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FREQUENCY OF RETINOPATHY IN HUNDRED CASES OF CHRONIC HEPATITIS C ON INTERFERON THERAPY AT LIAQUAT UNIVERSITY HOSPITAL HYDERABAD

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ABSTRACT

OBJECTIVE: *Chronic Hepatitis C is common problem world wide treated by combination of interferon alpha and ribavirin. Retinopathy is one of the side effects of interferon therapy. The aim of this study is to determine the frequency of retinopathy in patients treated by interferon alpha and ribavirin at Liaquat University Hospital Hyderabad.*
STUDY DESIGN: *Observational descriptive study.*
PLACE AND DURATION: *This study was conducted in the department of Medicine Liaquat University Hospital from July 2007 to June 2009.*
MATERIAL AND METHODS: *All chronic hepatitis C patients with positive HCV RNA by Polymerase Chain Reaction were included. Past medical history of hypertension and diabetes were taken. Full ocular examination was performed before start of treatment and at 3 months and 6 months interval.*
RESULTS: *Total 100 patients were enrolled amongst which 23 developed retinopathy. 12/82 (14.63%) with no co-morbid illness; 7/12(58.3%) in patients with hepatitis C diabetes; 2/3(66.6%) in patients with hepatitis C and hypertension and 2/3(66.6%) in patients with hepatitis C and both diabetes and hypertension.*
CONCLUSION: *Retinopathy may occur in patients with chronic hepatitis C receiving interferon alpha and ribavirin, commonly in patients with diabetes and hypertension.*

KEYWORDS: Retinopathy, Interferon and ribavirin, Chronic hepatitis C.

INTRODUCTION:

Chronic hepatitis C is a serious condition and prevalent through out the world. It affects more than 170 million (3.0% of world population) people in the world.[1] For most countries the prevalence of hepatitis C virus infection is less than 3.0%: the prevalence is higher (upto 15%) in some countries as in Africa and Asia and highest (over 15%) in Egypt.

Chronic hepatitis C if not treated properly may eventually leads to cirrhosis.[2] and hepatocellular carcinoma [3] in some cases. Therefore timely diagnoses and treatment of patients at risk for severe liver disease from the chronic hepatitis C is imperative to prevent life threatening illness. The main treatment for this intractable disease is interferon administration. Currently combination therapy of interferon alpha and ribavirin is the most successful treatment.[4]

Various adverse effect have been reported due to use of interferon. [5] Okanoue et al[6] observed flu like syndrome after using high doses of interferon ; Neuropsychiatric side effects like suicidal tendencies has been observed by Janssen HLA et al[7] ; Bone marrow suppression has been seen by Wong S [8] ; similarly gastrointestinal[9], urinary[10], dermatologic[11] side effect has been observed by various researchers. Endocrinological disorders has been observed by Imagawa A et al[12].

Recently ophthalmic side effects have been reported during interferon therapy particularly retinal lesions and neurovisual impairment. Interferon associated retinopathy was first described in 1990 by Ikebe et al.[13] Features include hemorrhages and cotton wool spots around the disc and through the posterior pole, optic disc hyperaemia and macular oedema. The reported incidence of retinopathy as a side effect of interferon varies widely in the literature. The aim of this study was to assess the nature and frequency of such lesions during alpha interferon therapy for chronic hepatitis C at Liaqaut University

Hospital.

MATERIAL & METHOD:

This study was conducted at Liaquat University Hospital from July 2007 to June 2009. This was a prospective study. Pretreatment all patients were positive for HCV RNA by polymerase chain reaction and had chronic hepatitis with elevated alanine amino transferase level. Patients with evidence of decompsensated liver disease were excluded from the study.

Patients were considered to have hypertension if systolic / diastolic pressure exceeded 140/90 mmHg or patients were using antihypertensive drugs. Patients were considered to have diabetes mellitus if they were being treated with insulin or oral hypoglycemic agents of if fasting blood glucose exceeded 140 mg/dl. Patients with poorly controlled diabetes (HbA$_1$C >8%) and hypertension (systolic/ diastolic blood pressure > 160/100 mmHg were excluded. All patients underwent a baseline ophthalmic evaluation before they started Interferon treatment. Patients already with retinopathy, dense cataract, glaucoma or any other ocular abnormalities were excluded. Total hundred patients who fulfilled the criteria were included in this study and ophthalmic examination was repeated after 3 months and 6 months after the start of in interferon and ribavirin therapy.

STATISTICAL ANALYSIS:

The data were entered in statistical program SPSS version 16.0. Qualitative data (frequencies and percentage) was presented as n(%). All the data were calculated on 95% confidence interval. As this study was descriptive, no any statistical test was applied for any comparison.

RESULT:

Total hundred patients were enrolled in this study amongst which 72 were males and 28 were females with ages ranging from 26 to 58 years (Table No. I). No comorbid illness was present in 82 patients. Diabetes mellitus was present in 12 patients, 3 patients were hypertensive and 3 patients were having both diabetes mellitus and hypertension.

