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Journal
International Journal of Medical Sciences, 1(2)

ISSN
1449-1907

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Publication Date
2004

DOI
10.7150/ijms.1.92

International Journal of Medical Sciences
ISSN 1449-1907 www.medsci.org 2004 1(2):92-100

Research paper

Received: 2004.3.24
Accepted: 2004.5.05
Published:2004.6.01

Clinical Profiles of Chronic Hepatitis C in a Major County Medical Center Outpatient Setting in United States

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Abstract

The estimated prevalence of hepatitis C virus (HCV) infection in the US is 1.8 %. Data are limited on the clinical profile of the disease at first presentation and dynamic follow-up of ALT level, especially in publicly-funded patients. This information is critical for optimal management of these patients. The present study is aimed to assess the clinical profiles of chronic hepatitis C (CHC) at first presentation and clinical implication of dynamic follow-up of ALT level in a county medical center setting. A total of 294 patients were selected from the population consecutively evaluated in the Hepatitis Clinic at Los Angeles County-USC Medical Center between Jan. 1990 and Dec. 1998. Ethnicity of the patients was Hispanics-49.0%, Caucasian-28.6%, African American-13.6%, and Asian-8.8%. Risk factors were identifiable in 84.0% of patients, and injection drug use (IDU) represented the leading risk factor for HCV acquisition (47.4%). History of alcoholism was present in 39.1%. The initial clinical diagnoses were chronic hepatitis 76.9%; compensated cirrhosis 20.4%; and decompensated cirrhosis 2.7%. Elevation of ALT, alpha fetoprotein (AFP), ferritin, and anti-nuclear antibody (ANA) titer were seen in 219/294 (74.5%), 60/194 (30.9%), 20/83 (24.1%), and 35/97 (36.1%) patients, respectively. Anti-HBc (total) test was positive in 65/129 (50.5%) patients. The presence of cirrhosis was significantly associated with age greater than 55 years at entry, female gender, non-African American ethnicity, history of transfusion, lower level of albumin and elevated level of AFP. Longitudinal observation of ALT changes in 178 patients who had neither evidence of cirrhosis at entry nor received interferon treatment showed persistently normal, intermittently or persistently elevated ALT level in 15.2%, 38.3%, and 46.6% patients, respectively. The frequency of developing clinical evidence of cirrhosis during follow-up was significantly higher in patients with persistently (16.0%) or intermittently (7.0%) elevated ALT than that in patients with persistently normal ALT (4.0%). In conclusion, the present study analyzed the clinical profiles of CHC, assessed risk factors for developing cirrhosis, and demonstrated the clinical value of dynamic follow-up of ALT level in a cohort of publicly-funded patients. These data have major implications in designing optimal strategies for disease management, antiviral therapy, and screening for hepatocellular carcinoma in patients with CHC.

Key words chronic hepatitis C, clinical profiles, US publicly-funded patients

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1. INTRODUCTION

Hepatitis C virus (HCV) infection affects approximately 4 million people in the United States [1]. Studies have shown that more than 80% of the HCV infections become chronic, which may progress to cirrhosis and complicated by hepatic decompensation and hepatocellular carcinoma (HCC) [2-4]. HCV-related end-stage liver disease is currently the leading cause of liver transplantation in this country [5]. A computerized projection study showed a rapidly increasing health burden of HCV-related diseases in the next two decades [6]. Treatment of chronic hepatitis C (CHC) with either conventional or pegylated alpha interferon and ribavirin can induce a sustained virologic response [7-10], which is associated with subsequent marked improvement in liver histology [11]. It is therefore necessary to determine which patients may benefit from the treatment.

Extensive studies have focused on the natural history of HCV infection [12-23]. An early study indicated a poor prognosis of HCV cirrhosis [14]. However, subsequent large cohort studies showed that the long-term outcomes of HCV cirrhosis, although progressive, are more variable [17, 19-21, 23-25]. Our knowledge about clinical profiles of CHC at the initial presentation and the factors which affect disease progression, especially from CHC to cirrhosis, remains limited. Data on these issues are particularly lacking in publicly-funded patients. However, such data are essential for us to provide these patients with improved quality and cost-effective care.

It is well known that CHC is associated with a wide variation in ALT, from normal ALT to persistent elevation of ALT. Although studies have shown that patients with persistently normal ALT usually have slower progression and lower prevalence of cirrhosis [23], the clinical importance of dynamic ALT follow-up for the disease activity and predict disease progression remains to be defined.

