ORIGINAL ARTICLE

HYPOTHYROIDISM IN HEPATITIS C PATIENTS ON PEGYLATED INTERFERON THERAPY

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Background: Chronic hepatitis has become a major health problem all over the world especially in the third world countries. The most common cause of chronic hepatitis in Pakistan is hepatitis C which can lead Toliver cirrhosis and hepatocellular carcinoma. In Pakistan Pegylated Interferon Alpha is still corner stone of therapy for chronic hepatitis C. One of the major side effects of this therapy is the development of thyroid dysfunction, i.e., hypothyroidism and hyperthyroidism. This study was done to assess the frequency of hypothyroidism in hepatitis C patients after three months of pegylated interferon therapy. **Methods:** This study was conducted from 1st October 2013 to 31st march 2014 at outpatients department (OPD) of Gastroenterology and Hepatology, Lahore General Hospital Lahore. Descriptive case series study design was used. The sample of 200 patients was taken from the patients who visited OPD and fulfil the inclusion criteria of the study. Serum thyroid stimulating hormone level (TSH) was done before and after completion of three months therapy at centre for Nuclear Medicine (CENUM) laboratory, Mayo Hospital, Lahore by immune-radiometric assay (IRMA) and patients having TSH>4.0 mIU/L (normal range: 0.2–4.0 mIU/L) were considered hypothyroid. **Results:** The mean age of the patients was 36.29±8.5 years. One hundred and twenty-three (61.5%) were male and 77 (38.5%) were female. After 3 months of interferon therapy, 163 (81.5%) patients were euthyroid and 37(18.5%) patients were having thyroid dysfunction. There were total 29 (14.5%) hypothyroid patients; 8 (27.6%) were male and 21 (72.4%) female. **Conclusion:** It is concluded from this study that frequency of hypothyroidism in patients with chronic hepatitis C was 14.5% after treatment with pegylated interferon therapy for 3 months. Female patients were more prone to develop hypothyroidism as compared to male patients.

Keywords: Hepatitis C Virus; hypothyroidism; pegylated interferon therapy

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INTRODUCTION

Chronic viral hepatitis is necro inflammatory disease of the liver lasting more than 6 months. Different viruses causing chronic viral hepatitis are Hepatitis B, C, and D. The rate of spontaneous clearance varies according to the virus, the age at the onset of infection and various other factors. Hepatitis C virus (HCV) is the most common cause of chronic viral hepatitis in western world.[1] Hepatitis C is the leading cause of chronic liver disease, cirrhosis, and hepatocellular carcinoma, as well as the most common indication for liver transplantation in many countries.[2]

The prevalence of Hepatitis C in the United States is 1.6%.[3] Hepatitis C is estimated to result in 366 000 deaths annually worldwide.[4] Similarly in Pakistan Hepatitis C is the most common cause of chronic viral hepatitis involving three out of 10 person and more than 10 million people are living with this disease.[5,6] A joint publication by WHO and Pakistan medical association revealed that in Pakistan prevalence of hepatitis C virus is 2.5% in children, 5.2% among pregnant women, 5.3% in general population, 3.1% in army recruits, 3.6%in blood donors, 5.4%in health care workers, 10.3% in high risk groups, 12% in patients with provisional diagnosis of hepatitis and 54% in patients with chronic liver disease.[7]

Hepatitis C virus infection is associated with both the organ specific and systemic autoimmune diseases. Thyroid disease may be subclinical. A variety of thyroid diseases have been described in association with chronic viral hepatitis. Patients who test positive for ANA are more prone to developing thyroid disorders, particularly when treated with interferon. These thyroid disorders, however, are generally reversible.[1]

Pegylated Interferon is the cornerstone therapeutic agent for chronic hepatitis C virus (HCV) infection.[8] In addition to many other side effects of interferon therapy like flu-like symptoms, haematological toxicity, elevated transaminases, nausea, fatigue, and psychiatric sequalae, it also causes thyroid dysfunction i.e. hyperthyroidism and hypothyroidism.[9]

In Pakistan limited studies have been done to see the frequency of hypothyroidism in hepatitis C patients on interferon therapy. By doing so we will be able to encourage our healthcare personnel to monitor all hepatitis C patients on pegylated interferon therapy for hypothyroidism and manage them aggressively in order to improve therapy compliance.

MATERIAL AND METHODS

This descriptive case series was conducted at outpatient department of Gastroenterology and Hepatology, Lahore General Hospital Lahore and study design was descriptive case series. There were two hundred patients enrolled in this study by calculating sample size under ninety five percent confidence level, six percent margin of error. This study was continued for the period of three months by using purposive non probability sampling technique. The inclusion criteria was set that only patients of hepatitis C who had age range from 15–65 years (both inclusive) were enrolled in the study and this inclusion criteria was strictly followed from start to close up of study. Pegylated interferon therapy was given to hepatitis C patients. The patients who had decompensated chronic liver disease, thyroid disorder, getting amiodarone therapy, EF less than 30% were not enrolled in this study. The patients whose TSH level was more than 4.0 mlU/L, after 3 months of therapy were considered hypothyroid. Objective of study is to assess the frequency of hypothyroidism in hepatitis C patients after three months of pegylated interferon therapy.

There were two hundred patients enrolled who strictly follow the defined inclusion criteria and visited outpatient department of Gastroenterology and Hepatology, Lahore General Hospital Lahore. TSH level was performed in the centre for nuclear medicine laboratory and also repeated after three months of interferon therapy. Normal value of TSH was considered 0.20–4.0 mlU/L. Demographic data of each patient was collected by using designed Performa. The collected data was entered in SPSS version 15 for analysis. Mean and standard deviation was calculated of quantitative data and frequency analysis was conducted for qualitative variables.

