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Hepatitis C Virus Infection: A Single Center Experience

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Background: HCV infection is increasing and the number of patients evaluated is a fraction of the total population. There is no previous study in Bahrain documenting the characteristics of these patients, their risk factors, presentation, source of referral, viral load and genotyping, response to therapy and their follow up.

Objective: The aim of this study is to evaluate the characteristics of patients with hepatitis C virus infection and their response to therapy.

Setting: Gastroenterology Unit, Department of Internal Medicine at SMC.

Design: Retrospective study.

Method: One hundred and eighty-three patients with hepatitis C virus infection identified based on positive HCV RNA test, were reviewed between January 2002 and March 2006. Only adult patients with records have been included. Children were excluded.

Result: One hundred and twenty-five males (68.3%) and 58 (31.7%) females with HCV infection were reviewed. The mean age was 42 years. The most common risk factor was history of blood transfusion in 64 patients (35%). Primary health care was the main source of referral in 39 (21.3%). The average period between exposure to presentation was 12.7 years. Many patients 77 (42.1%) had signs or symptoms of liver disease at presentation. The HCV RNA viral load was low (<600,000 IU/ml) in 79 (43.2%) patients. Most patients had genotype one 67 (36.6%). Only 54 patients had their treatment documented and their records were available for analysis. Twenty-three patients 23/54 (42.6%) had achieved sustained viral response (SVR). One hundred and twenty-nine patients (70.5%) had inadequate records on treatment and follow-up.

Conclusion: This study showed that blood transfusion is the main risk factor for HCV infection in Bahrain. HCV genotype one is the most common and many patients presented with low viral load. Many patients with HCV were not on treatment and many were not referred for further evaluation.

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Hepatitis C is the most common chronic blood-borne infection. It is transmitted primarily through blood or blood products. Hepatitis C chronically infects 130 million people

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worldwide, with an additional three to four million people newly infected each year[1-2]. It is a major cause of liver disease worldwide and a potential cause of substantial morbidity and mortality[3]. The prevalence of hepatitis C virus (HCV) varies throughout the world, with the highest number of infections reported in Egypt 6 – 28% (mean 22%)[4-8].

The majority of patients infected with HCV acquired the disease through intravenous drug use or blood transfusion[9]. The latter has become rare since routine testing of the blood supply for HCV had began in 1990[10-11]. Patients who had multiple transfusions, including those with thalassemia or hemophilia are at a higher risk of developing hepatitis C[12-14]. Since the use of treated or recombinant clotting factors, new cases of hepatitis C infection have become uncommon in those patients. The continued high prevalence of anti–HCV in thalassemia or hemophilia is due to past exposure to untreated concentrates[15-16].

Several co-factors like hepatitis B Virus (HBV) infection and alcohol consumption have been associated with an accelerated progression of hepatic fibrosis among HCV patients. There is also an increased incidence of HCV–related complications of chronic liver disease and hepatocellular carcinoma (HCC)[17-21].

Currently, there are six major genotypes of HCV. Although genotype one is the most common worldwide; there is considerable variation in different parts of the world[22-24]. Eighty-six percent of Saudi chronic hepatitis C cases are due to genotype one and four[25].

Treatment of hepatitis C had improved during the last two decades[26]. With the advent of successful therapy for hepatitis C, factors associated with treatment outcome had received further consideration.

Factors that can influence treatment success include genotype, age, sex, stage of liver disease, baseline hepatitis C viral load and prior treatment failure[27]. In particular, advanced liver disease, characterized by bridging fibrosis on biopsy and manifestations of cirrhosis clinically, is associated with a worse treatment outcome. In addition, hepatitis C genotype one is substantially more difficult to treat compared with genotype two and three[28].

The aim of this study is to evaluate the characteristics of patients with hepatitis C virus infection and their response to therapy.

METHOD

Medical records of patients with positive HCV RNA were retrieved from the Salmaniya Medical Complex archives. Four hundred and seventy-eight HCV RNA positive test results were found between January 2002 and March 2006. Only adult patients with positive HCV RNA and available medical records were included in the study; children were excluded.