Occult or latent hepatitis B virus (HBV) infection is defined as the detectability of HBV DNA in the absence of HBsAg. Recent studies have raised the concern that occult HBV infection may play a role in disease progression and treatment response of CHC [26-28]. However, the prevalence of occult HBV infection in these patients and its true role in HCV pathogenesis remains to be determined.

The present study was aimed at assessing the clinical profiles of CHC, including the initial presentation, spectrum of the disease, factors associated with HCV cirrhosis, and prevalence of previous HBV infection as evidenced by total anti-HBc in publicly-funded patients in a major county medical center outpatient setting. The dynamic changes in ALT and their correlation with development of clinical evidence of cirrhosis was also assessed.

2. PATIENTS AND METHODS

Patient Population

Patients were consecutively collected from the Hepatitis Clinic at Los Angeles County-USC Medical Center between January 1990 and December 1998. The inclusion criteria included: chronic HCV infection demonstrated by anti-HCV and/or HCV RNA reverse-transcriptase polymerase chain reaction (RT-PCR); negative serologic test for hepatitis B surface antigen (HBsAg); exclusion of HCC by either ultrasonography, alpha fetoprotein (AFP) level, or pathological evidence; absence of evidence for other non-HCV-related liver diseases (i.e. autoimmune hepatitis in the absence of CHC, hemochromotosis etc.), and minimal follow-up of 12 months with regular ALT monitoring approximately every 6 (ranging 5-7) months. All enrolled patients with history of injection drug use (IDU) also had documented negative serology for anti-HIV. A total of 294 patients who fulfilled the criteria were included in the present study.

Patients were classified as having CHC, cirrhosis or hepatic decompensation based on either clinical or pathological criteria on initial presentation as previously reported [21]. Seventy-nine patients underwent liver biopsy. CHC was defined as positive serum anti-HCV and/or HCV RNA PCR lasted for longer than 6 months with either elevated or normal transaminases. HCV-cirrhosis was based on either liver biopsy evaluated by international pathological criteria [29], or a clinical discriminant score as reported by Bonacini et al [30]. The discriminant score consists of levels of platelet count, prothrombin time (PT), and ALT/AST ratio. A score of higher than 8 is the criteria for diagnosing cirrhosis. The specificity of the discriminant score in diagnosing advanced fibrosis or cirrhosis was reported to be 98% [30]. The criteria for decompensation were as previously reported [14, 20], and included the presence of ascites, jaundice (total bilirubin > 3 mg/dL or 51 μmol/L), variceal bleeding, or hepatic encephalopathy. Clinical evidence of cirrhosis was reassessed with discriminant score [30] during follow-up in a subgroup of patients (n=178) who neither received interferon treatment, nor had a diagnosis of cirrhosis at entry. The term “entry” was defined as the first time when patients were seen in the hepatitis clinic.

To verify the accuracy of clinical discriminant score in diagnosing cirrhosis, the clinical diagnosis was further assessed in 79 patients who had pathological diagnosis. Compared to pathological diagnosis, the sensitivity and specificity of the clinical discriminant score in diagnosing cirrhosis were

81.3% and 100%, respectively. Thus, the clinical discriminant score may underestimate the incidence of cirrhosis, but provide a reliable clinical diagnosis in these patients as previously reported [30].

Variables and Follow-up

To identify the factors associated with clinical presentation and disease progression in patients with chronic HCV infection, a series of epidemiological, clinical and biochemical variables were collected at entry through a retrospective chart review. The clinical variables collected included age at entry, gender, risk factors for HCV acquisition, presumed age at initial exposure and duration of HCV infection, history of alcoholism. The biochemical variables collected included serum levels of ALT, AST, ALT/AST ratio, albumin, PT, platelet counts. A portion of patients had also received assays of alpha fetoprotein (AFP, n=194), anti-nuclear antibody (ANA, n=97), and ferritin (n=83). The virological variables collected included anti-HCV by second generation of immunoenzyme assay, HCV RNA by RT-PCR, HBsAg, and anti-HBc total (simplified as anti-HBc below). Anti-HBc was assessed in 129 patients in the present study. For patients with high risk for HIV infection, anti-HIV was also tested.

