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RESEARCH ARTICLE

RETINAL COMPLICATIONS IN PATIENT WITH CHRONIC HCV ON INTERFERON THERAPY IN EGYPT

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ABSTRACT

Introduction: Hepatitis C virus (HCV) infects up to 170 million people throughout the world causing chronic liver disease, liver cirrhosis and hepatocellular carcinoma. According to recent guidelines, the combination of pegylated interferon (PEG- IFN) α and ribavirin is still regarded as the standard chemotherapy for chronic hepatitis C (CHC). Various adverse effects, including ophthalmological side effects have been reported with the use of IFN.

Aim of the study: To evaluate retinal complications in patient with chronic HCV on interferon therapy.

Patients and methods: The study included 300 patients with CHC who received interferon therapy for 48 weeks at the outpatient clinic of hepatology and gastroenterology in the Ain Shams University hospital and Elqahira Elfatemya hospital. Patients were divided into two equal groups; group A responders to interferon therapy and group B non-responding to Interferon therapy. Patients were subjected to full history taking, clinical examination, laboratory investigations; liver function test, kidney function tests, urine analysis, complete blood count (CBC) , anti-nuclear antibody (ANA), anti-bilharzial antibody, thyroid function tests, viral markers, PCR for HCV, abdominal ultrasound, assessment of visual acuity, fundus examination, assessment of intra-ocular pressure, and liver biopsy.

Results: The study included 300 patients; 269 (89.7%) males and 31 (10.3%) females. The mean age of the studied patients was 45.73±5.47. Patients were divided into two equal age and sex matched groups; group A and B. Forty seven (15.7%) developed Retinal complications; 31 patients with cotton wool spots, 3 patients with macular oedema and 13 patient with bilateral retinal exudate. There was no relation between retinal complications and the stage of liver fibrosis by histopathology (X^2=6.29, p=0.179). There was statistical significant relation between retinal complications and liver examination by ultrasonography (X^2=11.92, p=0.003).

Conclusion: Fundus examination is recommended in chronic HCV patients on intereferon therapy.

INTRODUCTION

Infection with hepatitis C virus (HCV) is one of the leading causes of liver disease. Worldwide, it is estimated that HCV affects 170 million people, with a higher prevalence in Asia than in Europe or in the United States.[1] Within the United States, approximately 4.1 million have antibodies to HCV, which indicates an ongoing or previous infection with the virus. HCV accounts for about 15% of acute viral hepatitis, 60% to 70% of chronic hepatitis, up to 50% of cirrhosis, liver cancer, and end- stage liver disease.[2] Recently, there have been significant advances in the treatment of HCV infection. There are many new agents on horizon and the novel interferon (IFN)-free regimens are being explored, but IFN-based regimens along with the new direct acting antiviral agents are likely to stay as part of HCV treatment for the next few years.[3] Currently, pegylated interferon alpha (PegIFNα) is a part of all the standard regimens for the treatment of HCV. The development of retinopathy is a well-known side effect of the PegIFNα therapy. However, the data report discordant results about the frequency and clinical significance of retinopathy seen during PegIFNα-based therapy. Retinopathy has been reported in 18–86% of patients with chronic HCV who received IFN-based treatment regimens, and the risk is even higher in diabetic and hypertensive patients. The wide range of frequency reported in the literature reflects the limitations of small studies,

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which are heterogeneous in selection of the patients and screening protocols for retinopathy.[4]

Etiopathogenesis of interferon-induced vision changes is not clear. There are few theories. Ischemic: interferon activates endothelial growth factors and stimulates growth of high permeability microvessels followed by swelling of the surrounding tissue. This can also cause optic nerve ischemia and fiber swelling, progress to retinal vein occlusion and hemorrhage, anterior ischemic optic neuropathy with permanent losses of visual field and visual acuity.[5]

PATIENTS AND METHODS

The study included 300 patients with chronic HCV received interferon therapy for 48 weeks in the outpatient clinic of hepatology and gastroenterology in the Ain Shams University hospital and Elqahira Elfatemya hospital. Patients were divided into two groups; group (A) 150 responders to interferon therapy and group (B) 150 non-responders to interferon therapy.