The medical records of 183 patients with HCV infection were reviewed retrospectively. Characteristics data documented included the following: patient's age, sex, birth nationality, source of referral, date of diagnosis of hepatitis C virus infection, symptoms and signs on presentation, risk factors and co-factors like (hepatitis B virus, alcohol, and HIV), investigations done (ultrasound abdomen, liver biopsy), HCV RNA viral load, HCV genotype, treatment given, response and follow–up when available.

The data were analyzed using the Statistical Package for the Social Sciences (SPSS).

RESULT

The medical records of 183 patients (125 males and 58 females) with Hepatitis C virus infection were reviewed. The mean age was 42 years ranging from 16 to 63 years. The age and gender distributions of the patients are illustrated in Table 1.

Table 1: General Characteristics

Characteristics		Total	Percentage
Age	<29	32	17.5
	30 – 39	36	19.7
	40 – 49	68	37.2
	≥50	47	25.7
Sex	Male	125	68.3
	Female	58	31.7
*Nationality	Bahraini	168	91.8
	Non Bahraini	15	8.2
Referral	Unknown	69	37.7
	PMH	39	21.3
	Hospital's Clinics	23	12.6
	Accident and Emergency	20	10.9
	Other hospitals	16	8.7
	Hospital's Wards	10	5.5
	Blood Bank	6	3.3
**Risk factors	Unknown	73	39.9
	Blood Transfusion	64	35
	***IVDU	31	16.9
	Hemoglobinopathy	24	13.1
	Tattoos	9	4.9
	Sexual	6	3.3
	Dialysis	6	3.3
	Operation	3	1.6
	Bleeding Disorders	3	1.6
Other risk factors	Alcohol	37	20.2
	Hepatitis B	6	3.3
	HIV	1	0.5
Total		183	

** Twenty patients of the Bahraini group had attained nationality at a later stage.*
*** Some patients had more than one risk factor.*
**** IVDU: Intravenous Drug Use.*

The majority were Bahraini. However, out of the 168 Bahraini patients, 20 patients had acquired the nationality at a later stage in their lives. Most of them were born in either Egypt or Syria; countries which are known to have high HCV prevalence (see Table 1).

The majority were referred from primary health care 39 (21.3%) followed by referrals from other clinics within the same hospital 23 (12.6%). Only 20 (10.9%) patients were referred from the emergency department. Ten (5.5%) patients were diagnosed as HCV

during their hospital admission. Only 6 (3.3%) of the referrals were from the Blood Bank, where candidates for blood donation are tested for HCV.

Seventy-three (39.9%) patients had no identifiable risk factor. History of blood transfusion was the most common cause of HCV infection and was found in 64 (35%) patients. Thirty-one (16.9%) patients were IV drug users, 24 (13.1%) patients had hemoglobinopathy with Sickle Cell Disease. Nine (4.9%) patients had tattoos, 6 (3.3%) patients had extramarital sexual contact, 6 (3.3%) patients were on hemodialysis for chronic renal failure, 3 (1.6%) patients had previous surgery, and 3 (1.6%) patients had bleeding disorders (see Table 1).

Thirty-seven (20.2%) patients were alcohol consumers; 6 (3.3%) patients had Hepatitis B, and only one patient had HIV (0.5%). Seventy-seven patients (42.1%) had symptoms and/or signs of chronic liver disease. Abdominal Ultrasounds were available for 102 (55.7%) patients; the results were normal in 63 (34.4%) and the rest showed some abnormalities, which indicates late presentation (see Table 2).

Table 2: Investigations

		Total	**Percentage**
*US abdomen	Not Done	81	44.3
	Normal	63	34.3
	Splenomegaly	27	14.8
	Hepatomegaly	19	10.4
	Cirrhosis	10	5.5
	Portal Hypertension	7	3.8
	Ascites	6	3.3
RNA load	<600.000 IU/ml	79	43.2
	>600.000 IU/ml	62	33.9
	Unknown	42	22.9
Genotype	Genotype 1	67	36.6
	Genotype 3	34	18.6
	Genotype 4	18	9.8
	Genotype 2	10	5.5
	Unknown	54	29.5
Liver biopsy	Not done	102	55.7
	Chronic Active Hepatitis (CAH)	54	29.5
	CAH + Fibrosis	11	6
	CAH + Cirrhosis	6	3.3
	Cirrhosis	5	2.7
	CAH + Fibrosis + Cirrhosis	2	1.1
	Fibrosis	2	1.1
	Normal	1	0.5
Total		**183**	