History of alcohol consumption was collected, and alcoholism was defined as daily heavy drinking (> 50 g) for longer than 5 years [17, 20]. However, we were unable to distinguish active drinking from inactive drinking due to the limitation of retrospective chart review. In evaluating risks of parenteral exposure, the time of first exposure to either IDU, transfusion or tattoos was presumably the time of acquisition of HCV infection as previous reports [20]. If a patient had more than one risk, or more than one episode of the same exposure, the time when the patient initially experienced the first risk or first occasion of exposure was considered as presumed acquisition of HCV infection.

Statistical Analysis

The descriptive statistics were provided with mean ± SD or range. Either the χ^2 test or Wilcoxon nonparametric test was employed for analysis of qualitative or quantitative variables, respectively. Logistic regression [31] was used for both univariate and multivariate analysis. Both Chi-square test for trend and Kaplan-Meier survival analysis were used for analyzing the correlation of dynamic ALT follow-up with development of cirrhosis. Statistical software used in the present study was SAS program as previously reported [20].

3. RESULTS

Demographic and Epidemiological Profiles at Entry

Table 1 summarizes the initial demographic features of the cohort of patients enrolled into the present study. A total of 294 patients were included with a mean follow-up of 36.2 (12-108) months, and mean age of 46.2 (18-75) years at entry. The male to female ratio was 1.45:1 (174:120); 84 (28.6%) were Caucasians, and 210 (71.4%) were minorities, including 144 (49.0%) Hispanics, 40 (13.6 %) African Americans, and 26 (8.8%) Asians.

All 294 patients had documented positive anti-HCV antibodies, and 262 (89.1%) of these patients had also positive serum HCV RNA. All patients with history of IDU or other risk factors for HIV infection had a negative anti-HIV test. Fifty-one (17.3%) patients received 6-12 months duration of interferon (IFN) monotherapy during follow-up, and 14 (27.5%) patients achieved sustained viral response as defined by negative HCV RNA PCR 6 months after IFN treatment.

Of the 294 patients, 247(84.0%) had identifiable risks of exposure to HCV infection. History of IDU was present in 117 patients (47.4%) representing the most common risk of exposure in this cohort of patients. The other risks included blood transfusion in 94 cases (38.1%); tattoos in 27 (10.9%) case, intranasal cocaine in 5 (2.0%), and needle sticks related to health care in 4 (1.6%) cases. More than one risk factor was identified in 71 (28.7%) patients. History of IDU was significantly common in male patients (52.3%) than in female patients (21.7%, $p = 0.001$). History of transfusion whereas was significantly more common in female patients (49.2%) than in male patients (20.1%, $p = 0.001$). The mean age at first exposure was significantly younger in patients with IDU (24.3 years) than those with transfusion (31.7 years, $p = 0.0003$).

History of alcoholism was present in 115 (39.1%) patients, who were significantly younger than those without history of alcoholism ($p = 0.007$). History of alcoholism was significantly more common in male patients (50.6%) than female patients (22.5%, $p = 0.0001$). Multivariate logistic analysis showed that both age and male sex were independently associated with the history of alcoholism.

Clinical Profiles at Entry

As summarized in Table 1, 219 (74.5%) patients presented with elevated ALT, which was < 2.5 times of the upper limit of normal (ULN) ALT level in 130 (59.4%) patients, 2.5- 5 times ULN in 68 (31.1%) patients, and > 5 times ULN in 21 (9.6%), respectively. Initial normal ALT was seen in 75 (25.5%) patients. The initial diagnosis included CHC in 226 (76.9%) cases, compensated cirrhosis in 60

(20.4%) cases, and decompensated cirrhosis in 8 (2.7%) cases. In 226 patients with chronic hepatitis C, 56 (24.7%) had normal ALT at initial presentation. We were able to estimate the time interval between initial exposure and entry to the study in183 patients. The mean intervals from initial exposure to entry for patients with CHC, compensated cirrhosis, and hepatic decompensation were 17.1 (±8.5) years, 20.5 (± 8.0) years, and 30.0 (±5.5) years, respectively.

As shown in Table 1, 60/194 (30.9%) had elevated AFP at entry; 20/83 (24.1%) had elevated ferritin, and 35/97 (36.1%) had ANA titer greater than 1:80. Five (1.7%) had pathologically confirmed overlap syndrome, 4 with coexisting autoimmune hepatitis and 1 had coexisting autoimmune cholangiopathy.