All patients were subjected for

Full history taking

- Personal history: for age, gender, occupation, residence, special habits of medical importance and menstrual history for females.
- Present history of the following complaints:

Symptoms suggestive of chronic liver disease and liver cell failure e.g., yellowish discoloration of skin and sclera, enlargement of the size of the abdomen, bleeding tendency, swelling of both lower limbs, disturbed level of consciousness, hematemesis and/or melena.

Clinical examination stressing on

General examinations including

- Vital data (pulse, blood pressure, temperature & respiratory rate).
- Signs of liver cell failure: as jaundice, flapping tremors, palmar erythema, lower limb edema & deteriorated level of consciousness.

Abdominal examination

For abdominal contour, liver size, spleen size, degree of ascites and abdominal mass.

Chest examinations

For chest contour, air entry equality, additional air sounds and any abnormalities.

Heart examinations

Heart sounds and additional heart sounds Laboratory investigation including.

- Liver function tests: Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), serum albumin, prothrombin time (PT), partial thromboplastin time (PTT), International normalized ratio (INR) and bilirubin (total and direct).
- Kidney function tests: Serum creatinine and urea.
- Urine analysis.
- Complete blood picture (CBC) including platelet count, hemoglobin and leucocytic count.
- Antinuclear antibody (ANA) and antibilharzial antibody.
- Thyroid stimulating hormone (TSH).
- Viral markers: Hepatitis C virus antibody (HCV Ab) and Hepatitis B surface antigen (HBsAg).
- PCR for HCV quantitative pretreatment, after 12, 24,36, 48 and 72 weeks of treatment.
- Abdominal ultrasound with full comment on liver, spleen and portal vein diameter.
- Ocular examination: visual acuity, Intra-occular pressure for both eyes and fundoscopy to exclude retinal complications before interferon therapy and after 12, 24, 36 and48 weeks of treatment.

5- Liver biopsy and histopathology for grading and staging.

Statistical analysis

Data was collected, tables and statistically analyzed using SPSS v. 15. Parametric data was expressed as minimum, maximum, mean± standard deviation. Non parametric data was expressed as number and percentage. Comparison of parametric data between two groups was done used unpaired t test. Comparison of non-parametric data between two groups was done using Chi-square. Two tailed p value of ≤ 0.01 was considered highly significant, $p \leq 0.05$ significant and $p > 0.05$ insignificant.

RESULTS

The study included 300 patients; 31 (10.3%) females and 269 (89.7%) males. Their age ranged from 34 to 57 years with a mean of 45.73±5.47. Patients were divided into 2 groups;

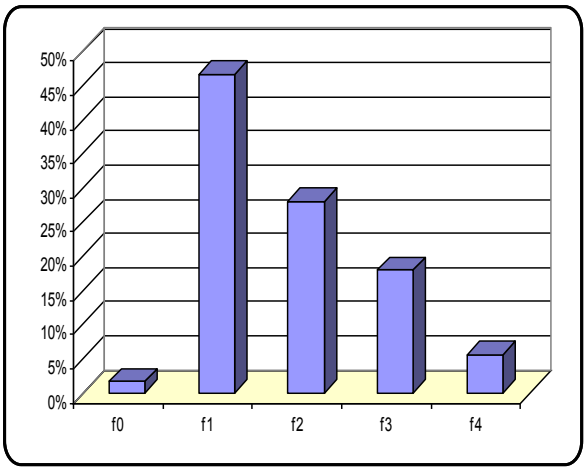

Figure 1 Stage of liver fibrosis by histopathology

group A included 150 patients responders to Interferon therapy and group B included 150 patients non-responders to Interferon

therapy. According to the stage of liver fibrosis by histopathology, f0 represent 5 patients (1.67%), f1 represent 140 patients (46.67%), f2 represent 84 patients (28%), f3 represent 54 patients (18%) and f4 represent 17 patients (5.67%) as shown in figure 1.

