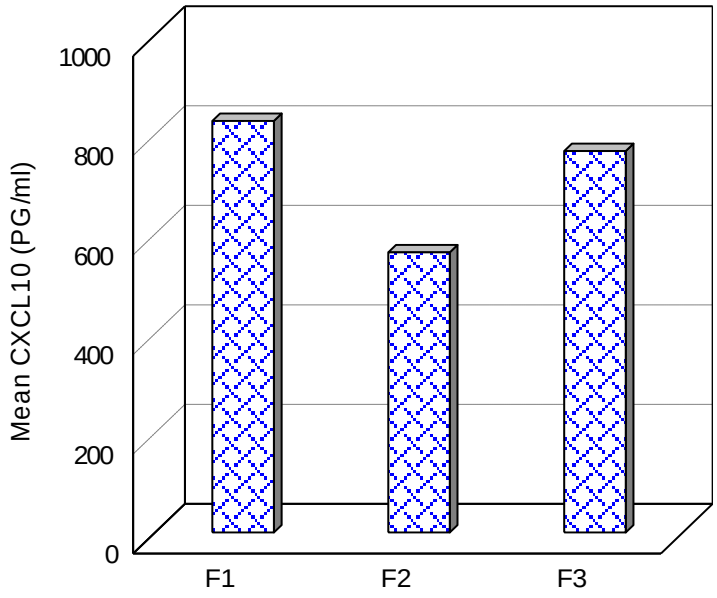


Fig. (12): Plasma CXCL10 before starting treatment in relation to fibrosis score.

VI-Response to treatment:

Viral loads were assessed after 12 weeks of initiation of the antiviral therapy, at 24 weeks during treatment and after 24 weeks of completion of treatment and the results were 31 patients (73.8%) had EVR and 27 patients (64.3%) had SVR and where as 4 patients (9.5%) had relapse (Table 14, Fig. 12).

Table (14): Distribution of the studied patients regarding their response.

	Frequency	Percent %
No response (NR)	11	26.2
Responders :		
(SVR)	27	64.3
Relapse	4	9.5
Total	42	100.0

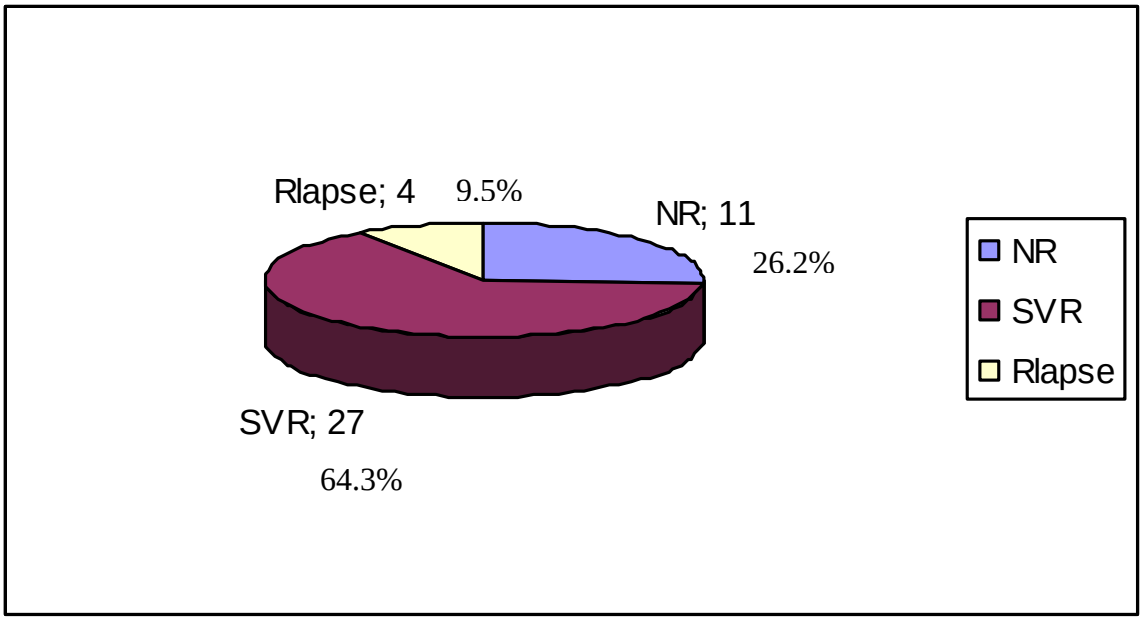


Fig.(13): Distribution of the studied patients regarding their response to anti-viral therapy