In the present study, decreased ALT/AST ratio, prolonged PT and thrombocytopenia were used for the clinical diagnosis of cirrhosis [30]. This would limit the value of these three variables to predict development of cirrhosis in the present study. Thus, they were excluded from the following univariate and multivariate analysis. Univariate analysis of the remaining factors showed that presentation of cirrhosis, including hepatic decompensation, was significantly associated with age greater than 55 years at entry, time interval from exposure to entry, female gender, ethnicity, history of transfusion as risk of HCV requisition, albumin level lower than 3.5 mg/dl and AFP level great than 20 μg/L (Table 2). Cirrhosis was more frequently seen in patients with history of transfusion than those with history of IDU, but difference was not significant (Table 2). The presence of cirrhosis was not significantly associated with age at initial exposure, history of alcoholism, initial levels of ALT, AST, ferritin or ANA titer (data not shown). Multivariate logistic analysis showed that after adjusting gender, risk of HCV exposure, and albumin level, age at entry was independently and positively associated with cirrhosis (p=0.0001), but African American ethnicity was independently and negatively associated with presence of cirrhosis (p=0.014, data not shown).

Although none of this cohort of patients had detectable HBsAg, 129 patients were tested for total anti-HBc and 65 (50.5%) had positive results. Univariate analysis showed that positive anti-HBc was significantly correlated with history of IDU (OR=3.2, p = 0.008) as compared with history of transfusion. In addition, positive anti-HBc was more common in Hispanics than in Caucasians (63.2% vs. 38.5%, p = 0.015). Although Asian ethnic group appeared to have an increased frequency of anti-HBc (90.9% vs. 63.2%) this difference did not attain statistical significance (p=0.079). Anti-HBc status was not statistically associated with age at entry, history of alcoholism, diagnosis of cirrhosis, levels of ALT, AST, albumin, PT, AFP, or platelet counts.

Dynamic ALT Changes and the Clinical Implication

In order to evaluate the relationship between ALT changes and HCV-related disease progression, we analyzed dynamic changes of ALT in a subgroup of patients (n=178), who had neither cirrhosis at entry nor received IFN treatment during follow-up. These patients were longitudinally observed for ALT changes approximately every 6 months. The initial ALT was normal in 50/178 (28.1%) patients. During follow-up (mean 35.2 months, range 12-108), 27 (15.2%) showed persistently normal, 68 (38.2%), fluctuated, and 83 (46.6%), persistently elevated ALT levels. Twenty-three (12.9%) patients developed clinical evidence of cirrhosis [30], which is approximately 4.3% annually. The mean interval from entry to diagnosis of cirrhosis was 40.8 ± 27.9 months (i.e. 3.4 ± 2.3 years). The incidence of developing cirrhosis was 4.0% in patients with persistently normal ALT, 7.0% in patients with fluctuated ALT, and 16.0% in patients with persistently elevated ALT. The statistical analysis was significant by both Chi-square test for trend (p=0.043) and Kaplan-Meier survival analysis (p=0.0013).

4. DISCUSSION

Chronic HCV infection represents one of the major public health problems in the United States and worldwide. Approximately 20-30% of patients with chronic HCV infection will progress to cirrhosis [2, 3], which can be further complicated by hepatic decompensation and development of HCC [2-4]. While remarkable knowledge of the natural history of this disease have been gained in the past few years, data on special groups of the patients, including the US veterans and publicly-funded patients, remain limited. Yet, this information is essential for providing these patients with better quality and cost-effective care. This study assessed the clinical profiles and natural history of CHC in a cohort of publicly-funded patients.

The present study included 294 patients with CHC who were followed in the Hepatitis Clinic at USC-LAC Medical Center. In these patients, 71.4% were minorities, including African American, Hispanic, and Asian patients, indicating that a high prevalence of HCV infection is also present in the minorities of publicly-funded patients in the United States. The frequency of identifiable risk factors for HCV acquisition in our patients was 84.0%, which is similar to those as previously reported [15, 32]. Although studies indicated blood transfusion was the leading risk factor for HCV acquisition [15, 20, 32], IDU was the most frequent risk factor for HCV acquisition in our patient group. Consistent with a previous report [32], the male patients tended to have history of IDU, whereas, female patients tended to have history of transfusion in this cohort of patients.

At entry, 74.5% of patients presented with elevated ALT, and majority (59.4%) of them had ALT elevation less than 2.5 times of ULN. Pathological, clinical or unltrasonopraphic evidence of cirrhosis was present in 23.1% of patients, including 2.7% with hepatic decompensation. The frequency of elevated ALT and cirrhosis in this cohort of publicly-funded patients is almost same as other patient groups as previously reported [2, 3, 15, 19]. However, it should be noted that our results might underestimate the frequency of cirrhosis since clinical diagnosis based on clinical discriminant score is less sensitive than histopathologic diagnosis. The estimated mean intervals from initial exposure to cirrhosis and hepatic decompensation were 20.5 years and 30.0 years, respectively, which fell into the ranges as previously reported [14, 17, 20]. These findings suggest that the disease progression of CHC in publicly-funded patients appears similar to other patient groups.

