ORIGINAL ARTICLE

Chronic Hepatitis C - A Study of 105 Cases Between 1990 - 2000

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Summary

An analysis of 105 consecutive patients with chronic hepatitis C at the gastroenterology outpatient's clinic in Hospital Kuala Lumpur was performed. The clinical, laboratory and virological data was prospectively recorded in the case notes and comprised of data on patient characteristics, risk factors, clinical features, laboratory features, virology screen and management.

Chronic Hepatitis C cases accounted for 2.1% of the total number of cases seen at this clinic during the entire period. There were 78 (74%) males and 27 (26%) females. The ethnic breakdown consisted of Chinese (44.2%), Malays (39.4%), Indians (15.4%) and others (1%). There was higher male preponderance in all the ethnic groups. The main mode of transmission was blood transfusion comprising 51 patients (48.8%).

A total of 35.2% of cases underwent treatment, of which a proportion had interferon monotherapy for 6 or 12 months and a subsequent group of naïve patients and non-responders underwent combination therapy with interferon and ribavarin.

Key Words: Chronic Hepatitis C, Interferon, Ribavarin

Introduction

The hepatitis C virus (HCV) is the leading cause of chronic liver disease worldwide[1]. It is estimated that about 170 million people are chronically infected with HCV. Chronic hepatitis C is a major cause of cirrhosis, and hepatocellular carcinoma. HCV- related end stage liver disease is, in many countries, the commonest cause of liver transplantation[1]. HCV exhibits high genetic variability, and therefore it has the capability to escape the immune response of the host. Some studies suggest that HCV persistence is related to the high mutation rate of HCV and the continual turnover of complex viral quasispecies that are able to evade the immune response of the host[2,3].

The interval between HCV infection and the subsequent development of significant liver disease can indeed be very long. The mean interval time between blood transfusion and the diagnosis of HCC was about 29 years. In those with cirrhosis without HCC it was about 21 years, while the development of chronic hepatitis was 10 years from the initial transfusion[4].

We report our experience of 105 cases over a period of 10 years.

Materials and Methods

One hundred and five consecutive hepatitis cases were seen were seen from late 1990 to March 2000 at the outpatients clinic, Department of Medicine, Hospital Kuala Lumpur. The data obtained was analyzed for patient characteristics, risk factors, clinical features, laboratory features, virology screen and management in order to formulate a database for chronic hepatitis C in Hospital Kuala Lumpur.

There were 78 males and 27 females. The mean age at presentation was 39.5 years, (range: 16 to 63 years).

Results

Hepatitis C accounted for about 2.1% of cases seen in the hepatobiliary outpatient clinics during the study period. The demographic characteristics, modes of transmission and clinical features are summarized in Figures 1 to 4.

Elevated alanine transaminases were seen in 89 patients (84.8%) compared to 16 patients (15.2%) who had normal transaminases. The normal transaminases were noted despite persistently testing positive for the virus.

In patients with elevated alanine transaminases, the level of elevation did not correlate with either severity or the presence of symptoms.

The mean serum albumin concentration in patients older than 40 years was significantly lower than that in younger patients. Portal hypertension was also more common in older patients.

Ultrasound was performed in 82 patients (78.1%). The rest of the cases had defaulted after their first or second visits.

Liver biopsies were performed on 62 patients (59.1%), with an intention to treat these patients with specific antiviral therapy. All cases that underwent biopsy had elevated alanine transaminases and invariably had chronic active hepatitis. Patients with normal alanine transaminase did not undergo liver biopsy. There were no complications of liver biopsy.

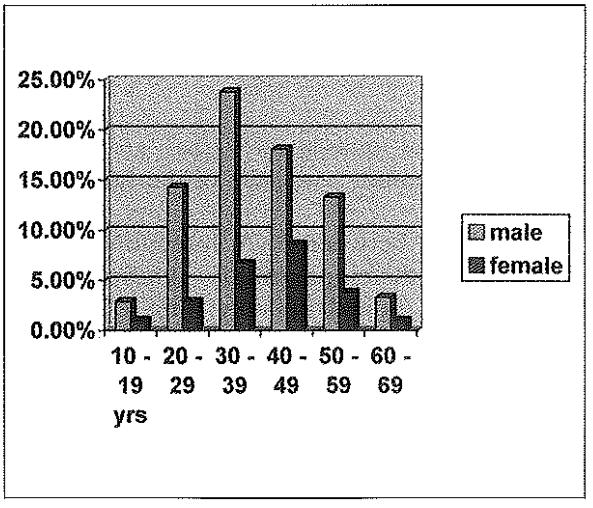

Fig. 1: Distribution of 105 Chronic Hepatitis C patients according to age and gender.