** Some patients had more than one finding on US.*

One hundred and forty-one (77%) patients had viral load at the time of referral. Seventy-nine (43.2%) patients had a low viral load (<600,000 IU/mL), whereas 62 (33.9%) patients had a high viral load (>600,000 IU/mL). Viral load was not available in 42 patients (23%).

Genotype one was the most common 67 (36.6%) followed by genotype three 34 (18.6%), genotype four 18 (9.8%), and genotype two 10 (5.5%) (see Table 2). Seventeen 17/29 (58.6%) patients with genotype three had high viral load compared to 24/57 (42.1%) of genotype one.

Table 3 shows the numbers and the percentages of each genotype in both HCV RNA groups. The genotypes of fifty-four patients were unknown and nineteen of those who had genotyping had no HCV RNA level, which makes a total of seventy-three patients.

Table 3: Genotypes and HCV RNA Levels*

	Genotype 1	**Genotype 2**	**Genotype 3**	**Genotype 4**	**Total**
HCV RNA <600.000 IU/ml	33/57 (57.9%)	4/7 (57.1%)	12/29 (41.4%)	7/17 (41.2%)	56/110 (50.9%)
HCV RNA >600.000 IU/ml	24/57 (42.1%)	3/7 (42.9%)	17/29 (58.6%)	10/17 (58.8%)	54/110 (49.1%)
Total	57/110 (51.8%)	7/110 (6.4%)	29/110 (26.4%)	17/110 (15.4%)	110

**The genotypes of fifty-four patients were unknown and nineteen of those who had genotyping had no HCVRNA level, which makes a total of Seventy-three patients.*

Liver Biopsy was done in 81 patients (44.3%). The most common finding was chronic active hepatitis (CAH) which was seen in 54/81 (66.6%) patients. Other histological findings are seen in Table 2.

Fifty-four patients received treatment and had adequate medical records for analysis. Some patients did not respond to the first course of treatment and thus given second and even third treatment course. Those who received only one treatment course were 36/54 (66.7%) patients; 19/36 (52.8%) patients had overall sustained viral response (SVR) that is negative HCV RNA six months post completion of therapy. Patients who received a second treatment course were 16/54 (29.6%) patients and 4/16 (25%) patients achieved SVR. Two patients (3.7%) were given the opportunity for a third treatment course and both were non-responders (see Table 4).

Table 4: Number of Treatment Courses Received

	Non – responder No. patients (%)	**Responder (SVR)* No. patients (%)**	**Total No. patients (%)**
1 Treatment course	17/36 (47.2%)	19/36 (52.8%)	36/54 (66.7%)
2 Treatment course	12/16 (75%)	4/16 (25%)	16/54 (29.6%)
3 Treatment course	2/2 (100%)	0/2 (0%)	2/54 (3.7%)
Total	31/54 (57.4%)	23/54 (42.6%)	54

** Sustained Viral Response.*

Fifty-four patients received 74 treatments. Each treatment group was evaluated separately. Ten patients received conventional Interferon monotherapy; only 1/10 (10%) patient achieved SVR while 9/10 (90%) were non-responders. Conventional Interferon

and Ribavirin was given to 23 patients whereby 9/23 (39.1%) achieved SVR and 14/23 (60.9%) were non-responders. Forty patients received Pegylated Interferon with Ribavirin. Peg-Interferon Alfa-2b (Peg-Interon) and Ribavirin were given to 19 patients; only 6/19 (31.6 %) achieved SVR. On the other hand, 21 patients received combination therapy with Peg-Interferon Alfa 2a (Pegasys) and Ribavirin; 7/21 (33.3%) achieved SVR. Only one patient received Peg-Interferon Alfa 2b (Peg-Interon) monotherapy and successfully responded to the treatment, see Table 5.

