Results

The study was conducted on 380 patients, 287 males (75.5 %of patient population) and 93 female (24.5%). Responders were 306 out of 380 patients (80.5%) while 74 patients (19.5%) failed to achieve response. (Table 5)

15 patients were diabetics (3.9 %) while the remaining 365 cases showed no history of diabetes or blood glucose level abnormalities (fasting blood Sugar below 115 mg/dl). (Table 8)

Ultrasound examination revealed that none of patients had ascites,197 (51.84%) had hepatomegaly and 69(18.1%) had splenomegaly.(Table 9)

The histopathological examination done for all 380 liver biopsies according to Metavir score and it revealed the following: (Table 12)

Necroinflammatory activity:

Grade A1 (mild activity) was detected in 171 patients (47.1 %) while grades A2-A3 (moderate and sever activity) were detected in 201 patients (52.9 %).

Stage of fibrosis:

Stages F1-F2 were detected in 259 patients (68.2%) while stages F3-F4 were detected in 121 patients (31.8%). The mean viral load was 469,250 IU/ml while the lowest detected viral load was 900 IU/ml and the maximum viral load was 7,600,000 IU/ml. 325 (85.5%) patients had low and moderate viraemia (PCR < 1 million IU/ml) while 55 (14.5%) patients had high viremia (PCR > 1 million IU/ml).

Table (1): Descriptive data of all studied variables.

	N	Mean	Std. Deviation	Minimum	Maximum
Age (years)	380	42.31	9.53	18.00	60.00
BMI (kg/m^2)	380	26.63	4.19	19.35	36.87
AST (IU/L)	380	55.58	40.64	10.00	254.00
ALT (IU/L)	380	57.94	41.56	10.00	265.00
Total bilirubin (mg/dl)	380	0.84	0.33	0.40	1.60
Alkaline phosphatase (IU/L)	380	82.67	35.63	13.00	185.00
WBCs	380	6499.96	1684.14	3500.00	11350.00
HB (gm/dl)	380	14.25	1.40	12.00	16.80
Platelets	380	197.23	64.14	100.00	410.00
AFP (ng/L)	380	10.34	12.75	0.40	76.30
Albumin (gm/dl)	380	4.13	0.47	3.50	5.00
PCR (IU/ml)	380	671416	101611	900	7600000

Baseline demographic & anthropometric data (Tables 1,2,3 & 4)

Table (2): Gender distribution in the studied patients.

Sex	Frequency	%
Male	**287**	**75.5**
Female	**93**	**24.5**
Total	**380**	**100.0**

Table(3): Age distribution of the studied patients

Age	Number	Percentage
≤ 40 year	188	49.5 %
> 40 year	192	50.5 %
Total	380	100 %

Table (4): Body Mass Index (BMI) of the studied group

BMI	Number	Percentage
BMI < 30 ($kg/m^{2)}$	294	77.4
BMI ≥ 30 ($kg/m^{2)}$	86	22.6
Total	380	100%

The mean age was 42.31 ± 9.53 years in the range of 18-60 years. Females represented 24.5% (93 patients) of the total number of studied subjects and males represented 75.5 (287 patients.). The mean body mass index was 26.63 ± 4.19 Kg/m^2. The maximum BMI was 36.87 kg/m^2 and the minimum was 19.35 kg/m^2. Patients were classified according BMI into patients with BMI< 30 kg/m^2 (294 cases) and patients with BMI: ≥ 30 kg/m^2 (86 cases).

Table (5): EVR in studied patients

Response	Number	Percentage
EVR	306	80.5 %
Non EVR	74	19.5%
Total	380	100 %

Table (6): Frequency of all studied variables.