Abdominal ultrasonography showed that 46 patients (15.33%) had coarse liver, 79 patients (26.33%) had fatty liver, 175 patients (58.3%) had normal liver, 18 patients (6%) had splenomegaly and 282 patients (94%) had no splenomegaly as shown in figure 2.

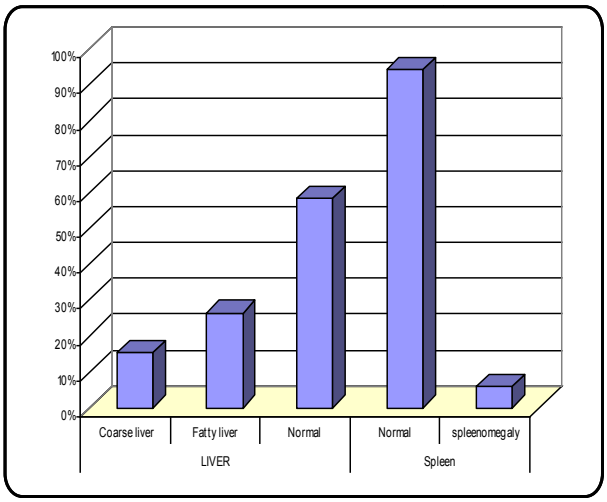

Figure 2 Abdominal ultrasonography finding

PCR results of the studied patients are shown in figure 3.

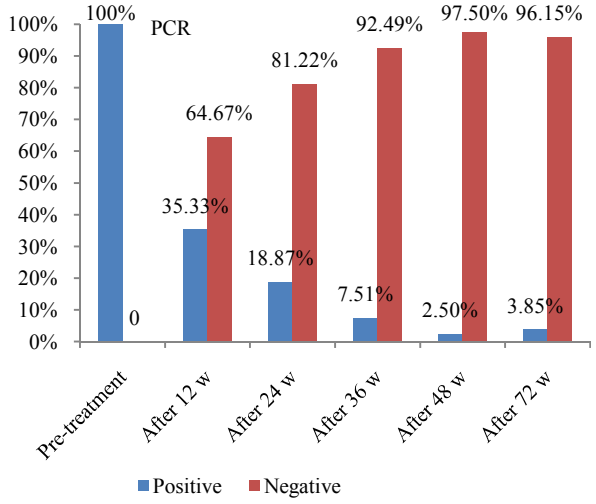

Figure 3 PCR of the studied patients

Complications during interferon therapy in all patients were 105 patients(35%) with anemia, 2 patients (0.67%) with depression,111 patients (37%) with neutropenia, 1 patients (0.33%) with pneumonitis, 1 patients (0.33%) with skin rashes and 69 patients (23%) with thrombocytopenia as shown in figure 4.

Retinal complications developed in 47 (15.7%) patients, as shown in figure 5.