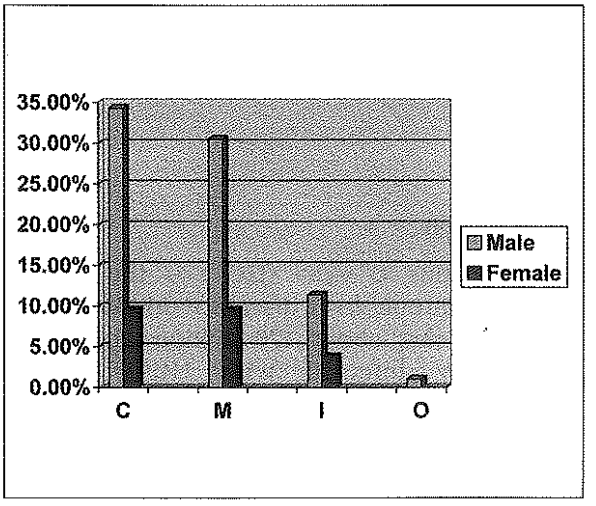

Fig. 2: The ethnic and sexual breakdown in the incidence of Chronic Hepatitis C (C-Chinese, M-Malay, I-Indian and O-Others).

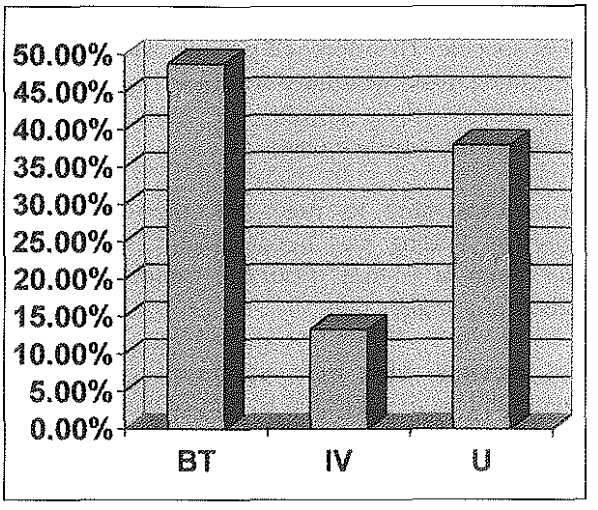

Fig. 3: Frequency of the different modes of transmission of the Hepatitis C virus in this series (BT- Blood Transfusion, IV- Intravenous Drug Abuse, U- Unknown).

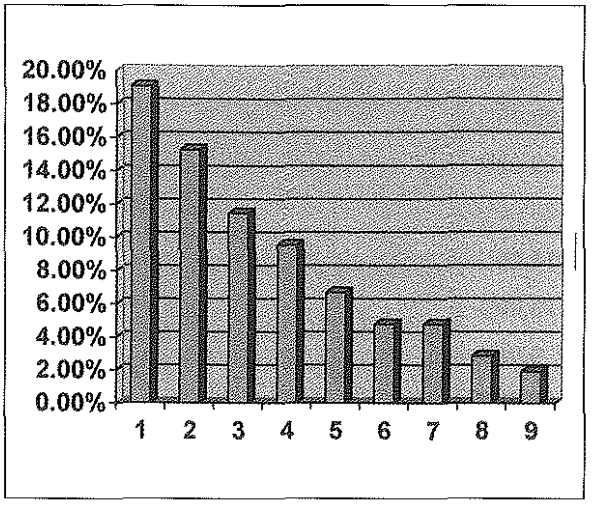

Fig. 4: Distribution of physical signs (1-hepatomegaly, 2-palmar erythema, 3-spider naevi, 4-splenomegaly, 5-ascites, 6-gynaecomastia, 7- clubbing, 8-scratch marks, 9-shiny nails).

The complications seen were oesophageal varices in 12 patients (11.4%) and hepatocellular carcinoma in 3 patients (2.9%). There was only one patient who exhibited extrahepatic manifestation and this was in the form of glomerulonephritis.

A total of 37 patients (35.2%) underwent a complete course of treatment with interferon for a duration of either 6 or 12 months. Treatment was offered to patients who fulfilled the virological and histological criteria.

End of treatment response, which was defined as absence of HCV RNA by polymerase chain reaction (PCR) at the end of the treatment course was seen in 16 patients (46%) and sustained response, defined as absence of HCV RNA by PCR at 6 months after treatment completion was seen in 11 patients (10.1%). A total of 27 patients (72%) received the one year treatment regime, while the remaining 10 patients (28%) received the 6 month treatment regime. Sustained response was more common in the subgroup treated with interferon for one year (83%).