Relation between different clinical findings and response :

- **As regard to age & sex**

variable	No.	Non responder (NR)	Percentage (%)
Age			
• **Above 40**	27	8	29.6
• **Below 40**	15	3	20
Sex			
• **Males**	34	9	26.5
• **females**	8	2	25

Table (15) shows patients age above 40 years were 27 , 8 patients (29.6%) were non respondrs while patients below 40 years were 15 with 3 patients (20%) were non respondrs **.**

34 male patients , 9 (26.5%) of them were nonresponders and 8 female patients , 2 (25%) were nonresponders .

- **Relation between age & sex and response :**

Table (16)

Variable		Non responder	Responders	Total
AGE	No.	8	19	27
Age > 40	% within responce	72.7 %	61.2 %	
	No.	3	12	15
Age < 40	% within responce	27.3 %	38.8 %	
Total	No.	11	31	42
	% within responce	100%	100%	
X^2	0.46			
P	0.496			
		NR	Responders	total
Sex	No.	9	25	34
Males	% within responce	81.8%	80.6%	
	No.	2	6	8
Females	% within responce	18.2 %	19.4 %	
Total	No.	11	31	42
	% within responce	100%	100%	
X^2	0.13			
P	0.93			

- **As regard the BMI & response :**

11 patients (26.1 %) had normal weight , all were responder to antiviral therapy , 12 patients (28.5 %) were overweight had 2 patients (16.6 %) non responder , 17 patients (40.4 %) were obese had 6 patients (35.2%) non responder , whereas 2 patients (4.8%) were underweight had 1 patient (50%) non responder .

Table (17): BMI & respons :

BMI		Non responder	Responder	Total
Normal	No.	0	11	11
	% within responce	0 %	33.3 %	26.2%
Overweight	No.	2	10	12
	% within responce	22.2 %	30.3 %	28.5 %
Obese	No.	6	11	17
	% within responce	66.7 %	33.3 %	40.5 %
Underweight	No.	1	1	2
	% within responce	11.1 %	3.1 %	4.8 %
Total	No.	9	33	42
	% within responce	100 %	100%	100%
X^2		6.07		
P		0.108		

Relation between elevation in ALT & AST & Response:

Table 18 and Fig. 24, show the association between increase in ALT&AST and response, it was found that there was a significant association between the patients with elevation in ALT&AST triple or more to be response, the normal value of ALT&AST. ($p < 0.05$).

Table (18): Increase in ALT & AST in relation to response :

Increase in ALT		**Response**		**Total**
		No response	**Responder**	
Normal	No.	9	17	26
	% within Response	81.8%	54.8%	61.9%
Elevated twice	No.	2	7	9
	% within Response	18.2%	22.6%	21.4%
Elevated 3 or more	No.	0	7	7
	% within Response	.0%	22.6%	16.7%
Total	No.	11	31	42
	% within Response	100.0%	100.0%	100.0%
X^2		6.512		
p		.017*		

Increase in AST		**Response**		**Total**
		No response	**Responder**	
Normal	No.	9	16	25
	% within Response	81.8%	51.6%	59.5%
Elevated twice	No.	2	10	12
	% within Response	18.2%	32.3%	28.6%
Elevated 3 or more	No.	0	5	5
	% within Response	.0%	16.1%	11.9%
Total	No.	11	31	42
	% within Response	100.0%	100.0%	100.0%
X^2		4.819		
p		.032*		