Consistent with previous studies [15, 20, 32, 33], cirrhosis is correlated with age at entry and lower level of serum albumin, but not with initial ALT and AST levels in our patients. The present study further supported most other [14, 15, 20, 32], but not all [19] reports that patients with history of transfusion are more likely to develop cirrhosis than those with history of IDU. However, this difference was not statistically significant. Studies have shown that male patients are more likely to develop fibrosis/cirrhosis than female patients [32, 33]. It remains to be determined whether a higher frequency of history of transfusion in the females had contributed to the disparate results. Nevertheless, our data indicated that a special attention should be paid to female patients in the publicly-funded setting due to a higher incidence of cirrhosis. We also found that African American patients tended to have a significantly low incidence of cirrhosis than other ethnic groups. Since African Americans represented a relative small portion of this cohort of patients, the clinical importance of this finding remains to be determined.

AFP is an embryotic protein which has been used for diagnosing HCC. Studies have shown that elevation of AFP is frequently seen in patients with CHC, especially in those with HCV-cirrhosis. However, the frequency of AFP elevation varied from 10% to 43% in those patients [14, 17, 34-36]. In our patients, 30.9% had AFP elevation greater than 20 μg/L. We also found that elevation of serum AFP to greater than 20 μg/L was present in as high as 42.1% patients with HCV-cirrhosis, which was significantly more frequent than in patients with CHC without evidence of cirrhosis. These data further supported our recent report that elevated AFP may serve as a clinical saraggate indicative of cirrhosis in patients with CHC, but without imaging evidence of hepatocellular carcinoma [36].

Approximately 14% to 37% of alcoholisms with liver disease have a positive anti-HCV test [37]. It has been well documented that alcohol consumption is associated with a more progression to HCV-fibrosis/cirrhosis [33, 37, 38]. However, the exact prevalence of alcoholism in patients with CHC remains to be determined, although a European study showed it was as high as 34.9% [15]. We found that history of alcohol consumption was present in 39.1% of our patients. Although the incidence of alcohol consumption was higher in patients with cirrhosis than in those without cirrhosis, the difference was not statistically significant. The similar results were reported in patients in Australia and New Zealand [39].

A positive, but low titer of ANA is reported as a common clinical presentation in patients with CHC [40, 41]. ANA titer greater than 1:80 was seen in 36.1 % of this publicly-funded cohort of patients, which is higher than previous reports from European patients [41]. Five patients also presented with typical overlap syndrome, 4 with coexisting ANA positive autoimmune hepatitis, and 1 with coexisting AMA negative cholangiopathy. All 4 patients with overlap syndrome of CHC and autoimmne hepatitis had ANA titer $\geq$ 1:320. Our finding supports the value of high ANA titer in diagnosing autoimmunity in patients with CHC [40]. As previously reported, similar frequency of elevated ferritin was present in our patients [42].

Occult HBV infection is defined as HBV infection in the absence of detectable serum HBsAg, which may aggregate the disease progression, development of HCC, and decrease anti-HCV treatment response of CHC as indicated by most [16, 26-28, 43], but not all [39] studies. The prevalence of anti-HBc in patients with CHC in the United States remains to be determined. In the present study, we found that anti-HBc was detectable in 50.5 % of our patients, which was similar to that reported from Australia and New Zealand (50.8%) [39]. The prevalence of anti-HBc was significantly higher in patients with history of IDU, which may be due to the shared trasmission route of the two diseases. Among patients with positive anti-HBc, it was reported that 46% had detectable HBV DNA by HBV PCR [26]. Since we were unable to assess serum HBV DNA in these patients, the prevalence of the true occult HBV infection is unknown at this point.

Although the elevation of ALT was reported to be associated with the severity and progression of HCV disease [44, 45], the value of dynamic follow-up of ALT remains unclear. In the present study, we assessed the clinical implication of dynamic ALT changes in 178 patients who had no clinical evidence of cirrhosis at entry and did not receive IFN treatment during follow-up. With approximately 3 years follow-up, 15.2% maintained normal ALT, 38.2% and 44.6% presented with intermittently and persistently elevated ALT, respectively. At the entry the frequency of abnormal ALT in this cohort of patients was 25.5%, it was dropped to 15.2% during dynamical ALT follow-up. In addition, the

incidence of intermittent elevation of ALT was as high as 38.2% in our patients. These results indicate that dynamic follow-up of ALT provides a more accurate clinical assessment of disease activity in these patients.