Studied variables	Total N. (380)	*Early virological response*			
		Responder (N=306)		Non responder (N=74)	
		No	%	No	%
Gender :					
- Male	(287)	232	80.8	55	19.2
- Fmale	(93)	74	79.6	19	20.4
Age group:					
- > 40 years	(192)	153	79.7	39	20.3
- ≤ 40 years	(188)	153	81.4	35	18.6
BMI ($kg/m^{2)}$ **:**					
- < 30	(294)	246	83.7	48	16.3
- ≥ 30	(86)	60	69.8	26	30.2
Type of interferon:					
- AlF a 2 a	(202)	164	81.2	38	18.8
- AlF a 2 b	(178)	142	79.8	36	20.2
Activity					
- A1	(179)	144	80.4	35	19.6
- A2 - A3	(201)	162	80.6	39	19.4
Fibrosis					
- F1 - F2	(259)	219	84.6	40	15.4
- F3 - F4	(121)	87	71.9	34	28.1
Hepatomegally in US					
- Yes	(197)	158	80.2	39	19.8
- No	(183)	148	80.9	35	19.1
Splenomegally in US					
- Yes	(69)	52	75.4	17	24.6
- No	(311)	254	81.7	57	18.3
Diabetes					
- Negative	(365)	299	81.9	66	18.1
- Positive	(15)	7	46.7	8	53.3

Table (6) (Continued): Frequency of all studied variables.

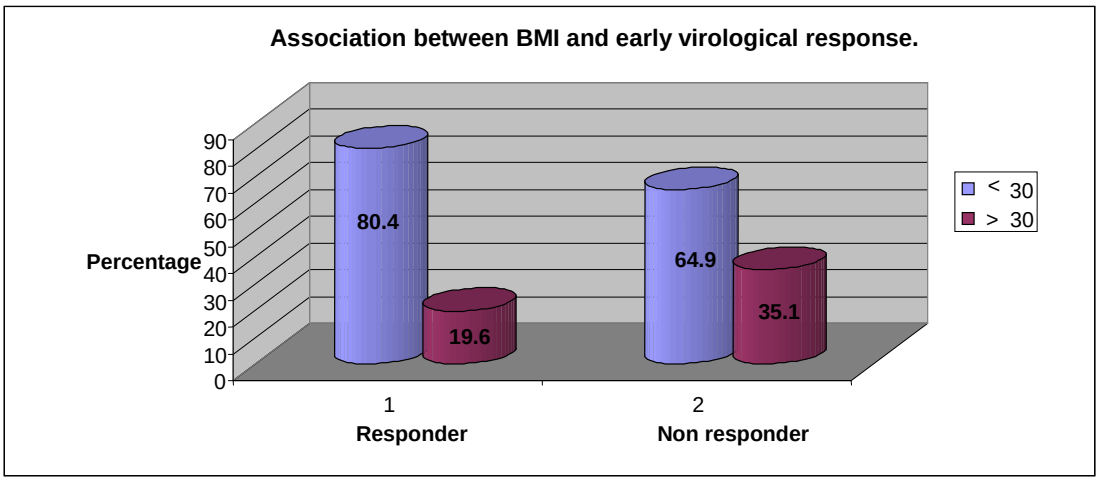
Studied variables	Total N. (380)	*Early virological response*			
		Responder (N=306)		Non responder (N=74)	
		No	%	No	%
AST:					
- ≤ 3 fold ULN	(353)	284	80.5	69	19.5
- > 3 foldULN	(27)	22	81.5	5	18.5
ALT:					
- ≤ 3 fold increase	(354)	285	80.5	69	19.5
- > 3 fold increase	(26)	21	80.8	5	19.2
Alkaline phosphatase:					
- ≤ ULN	(359)	289	80.5	70	19.5
- > ULN	(21)	17	81.0	4	19.0
Total bilirubin:					
- ≤ ULN	(317)	255	80.4	62	19.6
- > ULN	(63)	51	81.0	12	19.0
Albumin (g/dl) **:**					
- ≥ 4	(209)	169	80.9	40	19.1
- < 4	(171)	137	80.1	34	19.9
PCR (IU/ml)**:**					
- > 10^6	(55)	35	63.6	20	36.4
- < 10^6	(325)	271	83.4	54	16.6
AFP (ng/ml):					
- < 5	(159)	137	86.2	22	13.8
- 5 – 10	(106)	88	83.0	18	17.0
- > 10	(115)	81	70.4	34	29.6