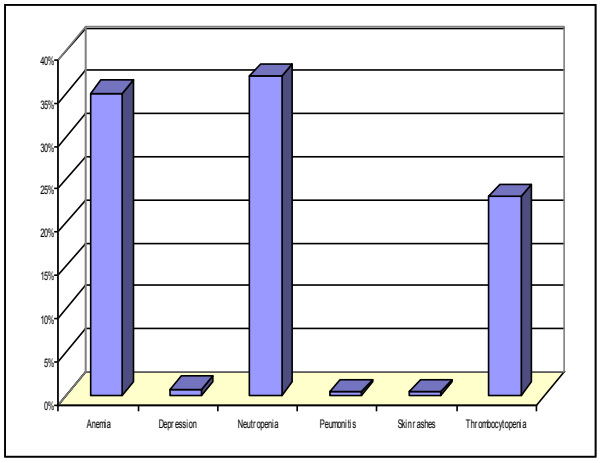

Figure 5 Complications during interferon therapy

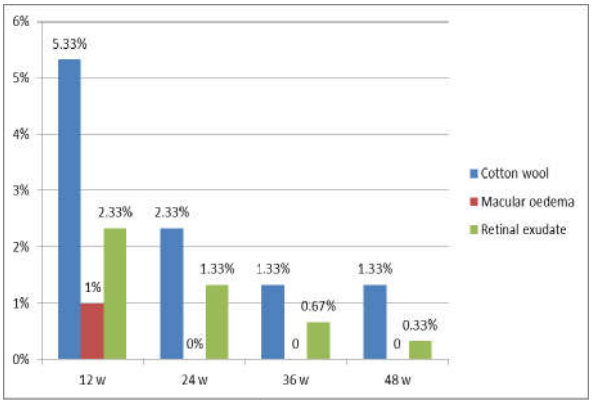

Figure 5 Retinal complications among the studied patients

Table 1 Comparison between the two groups as regard Antinuclear antibody (ANA)

	Non responder	Responder	Chi-square test	
	N (%)	N (%)	X2	P-value
ANA Positive	2 (1.3)	7 (4.7%)	2.864	0.091
BilharzialAb Positive	15 (10)	10 (6.7)	1.091	0.296

This table shows statistical no significant difference between both groups as regard (ANA). This tables hows statistical no significant difference between both groups as regard bilharzial antibody. There was statistical highly significant difference between both groups as regard stage of liver fibrosis by histopathology. Non responders have higher degree of fibrosis than responders group.

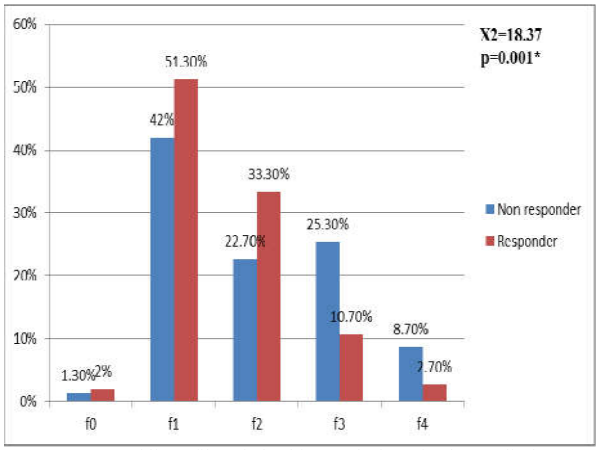

Figure 6 Stage of liver fibrosis by histopathology in the studied groups.

Table 2 Abdominal ultra-sonographic finding in the studied groups

Abdominal U\S		Non responder N (%)	Responder N (%)	Chi-square test X^2	P-value
liver	Coarse liver	35 (23.3)	11 (7.3)	17.644	0.000
	Fatty liver	42 (28)	37 (24.7)		
	Normal	73 (48.7)	102 (68)		
Spleen	Normal	139 (92.7)	143 (95.3)	0.946	0.331
	Splenomegaly	11 (7.3)	7 (4.7)		

This table shows statistical highly significant difference between both groups as regard ultra-sonographic finding of the liver. On the other hand there was no statistical significant difference between both groups as regard splenomegaly.

Table 3 Comparison between the two groups as regard retinal complications during interferon therapy

Fundus examination		Non responder N (%)	Responder No. %	Chi-square test X^2	P-value
12 week	Cotton wool	11 (7.30)	5 (3.3)	1.267	0.530
	Macular oedema	3 (2.00)	0		
	Retinal exudate	5 (3.30)	2 (1.3)		
24 week	Cotton wool	5 (3.3)	2 (1.3)	0.363	0.546
	Retinal exudate	2 (1.3)	1 (0.7)		
36 week	Cotton wool	2 (1.3)	2 (1.3)	0.000	1.000
	Retinal exudate	1 (0.7)	1 (0.7)		
48 week	Cotton wool	2 (1.3)	2 (1.3)	0.052	0.819
	Retinal exudate	1 (0.7)	0		

This table shows statistical no significant difference between both groups as regard fundus examination at 12, 24, 36 and 48 weeks of treatment.