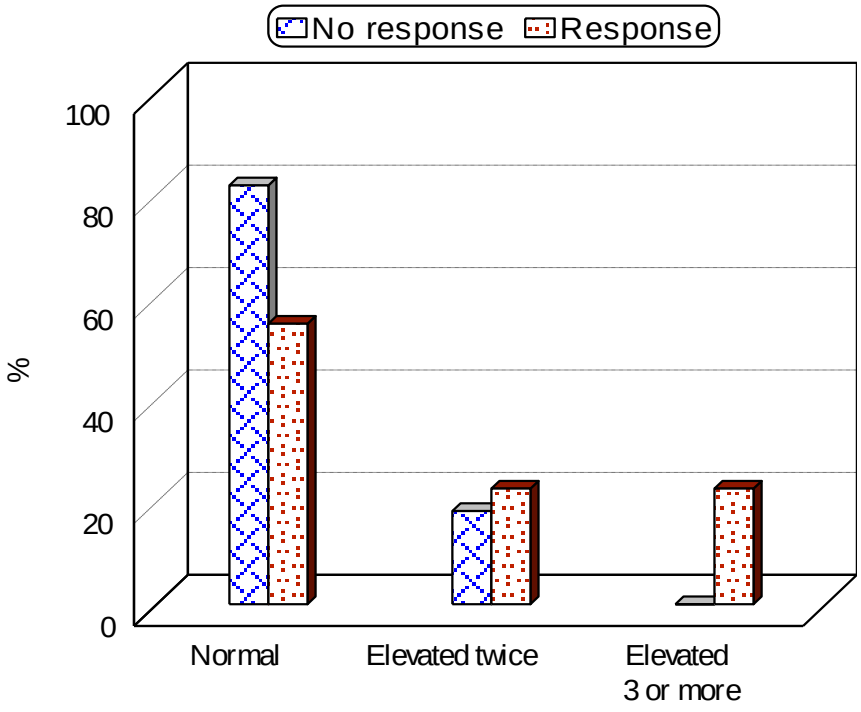


Fig. (14): Increase in ALT&AST in relation to Response

Relation between A stages & F score and response :

Relation between A stage and response:

Table (22), and Fig. (26), shows the relation between response and necroinflammatory changes, it was found that there was a significant relation between the necroinflammatory changes with response, all patients (13 patients) who was stage A1 had SVR, while the non-responder patients were in stage A2 and A3.

Table (19): Necroinflammatory changes in relation to Response

A stage		Response		Total
		No response	Response	
A 1	No.	0	13	13
	% within Response	.0%	41.9%	31.0%
A 2	No.	10	13	23
	% within Response	90.9%	41.9%	54.8%
A 3	No.	1	5	6
	% within Response	9.1%	16.1%	14.3%
Total	No.	11	31	42
	% within Response	100.0%	100.0%	100.0%
X^2		8.450		
p		.015*		