Table 5: Treatment Groups*

Treatments	Non – responder No. patients (%)	Responder (SVR) No. patients (%)	Total
Interferon	9/10 (90%)	1/10 (10%)	10
Interferon + Ribavirin	14/23 (60.9%)	9/23 (39.1%)	23
Peg – Interon + Ribavirin	13/19 (68.4%)	6/19 (31.6%)	19
Pegasys + Ribavirin	14/21 (66.7%)	7/21 (33.3%)	21
Peg - Interon	0/1 (0%)	1/1 (100%)	1

** Total treatment group is fifty-four, but some of these patients received more than one treatment. Therefore, the total number in this table is seventy-four.*

One hundred and twenty-nine patients (70.5%) had inadequate records of treatment and follow-up.

DISCUSSION

Bahrain based statistics of HCV showed that 349 new cases in the year 2003, 444 new cases in the year 2004, 588 new cases in the year 2005 and 426 new cases in the year 2006 were detected.

It seems that only small percentage is referred for further assessment. According to the blood bank records at SMC, 20 (0.14%) new Anti-HCV positive cases were detected after volunteering for blood donation in 2006 out of 14160 donors.

In this study, HCV infection was higher among males than females, which indicates high-risk behaviors among the former group. Most adults present with an age range of 40 to 49 years.

Since 1990, HCV has been rarely transmitted by blood transfusion[29]. Several studies had revealed that injection drug use is the single most important risk factor for HCV infection[30-31]. HBV, HCV and HIV infections remain a major hazard for children with hereditary hemolytic anemias, despite blood donor screening[32].

In this study, IV drug use is the second risk factor following blood transfusion. Blood transfusion is a major risk factor because of repeated blood transfusion for patients with thalassemia and sickle cell anemia, which are common blood disorders in Bahrain.

Only 21 patients had identified the time of probable exposure to HCV. The average time lapse was 12.7 years, which may explain the high percentage of patients presenting late with symptoms, signs or abnormal abdominal ultrasound.

The HCV genotype in the present study is similar to other studies in which genotype one predominates (36.6%) followed by genotype three (18.6%), genotype four (9.8%) and genotype two (5.5%). This study shows that HCV genotype one is the most common and is found in most patients infected during blood transfusion. HCV genotype three is found mainly in patients infected by IV drug use; it indicates that this genotype has been introduced concurrently with the spread of IV drug use and needle sharing. This finding is similar to several published studies[33-36]. Unlike many Middle Eastern countries, genotype four is uncommon in Bahrain.

In this study, most of genotype one patients had a low viral load at presentation while most patients with genotype three presented with high viral load. This may have an impact on their response to therapy and treatment plan.

Random International controlled trials have demonstrated an increasing sustained virological response (SVR) rate to interferon-based therapies in hepatitis-C-treated patients. Response rates of 6-20% in the era of interferon mono-therapy are compared with 42-82% using Pegylated Interferon plus Ribavirin. This is similar to our findings, where SVR was 10% in conventional Interferon mono-therapy group compared to 39.13% in combination therapy of Interferon and Ribavirin group[37-41]. SVR was almost the same (31.6-33.3%) in both groups of Pegylated Interferon combined with Ribavirin.

One hundred and twenty-nine patients (70.5%) had inadequate records on the treatment and follow-up. Those who had adequately documented treatment are only 54 patients, which is small number to draw any conclusion.

Certain limitations should be considered in the assessment of our findings. The loss of records and the difficulty of obtaining data from the available medical records resulted into the loss of valuable information needed for a better understanding and interpretation of the results. Another factor is the poor patient compliance and follow-up. Nearly half of the studied group missed their follow-up (54.6%). The newly diagnosed cases of HCV infection each year is around 400 cases. However, only few of them were seen in the gastroenterology unit. Further studies to analyze these patients may provide valuable information for understanding the magnitude of this disease.

CONCLUSION

Blood transfusion is the most common risk factor for contracting HCV in Bahrain. HCV genotype one is the most common in Bahrain. The majority of patients with HCV are not assessed or referred to tertiary care centers. There should be a stronger emphasis on the need for improving the maintenance of medical records and patient follow-up.

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