The relation between baseline : Age, gender, BMI, diabetes milletus, abdominal ultrasound finding (hepatomegaly & splenomegaly), liver profile (serum AST, ALT, total bilirubin, albumin, alkaline hosphatase), HCV viral load, type of pegylated interferon, liver histopathological state (activity grade & firosis stage), α-feto protein & CBC parameters (HB, WBCS, Platelet), and early virological response were studied in all patients.

Table (7): Study the relation between early virological response and (gender , age & BMI)

Studied variables	Total N (380)	*Early virological response*				X^2 test	p- value
		Responder (N=306)		Non responder (N=74)			
		No	%	No	%		
Gender :							
- Male	(287)	232	75.8	55	74.3	0.07	>0.05
- Female	(93)	74	24.2	19	25.7		
Age group:							
- > 40 years	(192)	153	50.0	39	52.7	0.17	> 0.05
- ≤ 40 years	(188)	153	50.0	35	47.3		
BMI (kg/m^2)**:**							
- < 30	(294)	246	80.4	48	64.9	8.2	< 0.01**
- ≥ 30	(86)	60	19.6	26	35.1		

Figure (1): Study the relation between BMI and EVR



As shown in the above table, Male represented 75.8% of responders and 74.3% of non responders (6/28), Compared to female the difference was not statistically significant (P> 0.05).

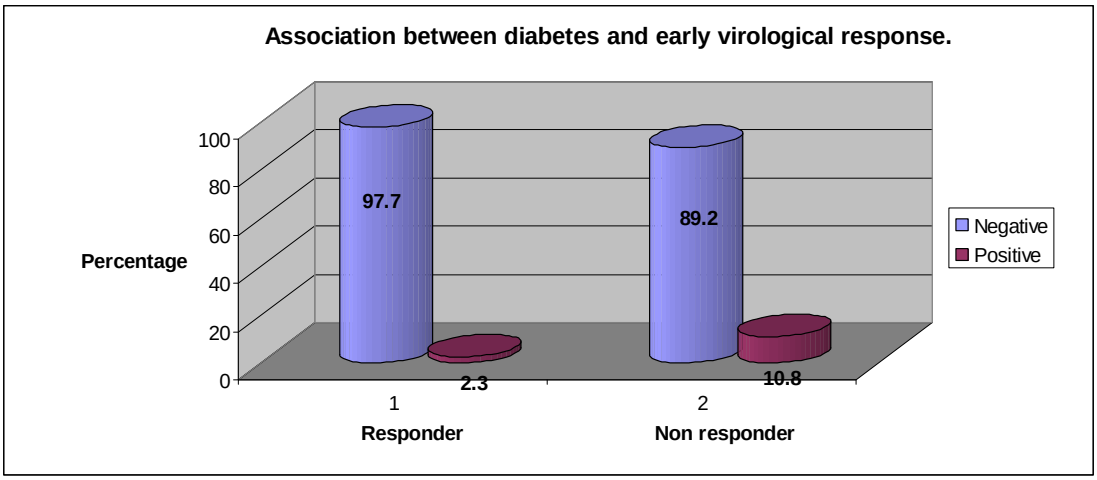
Patients with age > 40 years represented 50 % of responders and 52% of non responders, compared to patients with age ≤ 40 years the difference was not statistically significant (P> 0.05).