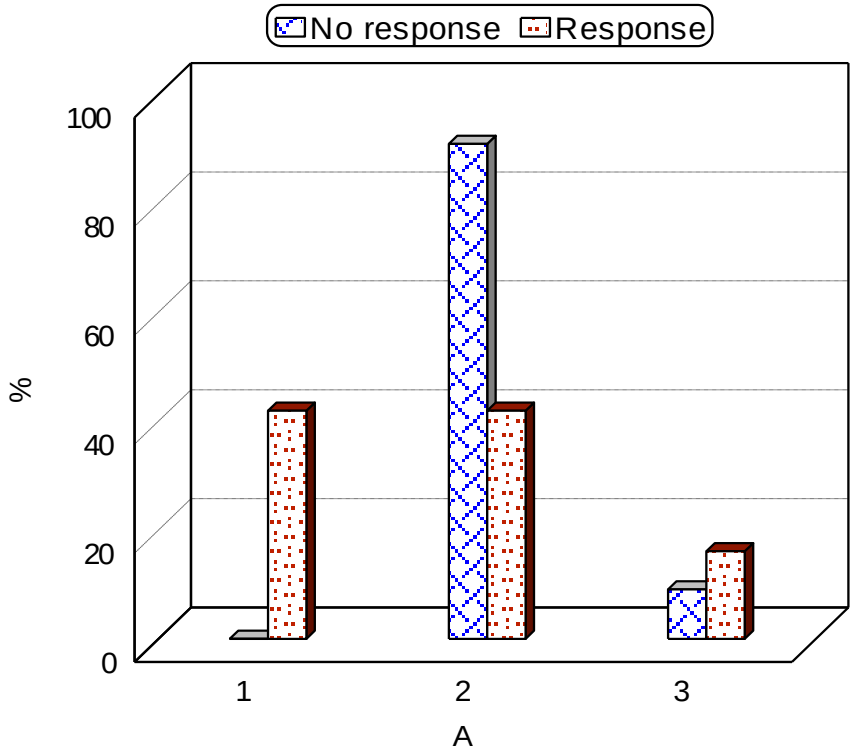


Fig. (15): Necroinflammatory changes in relation to response.

Relation between F score and response:

Table (20) and Fig. (27), shows the relation between stage F and response, it was found that there was no significant relation between the response and F scores.

Table (20): Fibrosis score in relation to response.

F score		Response		
		No response	Response	Total
F 1	No.	5	9	14
	% within Response	45.5%	29.0%	33.3%
F 2	No.	4	17	21
	% within Response	36.4%	54.8%	50.0%
F 3	No.	2	5	7
	% within Response	18.2%	16.1%	16.7%
Total	No.	11	31	42
	% within Response	100.0%	100.0%	100.0%
X^2		1.232		
p		.540		

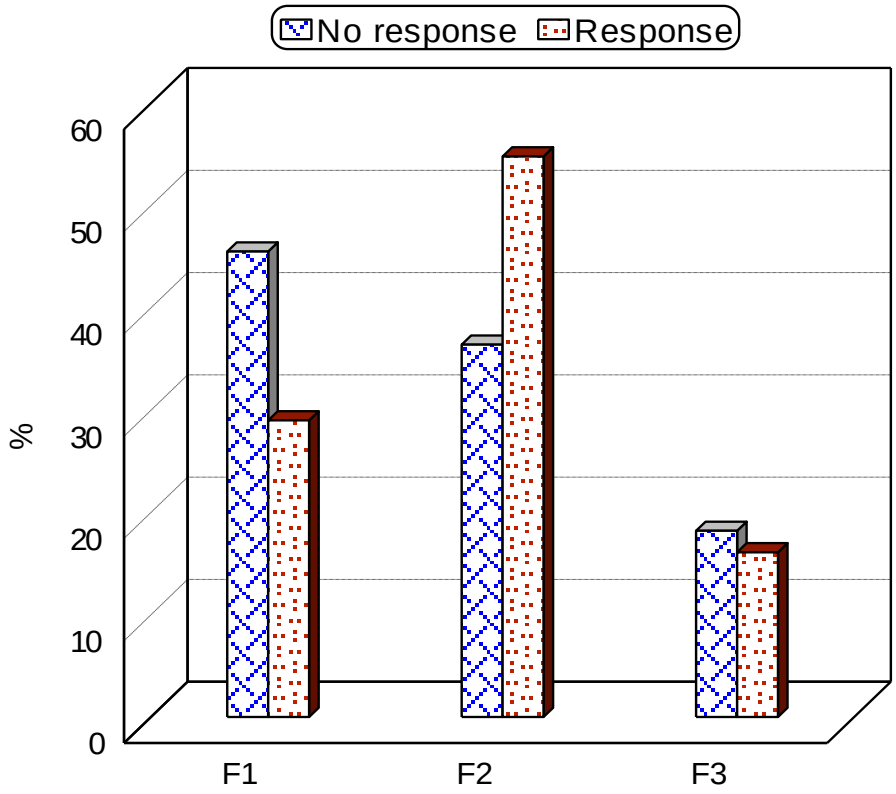


Fig.(16): Fibrosis scores in relation to response.