Table 4 Complications during treatment with interferon in the studied groups

Complications	Non responder N (%)	Responder N (%)	Chi-square test X^2	P-value
Anemia	62 (41.33)	43 (28.67)	3.603	0.607
Depression	2 (1.33)	0		
Neutropenia	64 (42.67)	47 (31.33)		
Peumonitis	1 (0.67)	0		
Skin rashes	0	1 (0.67)		
Thrombocytopenia	41 (27.33)	28 (18.67)		

This table shows statistical no significant difference between both groups as regard complications during treatment with interferon therapy.

Table 5 Comparison between the two groups as regard PCR during treatment

		Non responder N (%)	Responder No (%)	Chi-square test X^2	P-value
PCR pre tt	Positive	150 (100)	150 (100)	NA	NA
PCR 12w	Negative	63 (42)	131 (87.3)	65.488	0.000*
	Positive	87 (58)	19 (12.7)		
PCR 24w	Negative	23 (15.3)	150 (100)	113.133	0.000*
	Positive	40 (26.70)	0		
PCR 36w	Negative	10 (6.7)	150 (100)	83.719	0.000*
	Positive	13 (8.7)	0		
PCR 48w	Negative	6 (4)	150 (100)	143.388	0.000*
	Positive	4 (2.67)	0		
PCR 72w	Negative	0 0.00%	150 (100) 100.0%	130.132	0.000*
	Positive	6 4.00%	0 0.00%		

This table shows statistical highly significant difference between both groups as regard PCR throughout the treatment duration.

Table 6 Relation between retinal complications and both sex and age

		Retinopathy No	Retinopathy Yes		
Sex	Male N (%)	226 (89.33)	43 (91.49)	X^2 0.200	p-value 0.655
Age	Mean±SD	45.59±5.47	46.49±5.47	t 1.033	p-value 0.303

This table shows statistical no significant relation between retinopathy and both sex and age.

Table 7 Relation between retinal complications and laboratory investigations after 12 weeks of treatment

12 weeks follow up	Retinopathy No	Retinopathy Yes	Independent t-test	
	Mean± SD	Mean± SD	t	p-value
ALT	77.60± 18.51	77.55± 18.86	0.015	0.988
AST	48.60± 21.04	51.36± 21.95	-0.822	0.412
Serum Albumin	3.97± 0.17	3.98± 0.17	-0.576	0.565
PT	12.8± 0.61	12.89± 0.58	-1.028	0.305
PTT	32.81± 4.30	33.36± 4.47	-0.796	0.427
INR	1.16± 0.19	1.15± 0.20	0.335	0.738
Total bilirubin	0.89± 0.23	0.96± 0.18	-1.877	0.062
Direct bilirubin	0.42± 0.07	0.41± 0.09	0.672	0.502
Urea	25.98± 9.57	24.57± 9.39	0.930	0.353
Serum create	1.04± 0.17	1.01± 0.18	0.990	0.323
PLT	133.20± 29.55	132.60± 26.30	0.128	0.898
Hb	10.87± 1.13	10.52± 1.07	1.968	0.050
TLC	2.49± 1.03	2.14± 0.94	2.179	0.030

This table shows statistical significant relation between retinopathy and both hemoglobin and total leucocytic count. On the other hand no relation between retinopathy and other laboratory parameters at 12 weeks of treatment.