The correlation of dynamic ALT changes with development of cirrhosis was largely unknown. In the present study, we found that during an approximately 3-year of dynamic follow-up, 12.9% of patients developed clinical evidence of cirrhosis, which is approximately 4.3 % each year. More importantly, the development of cirrhosis was significantly more frequent in patients with either intermittently or persistently elevated serum ALT levels than those with persistently normal levels of ALT. Although these results need to be re-confirmed by large cohort of prospective studies, our findings support and extend previous reports [21, 44] that both the increment and dynamics of ALT levels are important clinical parameters to predict disease progression.

In summary, by retrospectively assessing a large cohort of publicly-funded patients with CHC, we found that the demography, clinical spectrum of the disease, disease progression and the related factors are comparable to those as previously reported. However, in this group of patients, minorities account for as high as 71.4%, the frequency of alcoholism is as high as 39.1%, prevalence of anti-HBc is 50.5%, and females tend to have higher risk for HCV-cirrhosis. Dynamic ALT follow-up appears to provide a more accurate assessment of and prediction to the disease progression of CHC. Persistently or intermittently elevation of ALT predicts to a higher incidence of developing cirrhosis.

Conflict of interest:

None declared.

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Tables

Table 1. Demographic and Clinical Profiles at Initial Presentation

Variables	Data
Total cases:	294
Mean age at entry (range):	46.2 (18-75) years
Male to female ratio:	1.45:1 (174:120)
Mean F/U length (±SD):	36.2 (12-108) months
Ethnicity:	
Caucasian	84 (28.6%)
Hispanic	144 (49.0%)
African American	40 (13.6%)
Asian	26 (8.8%)
Identifiable risk factors (n=247):	DU 117 (47.4%)
	Trans. 94 (38.1%)
	Tattoos 27 (10.9%)
	Others 9 (3.6%)
History of Alcoholism:	Yes: 115 (39.1%)
	No: 179 (60.9%)
Initial diagnosis:	
Chronic hepatitis C	226 (76.9%)
Compensated cirrhosis	60 (20.4%)
Decompensated cirrhosis	8 (2.7%)
ALT elevation:	219/294 (74.5%)
AFP elevation:	60/194 (30.9%)
Ferritin elevation:	20/83 (24.1%)
Positive ANA (>1:80)	35/97 (36.1%)

Table 2. Univariate Analysis of the Variables Associated with Cirrhosis

Variables	Total Cases	Cirrhosis		
		Cases	OR (95% CI)	P Value
Age at Entry				
< 55 yr.	221	39		
≥ 55 yr.	73	29	3.1 (1.7-5.4)	0.001
Interval from exposure to entry				
< 19 yr	95	15		
≥19 yr.	88	28	2.5 (1.2-5.0)	0.011
Gender				
Male	174	31		
Female	120	37	2.1 (1.2-3.5)	0.009
Ethnicity				
Caucasians	84	21		
Hispanics	144	34	0.9 (0.5-1.7)	0.813
African Americans	40	3	0.2 (0.1-0.8)	0.022
Asians	26	10	1.9 (0.7-4.7)	0.184
Transmission				
IDU	117	20		
Transfusion	94	26	1.9 (1.0-3.6)	0.065
Albumin (3.5 mg/dL)				
≥ 3.5	265	45		
< 3.5	29	23	18.7 (8.8-40.1)	0.001
AFP (20 μg/L)				
≤ 20	164	38		

> 20	30	16	3.8 (1.8-8.2)	0.0001

Table 3 Dynamic Patterns of ALT Changes and Development of Cirrhosis*

ALT Patterns		Development of Cirrhosis#		
	Cases (n=178)	Cases	(%)	Odds Ratio
Persistently normal	27	1	4.0	1.0
Intermittently elevated	68	5	7.0	2.06
Persistently elevated	83	13	16.0	4.83

*P=0.043 (Chi-square test for trend)

#Diagnosis of cirrhosis was based on clinical evidence and SDS scores. The clinical evidence of cirrhosis was demonstrated during follow-up after entering to the study.

Author biography (continued from front page)

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