There was statistical high significant difference (P< 0.01) between EVR in patients with BMI ≥ 30 kg/ m^2 and EVR in patients with BMI < 30 kg/ m^2. (Table 7 and Figure 1)

Table (8): Study the relation between EVR & DM

Studied variables	Total N (380)	*Early virological response*				X^2 test	p- value
		Responder (N=232)		Non responder (N=74)			
		No	%	No	%		
Diabetes:						Fisher exact test: 9.28	< 0.01**
- Negative	(365)	299	97.7	66	89.2		
- positive	(15)	7	2.3	8	10.8		

Figure (2): Study the relation between between EVR & DM



Diabetic patient represented 2.3% of responder and 10.8% of non responders, compared to non diabetic patients The difference was statistically highy significant (P< **0.01**). (Table 8 and Figure 2)

Table (9): Study the relation between early virological response & Ultrasound finding

Studied variables	Total N (380)	*Early virological response*				X^2 test	p- value
		Responder (N=306)		Non responder (N=74)			
		No	%	No	%		
Hepatomegaly in US							
- YES	(197)	158	51.6	39	52.7	0.03	> 0.05
- NO	(183)	148	48.4	35	47.3		
Splenomegally in US							
- Yes	(69)	52	17.0	17	23.0	1.43	> 0.05
- NO	(311)	254	83.0	57	77.0		

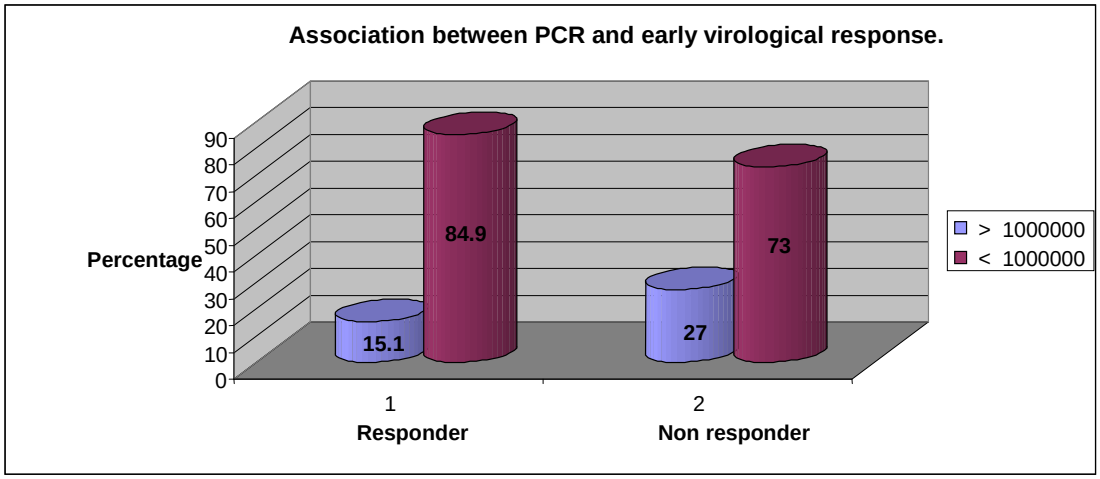
Ultrasound examination show no ascites in all patients. The presence of sonographic detected hepatomegaly was higher in non responders (**52.7**%) than responders (51.6%). The difference was not statistically significant (p > 0.05).

Sonographic detected splenomegaly was higher in non responders (23%) than responders (17%).Also, the difference was not statistically significant (p > 0.05). (Table 9)

Table (10): the relation between EVR and baseline Viral Load

Studied variables	Total N (380)	*Early virological response*				X^2 test	p- value
		Responder (N=306)		Non responder (N=74)			
		No	%	No	%		
PCR (IU/ml):							
- > **1 million**	(55)	35	15.1	20	27.0	11.7	< 0.01**
- < **1 million**	(325)	271	84.9	54	73.0		

Figure (3): the relation between EVR & baseline Viral Load



To study the effect of pretreatment viral load on EVR, patients were classified according to their level of viremia into patients with low and moderate viremia (PCR < 1 million IU/ml) and high viral load patients (PCR > 1million IU/ml). As shown in (Table 10 & Figure 3) , there was statistically significant difference in response to treatment regarding pretreatment viral load.

Table (11): The relation between EVR and liver biochemical profile.