Relation between response and level of PCR before treatment:

Table (21), shows the level of PCR before treatment in responder and non responder patients. The level of PCR in non-responders was 689541.54±665750.31 IU/ml, while in response patients the level of PCR was significantly lower 367602.22 ±436072.07 IU/ml. So, there was a significant decrease in PCR level in response patients than the non response. (Fig. 17).

Table (21): Comparison between response and level of PCR before treatment.

	Non-responders	**Responders (EVR and SVR)**
Min.	71000.00	267.00
Max.	2200000	1800000
Mean	689541.54	367602.22
S.D.	665750.31	436072.07
T	**3.321**	
p	**0.076**	

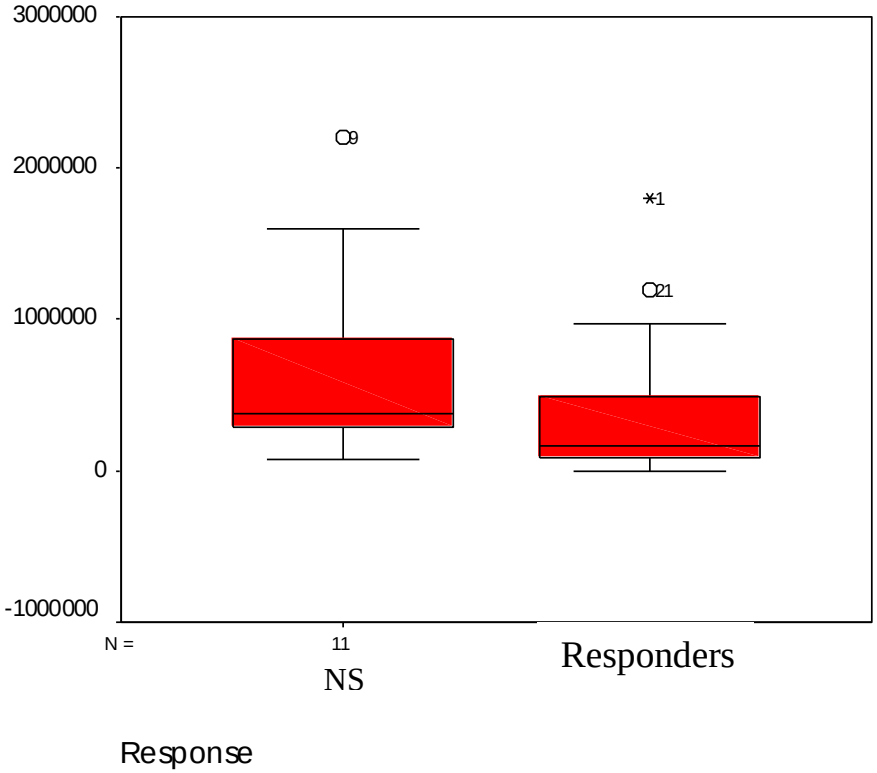


Fig. (17): The level PCR before treatment in relation to response.

ROC Curve to detect the cut off value of PCR before treatment and sensitivity and specificity:

The ROC curve to detect the cut off value of PCR level before treatment in prediction the response of the patients shows the area under the curve was 0.74, and the estimated cut of value was 225000 with a sensitivity 81.8% and specificity 78.1%.