RESULTS

The mean age of the patients was 36.29±8.5 years. There were 34 (17%) patients having age equal or less than 25 years, 56 (28%) patients were 26–35 years of age, 86 (43%) patients were of 36–45 years, 21 (10.5%) patients in age range of 46–55 years and 3 (1.5%) patients were equal or more than 56 years. There were123 (61.5%) male patients and 77 (38.5%) female patients. The mean value of Thyroid stimulating hormone (TSH) after 3 months of therapy was 1.72±1.54 mIU/L. There was 1 (0.5%) patient in TSH range of equal or less than 0.05, 7 (3.5%) patients in TSH range of 0.06–0.20, 141 (70.5%) patients in TSH range of 0.21–2.00, 22 (11%) patients in TSH range of 2.01– 4.00, 22 (11%) patients in TSH range of 4.01–6.00 and 7 (3.5 %) patients in TSH range of equal and more than 6.01. Regarding distribution of the patients with thyroid dysfunction at 3 months of therapy; 37 patients (18.5%) were having thyroid dysfunction whereas 163 patients (81.5%) were euthyroid. Out of 37 patients with thyroid dysfunction, 11 (29.73%) patients were male and 26 (70.27%) patients were female.

Table-1: Distribution of patients by TSH level groups at 3 months

TSH	Frequency	Percent	Cumulative percent
<=0.05	1	0.5	0.5
0.06–0.20	7	3.5	4.0
0.21–2.00	141	70.5	74.5
2.01–4.00	22	11.0	85.5
4.01–6.00	22	11.0	96.5
>6.01	7	3.5	100
Total	200	100	

Table-2: Distribution of patients having thyroid dysfunction by gender

Gender	n	Percent
Male	11	29.73
Female	26	70.27
Total	37	100

Table-3: Distribution of patients by thyroid status

Thyroid status	Frequency	Percent	Cumulative percent
Euthyroid	163	81.5	81.5
Hypothyroid	29	14.5	96.0
Hyperthyroid	8	4.0	100.0
Total	200	100.0	

DISCUSSION

The purpose of this study was to investigate the incidence of hypothyroidism in HCV infected patients after getting 3 month therapy of pegylated interferon. Female patients (14.5%) have significant higher rate of hypothyroidism than male patients. Hepatitis C is most common disease in both United States and Pakistan, having prevalence of 1.6% and three persons out of ten persons respectively.[3] Hepatitis C is related with various organ specific autoimmune diseases including variety of thyroid diseases. Interferon therapy may result in autoimmune destruction of thyroid gland leading to development of hypothyroidism.

Many western investigators conducted their research study on patients who have hepatitis C and getting interferon therapy by focusing thyroid dysfunction (hypothyroidism and hyperthyroidism). Ward *et al*, Bini *et al*, Foldes *et al*, Vezali *et al* and Yen *et al*, investigated that 3–14%, 10.7% patients, 8.7% patients, 18% patients and 11.5% patients developed thyroid dysfunction (hypothyroidism and hyperthyroidism) respectively. Kee *et al* concluded that approximately 2% patients had persistent thyroid dysfunction ina small group of patients.

In our study the mean age of the patients was 36.29±8.5 years which is comparable with the study of Vezali *et al*[11] and Yan *et al*. In our study, 123 (61.5%) patients were male and 77 (38.5%) patients were female but Vezali *et al*[11] enrolled 33 (54.1%) male patients and 28 (45.9%) female patients. The mean

Thyroid stimulating hormone (TSH) level of the patients was 1.74±1.62 mIU/L but the study of Vezali *et al* had mean TSH of 1.62±0.92 mIU/L. Hence it is comparable to our study. The frequency of thyroid dysfunction was 18.5% as 37 patients out of 200 developed thyroid dysfunction. According to Vezali *et al*[11] thyroid dysfunction was present in 13 (21.3%) out of total 61 treated patients whereas Foldes *et al*[15] showed that the incidence of thyroid dysfunction was 21.7%. The thyroid dysfunction was observed more in female population as out of 37 patients with thyroid dysfunction there were 11 (29.7%) males and 26 (70.3%) females. According to Vezali *et al* out of 13 patients with thyroid dysfunction 4 (30.8%) were male and 9 (69.2%) were female and Yan *et al*[12] out of 68 patients there were 21 (30.9%) males and 47 (69.1%) females. The results of both studies are comparable to our study. In our study the frequency of hypothyroidism was 14.5%. Out of 200 treated patients there were 29 (14.5%) hypothyroid, 8 (4%) hyperthyroid and 163 (81.5%) euthyroid. Vezali *et al*[11] showed the frequency of hypothyroidism was 18%. 61 patients received interferon therapy out of them 11 (18%) became hypothyroid, 2 (3.3%) hyperthyroid and 48 (78.7%) remained euthyroid. Yan *et al*[12] investigated the frequency of hypothyroidism was 6.4%. Out of 592 treated patients there were 38 (6.4%) hypothyroid, 30(5.1%) hyperthyroid and 524 (88.5%) euthyroid. Bini *et al*[13] concluded that 8% of patients developed hypothyroidism. There were 18 (8%) hypothyroid, 6 (2.7%) hyperthyroid and 201 (89.3%) euthyroid out of 225 patients. Foldes *et al*[15] showed that hypothyroidism was seen in 12 (8.7%) out of 138 patients. So it is concluded that the results of all previously conducted studies by different investigators are comparable with the results of this study.

CONCLUSION

It is concluded from this study that there is increase frequency of hypothyroidism in patients with chronic hepatitis C who are treated with pegylated interferon therapy. Frequency of hypothyroidism was found to be 14.5%. It is also concluded that females have greater risk of developing thyroid dysfunction, particularly hypothyroidism after interferon therapy as compared to male.

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