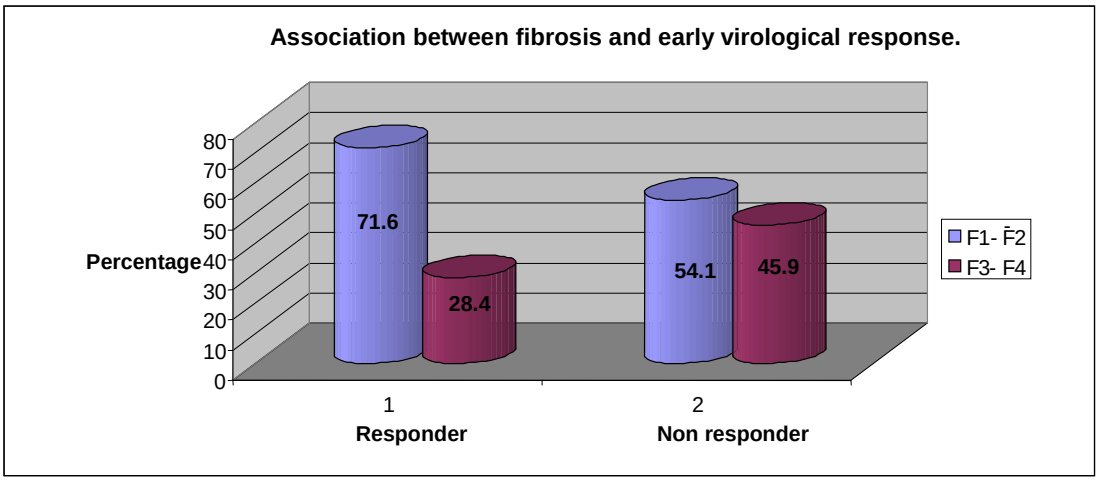
Studied variables	Total N (380)	*Early virological response*				X^2 test	p- value
		Responder (N=306)		Non responder (N=74)			
		No	%	No	%		
AST:							
- ≤ 3 fold ULN	(353)	284	92.8	69	93.2	0.02	> 0.05
- > 3 fold ULN	(27)	22	7.2	5	6.8		
ALT:							
- ≤ 3 fold ULN	(354)	285	93.1	69	93.2	0.001	> 0.05
- > 3 fold ULN	(26)	21	6.9	5	6.8		
Alkaline phosphatase:							
- ≤ ULN	(359)	289	94.4	70	94.6	0.003	> 0.05
- > ULN	(21)	17	5.6	4	5.4		
Total bilirubin:							
- ≤ ULN	(317)	255	83.3	62	83.8	0.009	> 0.05
- > ULN	(63)	51	16.7	12	16.2		
Albumin:							
- ≥ 4 gm/dl	(209)	169	55.2	40	54.1	0.03	> 0.05
- < 4 gm/dl	(171)	137	44.8	34	45.9		

The above table showed that there was no statistically significant difference in any of liver biochemical profile between patients with absent or present EVR ($p > 0.05$).

Table (12): Relation between EVR and liver histopathological state (activity grade & fibrosis stage) according to METAVIR score.

Studied variables	Total N (380)	*Early virological response*				X^2 test	p- value
		Responder (N=306)		Non responder (N=74)			
		No	%	No	%		
Activity grade							
- A1	(179)	144	47.1	35	47.3	0.001	> 0.05
- A2 - A3	(201)	162	52.9	39	52.7		
Fibrosis stage							
- F1 - F2	(259)	219	71.6	40	54.1	8.42	< 0.01**
- F3 - F4	(121)	87	28.4	34	45.9		

Figure (4): Relation between stage of fibrosis and SVR.



The above table and figure studied the relation between EVR and fibrosis stages. There was highly significant difference in EVR as regarding fibrosis stages(P < **0.01**). Fibrotic stages F1-F2 represented 71.6% of responders while fibrotic stages F3-F4 represented 28.4% of responders.

There was was no statistically significant difference in EVR as regarding activity grades in liver biopsy (p > 0.05).

Table (13): Relation between type of pegylated interferon and EVR.