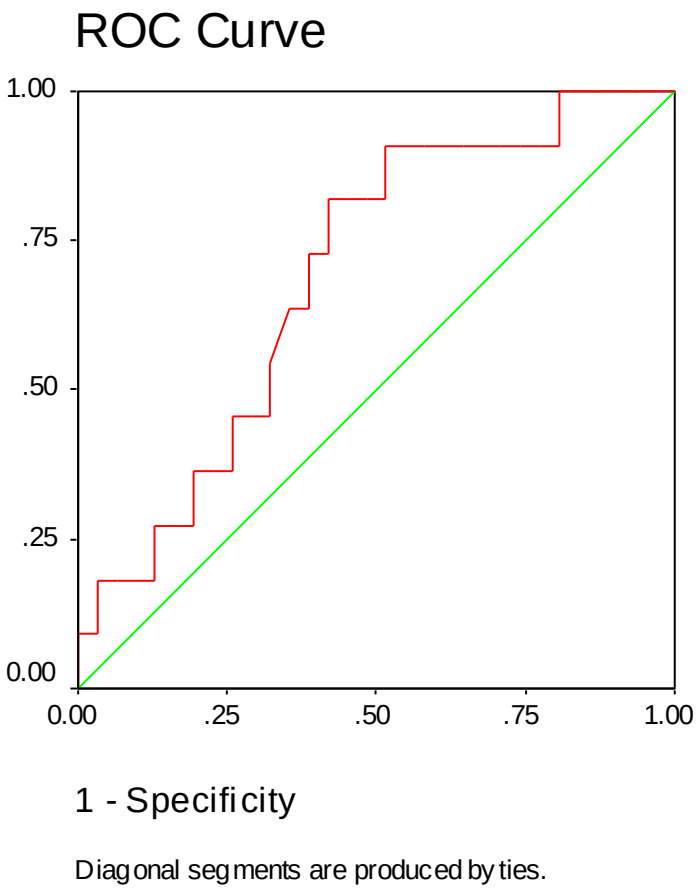


Fig. (18): ROC Curve to detect the cut off value of PCR before treatment and sensitivity and specificity.

Area Under the Curve

Table (22): Test Result Variable(s): PCR before

Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.74	.087	.063	.520	.861

Coordinates of the Curve

Table (23): Test Result Variable(s): PCR before

Positive if Greater Than or Equal To	Sensitivity	1 - Specificity
225000.0000	.818	.219

VII-Chemokine CXCL10 (IP10) plasma levels

Table (24), Fig. (19), show the plasma levels of CXCL10 (IP10) in healthy control group and in patients with CHC viral infection one week before starting antiviral therapy (PEG-IFNα-2a/Ribavirin) and sustained virological response (SVR) group.

In control group it was found that the plasma level of CXCL10 was ranged from 39-589 PG/ml with mean of 222.5±150.2 PG/ml, while in patients with CHC not currently on antiviral therapy, the plasma level of CXCL10 was ranged from 59-1940 PG/ml with mean of 684.93±491.25, and in patients who had already achieved an SVR, the plasma levels of CXCL10 was ranged from 65-918 PG/ml with mean of 318.79±252.78 PG/ml on comparing the data of the patients before starting antiviral treatment (n=42) with healthy control group (n=15) and patients with SVR (n=27), we found that there was a significant increase in CXCL10 in patients with CHC viral infection before start of antiviral therapy compared with either control subjects or sustained responders ($P< 0.05$).

Table (24): CXCL level in control and in patients before and after 24 weeks of treatment:

	Healthy (control)	**CHC viral infected**	**SVR (after 24 weeks of treatment)**
Range	39 – 589 PG/ml	59 – 1940 PG/ml	65 – 918 PG/ml
Mean	222.5 PG/ml	684.93 PG/ml	318.79 PG/ml
S.D.	150.2	491.25	252.78
U		3.65	1.88
p		0.013*	0.071