Table 8 Relation between retinal complications and laboratory investigations after 24 weeks of treatment

24 weeks follow up	Retinopathy No	Retinopathy Yes	Independent t-test	
	Mean±SD	Mean± SD	t	p-value
ALT	61.72± 19.15	62.40± 18.03	-0.228	0.819
AST	33.54± 13.01	36.34± 14.48	-1.332	0.184
Serum Albumin	4.12± 0.19	4.13± 0.20	-0.470	0.639
PT	13.06± 0.58	13.14± 0.58	-0.828	0.408
PTT	32.49± 2.89	33.66± 4.30	1.606	0.109
INR	1.12± 0.13	1.11± 0.12	0.433	0.665
Total bilirubin	0.87± 0.26	0.95± 0.22	-2.116	0.035
Direct bilirubin	0.47± 0.13	0.49± 0.12	-1.238	0.217
Urea	25.13± 8.67	24.47± 8.07	0.486	0.627
Serum create	0.92± 0.22	0.88± 0.22	1.306	0.193
PLT	127.40± 21.58	128.67± 21.07	-0.370	0.712
Hb	10.69± 0.96	10.33± 0.80	2.381	0.018
TLC	2.14± 0.84	1.82± 0.76	2.436	0.015

This table shows statistical significant relation between retinopathy and total bilirubin, hemoglobin and total leucocytic count. On the other hand no relation between retinopathy and other laboratory parameters at 24 weeks of treatment.

This table shows statistical significant relation between retinopathy and total bilirubin, INR, hemoglobin and total leucocytic count. On the other hand no relation between retinopathy and other laboratory parameters at 36 weeks of treatment.

This table shows statistical significant relation between retinopathy and AST and total leucocytic count. On the other hand no relation between retinopathy and other laboratory

parameters at 48 weeks of treatment.

Table 9 Relation between retinal complications and laboratory investigations after 36 weeks of treatment

36 weeks follow up	Retinopathy		Independent t-test	
	No	Yes		
	Mean±SD	Mean±SD	t	p-value
ALT	40.25±14.53	39.96±15.65	0.091	0.927
AST	25.97±7.54	27.88±10.60	-1.101	0.272
Serum Albumin	4.16±0.15	4.22±0.20	-1.610	0.109
PT	13.32±0.37	13.40±0.41	-0.863	0.390
PTT	37.23±3.15	37.14±2.97	0.113	0.910
INR	1.12±0.10	1.17±0.11	-2.091	0.038
Total bilirubin	0.89±0.23	1.01±0.15	-2.253	0.026
Direct bilirubin	0.49± 0.19	0.46± 0.18	0.757	0.450
Urea	26.18± 7.77	26.48± 8.27	-0.160	0.873
Serum create	1.04± 0.23	0.99± 0.24	0.940	0.349
PLT	121.64± 18.11	121.39± 17.35	0.088	0.930
Hb	10.60± 0.94	10.28± 0.83	2.230	0.026
TLC	2.11± 0.80	1.87± 0.68	1.960	0.051

Table 10 Relation between retinal complications and laboratory investigations after 48 weeks of treatment

48 weeks follow up	Retinopathy		Independent t-test	
	No	Yes		
	Mean± SD	Mean± SD	t	p-value
ALT	26.11± 13.14	25.55± 14.87	0.174	0.862
AST	23.16± 5.04	26.40± 7.27	-2.531	0.012
Serum Albumin	4.15± 0.15	4.15± 0.16	-0.010	0.992
PT	13.34± 0.36	13.46± 0.33	-1.457	0.147
PTT	36.06± 2.59	35.30± 3.13	1.189	0.236
INR	1.14± 0.12	1.14± 0.11	-0.010	0.992
Total bilirubin	0.85± 0.27	0.95± 0.25	-1.485	0.140
Direct bilirubin	0.44± 0.19	0.46± 0.19	-0.476	0.635
Urea	24.95± 8.02	23.45± 7.13	0.792	0.429
Serum create	1.04± 0.18	0.95± 0.19	2.148	0.133
PLT	116.68± 21.81	114.92± 20.49	0.511	0.610
Hb	10.67± 0.99	10.39± 0.90	1.761	0.079
TLC	2.21± 0.74	1.98± 0.65	1.993	0.047

Table 11 Relation between retinal complications and stage of liver fibrosis by histopathology

		Retinopathy		Chi-square test	
		No	Yes		
		N (%)	N (%)	X^2	P-value
Stage of Fibrosis	f0	3 (1.2)	2 (4.3)	6.290	0.179
	f1	121 (47.8)	19 (40.4)		
	f2	69 (27.3)	15 (31.9)		
	f3	48 (19.0)	6 (12.8)		
	f4	12 (4.7)	5 (10.6)		

This tableshows statistical no significant relation between retinopathy and stage of liver fibrosis by histopathology.