Studied variables		***Early virological response***				**X^2 test**	**p- value**
	Total N (380)	**Responder (N=306)**		**Non responder (N=74)**			
		No	**%**	**No**	**%**		
Type of interferon:							
- Alfa 2 a	**(202)**	164	53.6	38	51.4	0.12	> 0.05
- Alfa 2 b	**(178)**	142	46.4	36	48.6		

Pegylated interferon alfa 2a represented 53.6% of responders and 51.4% of nonresponders, compared to Pegylated interferon alfa 2b the difference was not statistically significant (P> 0.05).

Table (14): Relation between EVR and CBC parameters .

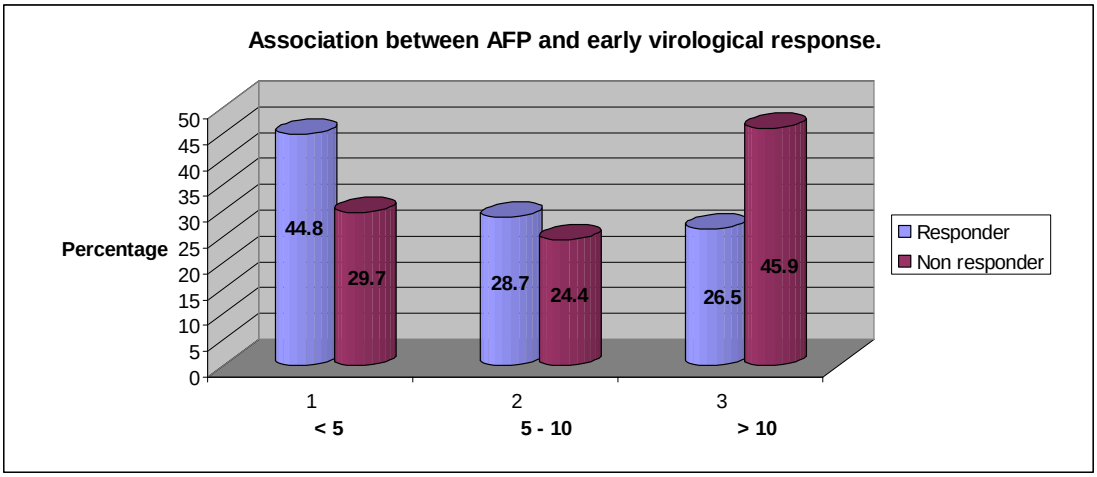
Studied variables	Early virological response	N	Mean ± SD	t- test	p- value
WBCs	**Responder**	306	6495.00±1643.01	0.12	> 0.05
	Non responder	74	6520.49±1856.46		
HB	**Responder**	306	14.25±1.41	0.12	> 0.05
	Non responder	74	14.23±1.39		
Platelets	**Responder**	306	195.75±65.29	0.92	> 0.05
	Non responder	74	203.38±59.11		

The above table showed that there was no statistically significant difference in any of CBC parameters and TSH between patients with absent or present SVR ($p > 0.05$)

Table (15): Relation between AFP and EVR.

Studied variables		***Early virological response***				**X^2 test**	**p- value**
	Total N (380)	**Responder (N=306)**		**Non responder (N=74)**			
		No	**%**	**No**	**%**		
AFP (ng/ml) **:**							
- < 5	**(**159**)**	137	44.8	22	29.7		
- 5 – 10	**(**106**)**	88	28.7	18	24.4	11.11	< 0.01**
- > 10	**(**115**)**	81	26.5	34	45.9		

Figure (5): Relation between AFP and EVR.



(Table 15 and figure 5) showed that there was significant difference between early virological responders and non responders as regarding baseline serum AFP ($p < 0.01$).

44.8% of responders had serum AFP < 5 ng/ml, 28.7% of responders had serum AFP between 5-10 ng/ml (10 ng/ml was the upper limit of normal according to the kit used) while 26.5% of responders had alfa feto protein >10ng/ml .