At 3 months ophthalmic examination, 22 out of 100 patients (22%) had evidence of retinopathy consisting of cotton wool spots in 12 patients, haemorrhages in 8 patients and cotton wool spots plus haemorrhages in 2 patients. One of these patient complained of blurring of vision.

Amongst the 12 patients having diabetes mellitus 4 patients had developed cotton wool spots, 2 patients developed haemorrhages and 1 patient developed both cotton wool spots plus haemorrhages.

Amongst 3 hypertensive patients 1 case developed haemorrhages and 1 case developed cotton wool spots. Amongst 3 patients having diabetes plus hypertension 1 case developed combined cotton wool spot ad haemorrhages. At the end of 6 months in repeat ophthalmologic examination retinopathy disappeared in 18 out of 22 cases but one case of diabetes mellitus and hypertension developed haemorrhage with visual symptoms. All patients except 2 completed their planned course of treatment without any dosage alteration. In two cases having visual impairment the therapy was terminated before time.

TABLE NO. I. SUMMARY OF PATIENT DETAILS AND FINDING (n = 100)

	No.	%
Gender:		
Male	72	72
Female	28	28
Age groups(range 26 to 58)		
20 to 29	6	6
30 to 39	37	37
40 to 49	52	52
50 to 59	5	5
Hemoglobin Level:		
< 8	2	2
8.1 – 10	12	12
10.1 to 12	72	72
> 12	14	14
Total leukocyte count		
< 4000	10	10
4001 to 6000	82	82
6001 to 11000	8	8
Platelet count		
< 100,000	8	8
100,001 to 200,000	52	52
200,001 to 400,000	40	40
Disease status:		
Patient with no co-morbid illness	82	82
Diabetic patient	12	12
Hypertensive patient	3	3
Diabetic + Hypertensive	3	3

TABLE NO. II INCIDENCE OF RETINOPATHY IN DIFFERENT GROUPS (n = 100)

	Patient with no comorbid illness	Diabetic	Hypertensive	Diabetic + Hypertensive
Number	82	12	03	03
Developed retinopathy	12	07	02	02
Percentage	14.63	58.3	66.6	66.6

DISCUSSION:

Combination therapy of alpha interferon and ribavirin is currently the most successful treatment for the patients of chronic hepatitis C. However patients must be monitored closely, as this therapy may produce serious

ocular and systemic side effects. Retinopathy is a well recognized side effect of interferon therapy and is characterized by retinal haemorrhages, cotton wool spots and macular oedema.[14]

Although most resolve while treatment continues and are asymptomatic[15], severe ocular complications can occur like macular oedema[16] which cause severe visual loss. Therefore baseline and ongoing assessment by ophthalmologist have been advocated in previous studies.

In our study 23 patients developed retinopathy out of 100 patients amongst which 7 patients were diabetic, 2 cases were hypertensive and 2 cases were combine hypertensive and diabetic. Retinopathy developed in 12 patients with no comorbid illness. This suggests that retinopathy is more common in patients having diabetic mellitus and hypertension.

As shown in our study amongst 12 diabetic patients 7 developed retinopathy (58.3%) and amongst 3 hypertensive patients 2 developed retinopathy (66.6%) and amongst 3 patients with Diabetic Mellitus and hypertension 2 developed retinopathy (66.6%); whereas amongst 82 patients with no comorbid illness only 12(14.63%) developed retinopathy.

This type of study was conducted also by Cuthbertson FM et al in 2004[15] and he found the retinopathy in 16% of patients receiving interferon and ribavirin which is considerable low than our study. Similar type of study was also conducted by Okuse C et al [17] and he found retinopathy in 19% of patients more commonly in patients suffering from hypertension which is comparable to our study.

Although the exact mechanism of interferon induced retinopathy is unknown but the fact that retinopathy is more common in patients with diabetes mellitus and hypertension and similarity of the clinical features to diabetic and hypertensive retinopathy suggest an ischaemic mechanism. This ischaemia may be caused by disrupted retinal microcirculation, as reported in studied using fluorescion angiography, that showed poorly perfused retinal areas in patients with interferon retinopathy.[18] It has also been reported that interferon alpha increased leukocyte adherence to the vascular endothelium, suggesting that the impaired retinal circulation may be associated with interferon induced retinopathy.[19] Similarly some other studies suggest interferon impairs endothelial function.[20] Some investigations have suggested deposition of immune complex at the vessels and immunological dysfunction[21] as possible mechanism of retinopathy.

Out study and other studies [22, 23] suggests that retinopathy is a common complication in patients receiving interferon and ribavirin in combination and is more common in patients suffering from diabetes mellitus and hypertension but is often reversible but severe in some cases. Therefore patients planned to start interferon therapy for chronic hepatitis C should have a baseline fundus examination before initiating treatment to identify any pre existing retinopathy. Patients should be monitored periodically for the development of retinopathy and followed up until retinopathy resolves.

CONCLUSION:

This study showed that retinopathy and neurovisual impairment may occur in patients receiving alpha interferon and ribavirin therapy especially in cases of diabetes mellitus and hypertension that are often reversible

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