Table 12 Relation between retinal complications and abdominal ultrasonography

AbdominalU/S		Retinopathy		Chi-square test	
		No	Yes		
		N (%)	N (%)	X^2	P-value
Liver	Coarse liver	31 (12.3)	15 (31.9)	11.929	0.003
	Fatty liver	70 (27.7)	9 (19.1)		
	Normal	152 (60.1)	23 (48.9)		
Spleen	Normal	238 (94.1)	44 (93.6)	0.014	0.904
	spleenomegaly	15 (5.9)	3 (6.4)		

This table shows statistical significant relation between retinopathy and liver examination by ultrasonography.

Table 13 Relation between retinal complications and PCR during treatment

PCR		No retinopathy	Retinopathy	Chi-square test	
		N (%)	N (%)	X^2	P-value
PCR 12w	Negative	167 (66.01)	27 (57.45)	1.271	0.259
	Positive	86 (33.99)	20 (42.55)		
PCR 24w	Negative	146 (80.66)	27 (84.38)	0.062	0.802
	Positive	35 (19.34)	5 (15.63)		
PCR 36w	Negative	142 (97.26)	18 (66.67)	26.443	0.000
	Positive	4 (2.74)	9 (33.33)		
PCR 48w	Negative	120 (98.36)	36 (94.74)	0.428	0.512
	Positive	2 (1.64)	2 (5.26)		
PCR 72w	Positive	2 (100)	2 (100)	NA	NA

This table shows highly statistical significant relation between retinopathy and PCR at 36 weeks. On the other hand there were no statistical significant relations between retinopathy and PCR at 12, 24 and 48 weeks.

DISCUSSION

Our study included 300 patients divided into 2 groups; 150 responders and 150 non responders. Their age ranged from 34 to 57 years old with 269 male (89. 7%) and 31 female (10.3%). In our study 47 (15.7%) developed Retinal complications; 31 patients with cotton wool spots, 3 patients with macular oedema and 13 patient with bilateral retinal exudate. Kim *et al.,*[2] that found 11 out of 32 patients(34.4%) developed retinal complications in the form of 6 patients with cotton-wool spots, 4 patients with retinal exudate and 1 patient with retinal vein occlusion. Panetta and Gilani[1] found that 7 of 183 patients (3.8%) developed retinal changes in the form of 3 patients showed cotton wool spots, 1 patient showed retinal exudate on follow-up and treatment was discontinued in 3 patients (1.6%). Mousa *et al.,*[6] found that among 98 studied patients; only 8 patients (8.16%) developed retinopathy, in the form of 5 patients with cotton wools and 3 patients with retinal exudate. Seven of 8 patients with retinopathy had no reduction in visual acuity. No dose reduction for management of retinopathy. Atypical adverse events: were reported as vitreous hemorrhage from retinal tears with retinal detachment requiring vitrectomy in 1 patient, final visual outcomes were not described.

In our study there was no statistical significant relation between retinopathy and both age and sex, in agreement with Mallolas and Laguno[7]. On the contrary with *Pemu and Ofili*[8]who had statistical significant relation between retinopathy and both age and sex, as retinopathy is more at older age and most common in female patients.

Vujosevic *et al.,*[4] found statistical significant relation between retinopathy and age, in this study 21 of 97 patients (22%) developed retinal complications but patients had pre-existing retinopathy, 9 patients, had worsening of retinopathy during treatment. Factors associated with developing retinopathy were age, metabolic syndrome, HTN, cryoglobulinemia and pre-existing intraocular lesions. Atypical adverse events: bilateral branched retinal vein occlusion in one patient with a background of HTN resulting in irreversible vision loss in the left eye only.