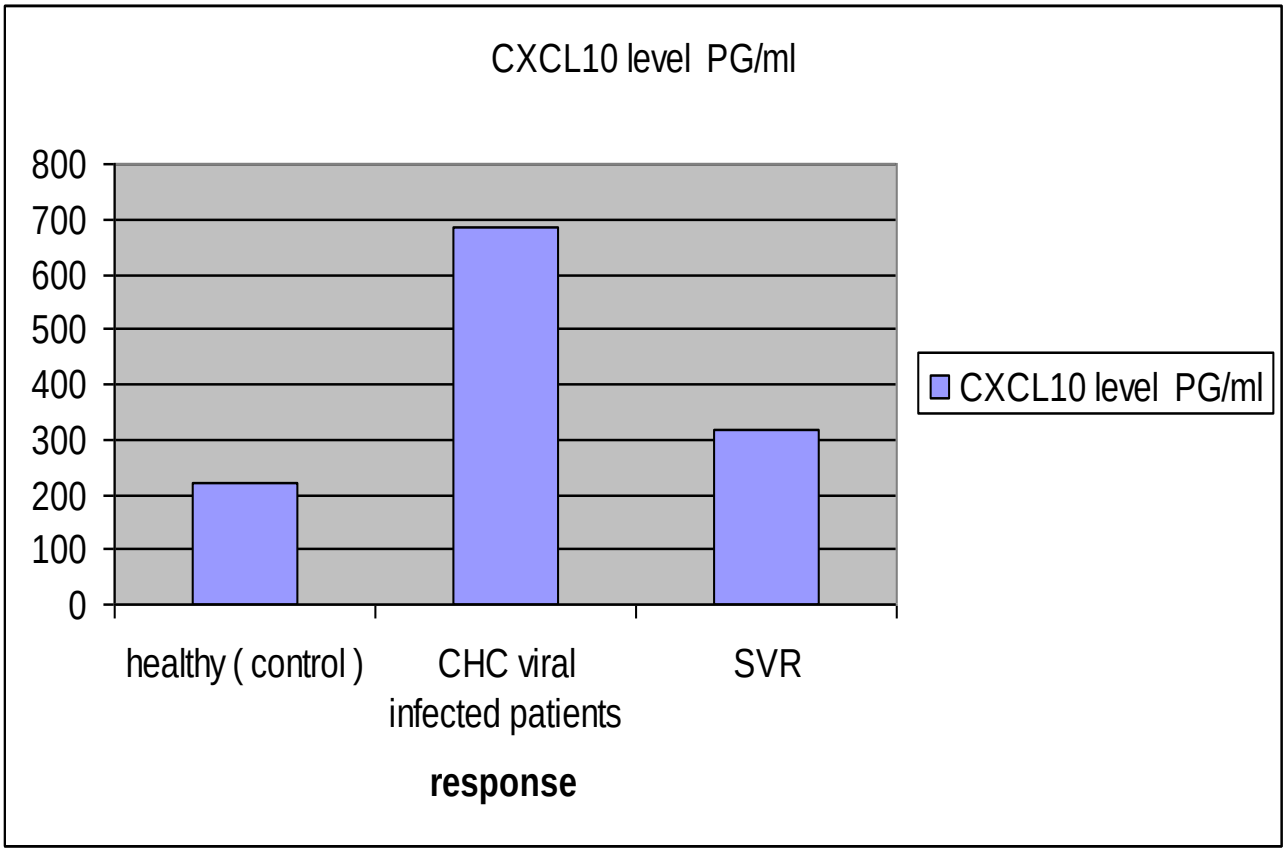


Fig. (19): CXCL10 levels in control and in patients before start of treatment and in patients with SVR.

Furthermore, the plasma CXCL10 levels declined in samples collected 6 months after completion of the antiviral therapy in patients who achieved sustained control of HCV infection (Fig. 20)