The combination therapy of interferon and ribavarin has been used in 21 cases. This group comprised of those who have failed interferon monotherapy (13 cases) and treatment naïve patients (8 cases).

At the present time, 10 patients have completed the full follow up period of 6 months post treatment. They comprise of 7 males and 3 females with a mean age of 42.5 years (range: 27 - 62 years). At the end of treatment, virological response was seen in 6 cases (60%) and subsequently 5 (50%) have shown a sustained virological response. The remaining 11 cases are still undergoing treatment or are in the follow up period.

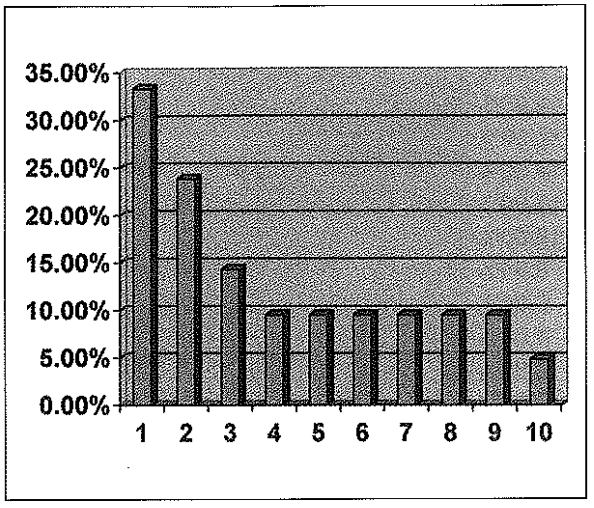

Fig. 5: Frequency of side effects in the combination (interferon + ribavarin) treatment group.
(1-fatigue, 2-headache, 3-diarrhoea, 4-anorexia, 5-dizziness,6-fever, 7-nausea, 8-depression, 9-rash, 10-hair loss).

Side effects are illustrated in Figure 5.
There was one patient who experienced a significant drop in haemoglobin (Hb) levels by 2.4gm/dl to below 10gm/dl. The dose of ribavarin was reduced and Hb levels normalized at the end of treatment.

Discussion

Chronic Hepatitis C is a significant cause of chronic liver disease. It can result in chronic liver disease and progression to liver cirrhosis with complications like portal hypertension and hepatocellular carcinoma. The duration of disease was important as complications were more frequently seen in the older age group.

It is a disease where a high index of suspicion should be maintained as it is largely asymptomatic and even when symptomatic, the symptoms are non-specific. Therefore, all patients with high risk including those who have had blood transfusions, intravenous drug abusers or multiple sexual partners must be screened.

It is interesting to note that the commonest physical finding was hepatomegaly, which was also seen in a study[5] from the United Kingdom, albeit at a higher rate.

All patients who were supposed to undergo treatment were subjected to a liver biopsy.

This was to determine the severity and activity of liver disease. It is also useful to help rule out other forms of liver disease such as concurrent alcoholic liver disease, medication induced liver injury and iron overload.

As a result of the high variability of reporting of liver histology in this series, it was not possible to stratify all the histology in terms of severity. However, at present time, histology scoring is being done and therefore in future, more comprehensive stratification will be possible. It is a safe procedure when performed under ultrasound guidance[6,7].

It is also a potentially treatable condition. Interferon monotherapy for 12 months was superior to 6 months therapy in this study[8]. It results in a significantly better sustained virological response which is crucial in ameliorating progression of liver disease. The combination of interferon with ribavarin has resulted in further improvements in response rates by up to 5 times in this database. This is generally higher than has been seen in other studies[9] but may reflect the smaller numbers in this treatment subgroup.

This treatment strategy for all patients who require treatment as first line therapy has been shown to be cost effective elsewhere[10]. Therapeutic strategy should include the monitoring of HCV RNA at 24 weeks of treatment.

We were not able to monitor genotype in all patients due the unavailability of this test readily and the costs involved. However, although we acknowledge that this will be the best treatment strategy[10,11] it was felt that treatment should not be denied to those patients where genotype was not available. Treatment was given to patients who had moderately severe or progressive liver disease.

Two large trials have confirmed the superiority of combination treatment with interferon and ribavarin[9,12].

In conclusion, Chronic Hepatitis C has significant healthcare implications. With the advent of more potent agents, the disease is becoming more effectively treatable. As screening methods become more efficient and disease awareness grows, we expect more cases to be detected and therefore more cases will require definitive antiviral therapy.

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