In our study there were statistical significant relations between

retinopathy and both hemoglobin and total leucocytic count at 12 weeks of treatment. Also there were statistical significant relations between retinopathy and total bilirubin, hemoglobin and total leucocyticcount at 24 weeks of treatment. There were statistical significant relations between retinopathy and total bilirubin, hemoglobin and total leucocytic count and INR at 36 weeks of treatment.

In addition there were statistical significant relations between retinopathy and AST and total leucocytic count at 48 weeks of treatment. There disagree with Yasser *et al.*,[9] who found no statistical significant relation between retinopathy and any laboratory investigations during treatment. This study showed 22 of 84 patients (26%) developed retinopathy. Retinal hemorrhage was observed in 8 patients. Four patients complained of visual disturbance. Retinopathy disappeared in 16 patients (73%) despite the continuation of combination therapy. However retinopathy persistent in 6 patients with retinal hemorrhage and three of them stopped treatment. In agreement with Yasser *et al.,*[9] we found no relation between retinal complications and the stage of liver fibrosis by histipathology.

In our study there was statistical significant relation between retinal complications and liver examination by ultrasonography, on the contrary with Božić *et al.*[10] that shows no statistical significant relation between retinal complications and liver examination by ultrasonography. This study showed 183 patients with chronic hepatitis C included in this multicenter trial from 8 reference centers in Serbia. In our study there was statistical significant relation between retinal complications and PCR at 36 weeks. On the other hand no statistical significant relation between retinopathy and PCR at 12,24 and 48 weeks, on the contrary with *Yasser et al.*[9] found no statistical significant relation between retinal complications and PCR during treatment.

In our study the patients were divided into 2 groups; 150 responders and 150 non responders to interferon therapy. There were statistical significant differences between groups as regard AST, ALT, Hb and total leucocytic count pretreatment. There was statistical significant difference between groups as regard ALT, hemoglobin and total leucocytic count after 12 weeks of treatment. There were statistical significant differences between both groups as regard ALT, AST, hemoglobin and total leucocytic count after 24 weeks of treatment. There were statistical significant differences between groups as regard ALT, hemoglobin and total leucocytic count after 36 weeks of treatment. Also there were statistical significant differences between groups as regard ALT, AST, hemoglobin and total leucocyticcount after 48 weeks of treatment, on the contrary with the result of Ali *et al.*[11] who showed no statistical significant difference between both groups in all laboratory investigations during treatment. In our study there was statistical significant difference between responders and non-responders as regard stage of liver fibrosis by histopathology, as non-responders had higher degree of fibrosis, in agreement with the study of Torriani *et al.*[12] whose study showed a statistical significant difference between both groups and stage of liver fibrosis by histopathology. On the contrary with Amanullah *et al.*[13] found no statistical significant difference between both groups and stage of liver fibrosis by histopathology.

In the current study, there was statistical highly significant difference between both groups as regard ultrasonographic finding of the liver in the form of fatty liver and coarse liver. On the other hand there was no statistical significant difference between both groups as regard splenomegaly. In agreement with Giordanino *et al.*[14], who found statistical significant difference between both groups as regard ultrasonographic finding of the liver, as the incidence of fatty liver and coarse liver was significantly higher among nonresponders (21.3%) compared with long-term responders (0.9%).

In our study there was statistical highly significant difference between both groups and PCR throughout the treatment duration, and this agree with Brillanti *et al.*[15], who found statistical significant difference between both groups and PCR during treatment. Our study showed statistically no significant difference between both groups as regard complications during treatment with interferon therapy. In concordance with *Di* Bisceglie *et al.*[16] who found no significant statistical difference between both groups as regard hematological and psychiatric adverse events. Meanwhile Bruix *et al.*[17] found statistical significant difference between both groups as regard Neutropenia and thrombocytopenia.

CONCLUSION

Patients with Chronic hepatitis C virus on interferon therapy are at risk of retinopathy, so fundus examinations is recommended in chronic HCV patients on intereferon therapy.

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