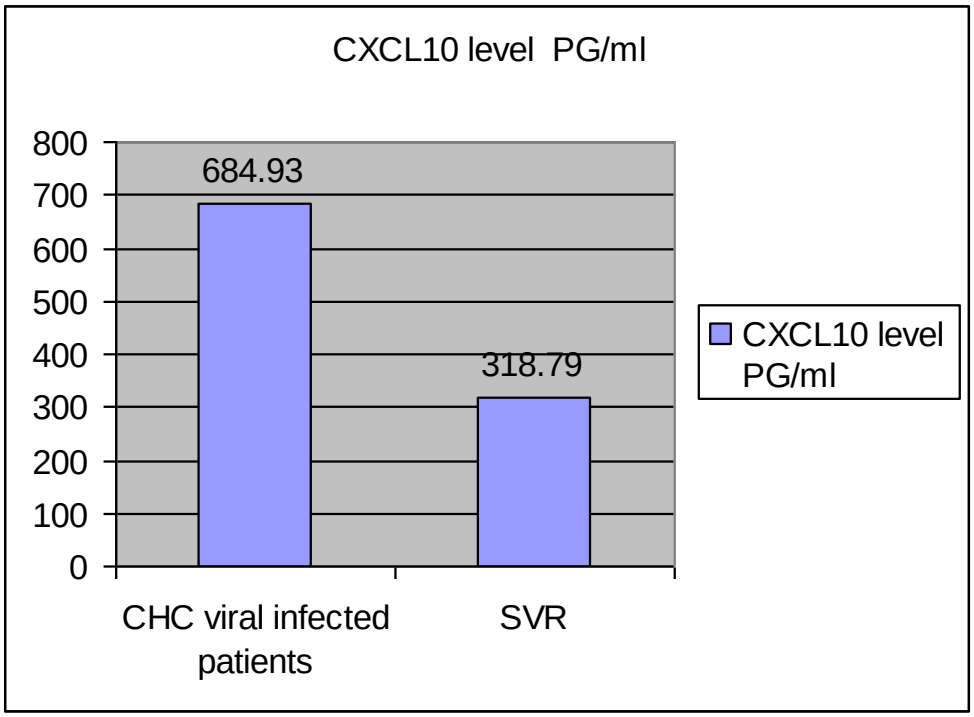


Fig. (20): Comparing the plasma level of CXCL10 in CHC patients before starting treatment and in there who achieved SVR after completion of treatment.

On comparing the baseline plasma levels of CXCL10 (one week before starting treatment in CHC patients who were complete non-responders (n=11) to that in patients who achieved SVR (n=27).

It was found that the baseline plasma levels of CXCL10 in non-responders was ranged from 692-1940 PG/ml with mean of 1131.4±404.01 PG/ml and the baseline CXCL10 in patients who subsequently achieved SVR was ranged from 65-918 PG/ml with mean of 318.79±252.78 PG/ml. So, the baseline plasma CXCL10 levels were lower in those patients who subsequently achieved an SVR. (Fig. 21).

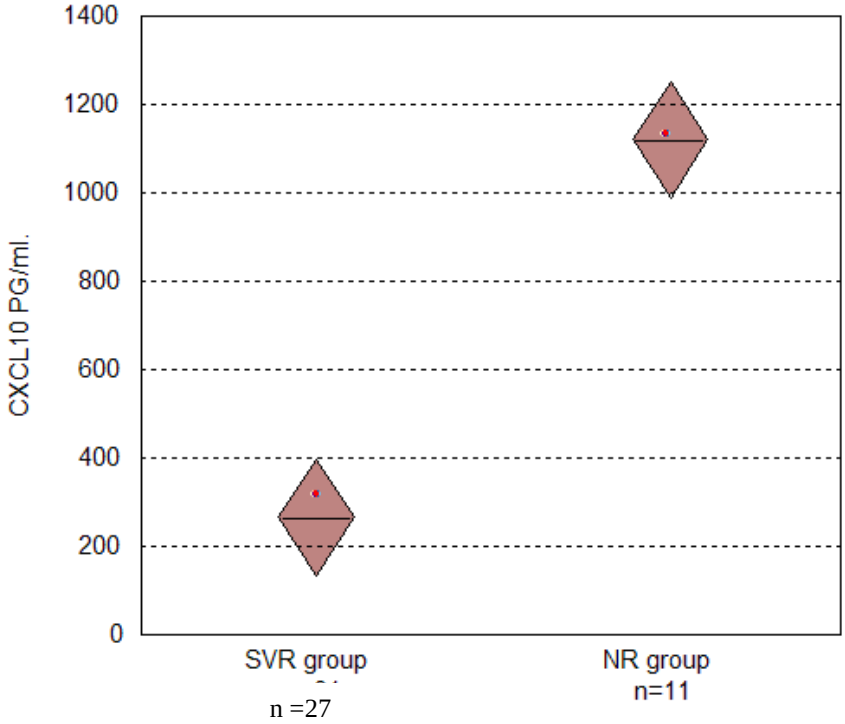


Fig. (21): Comparing the baseline plasma levels of CXCL10 in CHC patients who achieved SVR and in those who were complete non-responders.