Significantly, patients who achieved EVR had serum AFP readings less than those who did not achieve response.

Predictive variables at baseline associated with EVR

Table (16): Univariate logistic regression model of factors associated with EVR

Studied variables	Early response to interferon B0= - 1.4 R square = 0.35			
	β1	SE	OR	p-value
Gender: - Male - Female	- 0.16	0.37	0.85	> 0.05
Age group: - > 40 years - ≤ 40 years	0.26	0.45	1.29	> 0.05
BMI: - < 30 - ≥ 30	1.25	0.33	0.75	< 0.01**
Type of interferon: - Alpha 2 a - Alpha 2 b	- 0.79	0.52	0.45	> 0.05
Activity: - A1 - A2 - A3	- .19	0.24	0.3	> 0.05
Fibrosis: - F1 - F2 - F3 - F4	1.22	0.24	3.38	< 0.01**
Hepatomegally in US: - Yes - No	- 0.27	0.43	0.76	> 0.05
Splenomegally in US: - Yes - No	-0.71	0.45	0.49	>0.05
Diabetes: - Negative - Positive	2.18	0.61	8.84	< 0.01**
AST: - ≤ 3 fold ULN - > 3 fold ULN	0.44	2.48	1.55	> 0.05
ALT: - ≤ 3 fold ULN - > 3 fold ULN	- 0.73	2.49	0.77	> 0.05
Alkaline phosphatase: - ≤ ULN - > ULN	- 0.09	0.65	1.09	> 0.05
Total bilirubin: - ≤ ULN - > ULN	0.23	0.41	1.26	> 0.05
Albumin: - ≥ 4 - < 4	0.23	0.33	1.26	> 0.05
PCR: - < 10^6 - > 10^6	-1.14	0.38	0.32	< 0.01**
AFP: - < 5 - 5 – 10 - > 10	0.57	0.19	1.76	< 0.01**

Table (17): Multivariate logistic regression model of factors associated with EVR

Studied variables	Early response to interferon R square = 0.18					
	β0	**β1**	**SE**	**OR**	**CI**	**p-value**
BMI **- > 30** **- ≤ 30**	**- 1.59**	**0.88**	**0.3**	**2.42**	**(1.34 – 4.38)**	**< 0.01****
Fibrosis **- F3 - F4** **- F0 - F2**		**0.63**	**0.29**	**1.88**	**(1.07 – 3.31)**	**< 0.05***
Diabetes **- Positive** **- Negative**		**1.7**	**0.57**	**5.47**	**(1.79 – 16.8)**	**< 0.01****
PCR: **- ≥ 10^6** **- < 10^6**		**- 1.25**	**0.34**	**0.29**	**(0.15 – 0.56)**	**< 0.01****
AFP: **- > 10** **- 5 – 10** **- < 5**		**1.004** **0.78**	**0.33** **0.35**	**2.73** **2.18**	**(1.42 – 5.25)** **(1.09 – 4.35)**	**< 0.01****

By univariate analysis, Baseline factors strongly associated with early virological response (EVR) were BMI < 30 kg/m, AFP < 5 ng/ml, low and moderate viraemia (PCR< 1 million IU/ml.), non diabetic, mild fibrosis (F1-F2) according to METAVIR score. (Table 16).

These factors were entered into the multivariate logistic regression model to identify independent prognostic factors. The results of the multiple logistic regression are summarized in Table (17).

Baseline factors found to be independently predictive for the absence of EVR were:

- BMI ≥ 30 kg/m (OR=**2.4, CI :1.34 – 4.38)**
- Diabetes mellitus(OR=5.47, CI: **1.79 – 16.8**)
- High viraemia (PCR > 1 million IU/ml.) (OR=0.29 , CI: **0.15 – 0.56)**
- AFP >10 ng/ml(OR=**2.18**, CI: **1.09 – 4.35**)
- Advanced fibrosis (F3-F4) according to METAVIR score (OR=1.88, CI: **1.07 – 3.31**).