# Trends in epidemiological and clinical characteristics of HCV-infected patients over seven years: a french experience

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## Background

- To assess the impact of the first French national HCV control program implemented in 1999, a national hospital-based surveillance was set up in 2000 through Hepatology Reference Centres (HRC)
- We present its results in the context of ongoing preparation of harmonization and strengthening of Hepatitis C Virus (HCV) surveillance in Europe by the European Centre for Disease Prevention and Control (ECDC)

## Objectives

- To monitor changes in epidemiological and clinical characteristics of HCV-infected patients at first referral in HRC
- In order to contribute to the evaluation of the national HCV control program

## Methods

**Study period:** 2001-2007

**HRC definition:** 31 university hepatology wards specialized in the management of hepatitis C throughout France (26 participate to the network)

**Case definition:** newly referred (first contact) patients with positive anti-HCV antibodies attending any of the participating HRC (outpatient or inpatient)

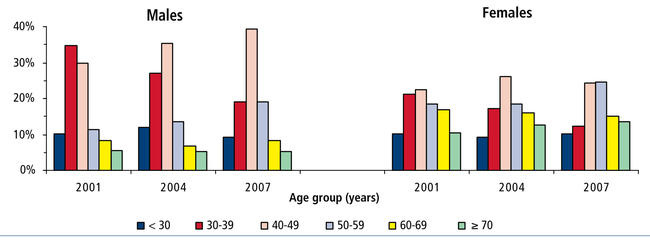
**Data collected**

- Patient's characteristics: age, gender, date of first referral to HRC
- Date and circumstances of anti-HCV testing: systematic screening, screening because of known risk exposure, diagnostic procedure
- HCV-risk exposures: IV or nasal drug use, blood transfusion before 1991, nosocomial exposure, occupational exposure, other (tattoo, piercing, travel in an endemic country…), unknown risk exposure
- Past excessive alcohol intake (>21 glasses/week for females; >28 glasses/week for males)
- Biological markers at referral: HCV RNA, genotype, HIV antibodies, HBs antigen
- Assessment of liver fibrosis by liver biopsy or non invasive method
- Clinical stage evaluation of the liver disease at referral

## Results

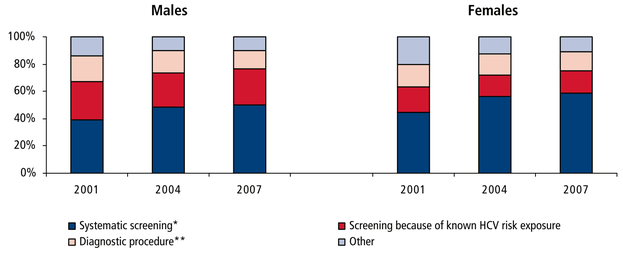
- Data are presented for the 23 continuously participating HRC during 2001-2007
- Number of patients declined: 3,336 in 2001 ; 2,791 in 2004 ; 2,423 in 2007
- Sex-ratio (M/F) remained stable: 1.3
- Median age increased from 41 to 45 in males and 48 to 52 in females (figure 1)

**Figure 1** Age distribution of anti-HCV patients newly referred to HRC by gender, France, 2001-2007




- Systematic screening:
  - main reason for HCV testing (figure 2)
  - increasingly reported (from 41.5 in 2001 to 53.9% in 2007) in males and females

**Figure 2** Distribution of circumstances of anti-HCV testing in anti-HCV patients newly referred to HRC by gender, France, 2001-2007




*For patients for whom only one circumstance was reported.*
** Systematic screening= during check-up, blood donation, before blood transfusion. ** Screening during diagnostic procedure for liver tests abnormalities, cirrhosis' complications, hepatocellular carcinoma investigation.*

- Major HCV-risk exposures (table 1): intravenous drug use for males; blood transfusion before 1991 for females

**Table 1** Reported HCV-risk exposures in anti-HCV patients newly referred to HRC by gender, France, 2001-2007

| | Males | | | | Females | | | |
|---|---|---|---|---|---|---|---|---|
| | 2001 n=1,870 | 2004 n=1,563 | 2007 n=1,367 | p | 2001 n=1,464 | 2004 n=1,228 | 2007 n=1,056 | p |
| Blood transfusion (<1991) | 23.4% | 21.1% | 17.8% | $<10^{-3}$ | 38.9% | 36.2% | 33.2% | $<10^{-2}$ |
| Intravenous or nasal drug use | 49.1% | 50.0% | 43.7% | $<10^{-2}$ | 21.9% | 20.4% | 18.4% | <0.05 |
| Occupational exposure | 1.9% | 1.3% | 1.2% | NS | 5.3% | 4.0% | 2.6% | $<10^{-2}$ |
| Nosocomial exposure* | 16.5% | 15.7% | 10.0% | $<10^{-3}$ | 22.3% | 25.8% | 14.8% | $<10^{-3}$ |
| Other risk exposure** | 14.6% | 16.4% | 14.1% | NS | 13.8% | 19.5% | 16.6% | <0.05 |
| None | 14.0% | 15.5% | 17.6% | $<10^{-2}$ | 15.5% | 16.0% | 19.9% | $<10^{-2}$ |

*Total>100%; NS=non significant (α=5%). - * Surgery, hemodialysis, endoscopy… - ** Tattoo, travel in an endemic country…*

- HCV genotyping increasingly performed: 70.0% in 2001 (available for 81%) 87.3% in 2007 (available for 87%)
- HCV genotype distribution was stable on 2001-2007, most frequent HCV genotypes remaining in 2007: 1b (31.2%), 3 (18.6%) and 1a (17.3%)
- Liver biopsy performed: 48.7% in 2001 (available for 95%) 15.7% in 2007 (available for 94%)
- Non invasive assessment of liver fibrosis: 27.6% in 2004 (available for 70%) 51.6% in 2007 (available for 83%)
- The proportion of patients reporting past excessive alcohol intake:
  - remained stable between 2001 and 2006 (34.7% in 2006) and decreased in 2007 (28.9%) in males
  - was constant in females over the 7-year period (10.3% in 2007)
  - was higher and stable among men and women who acknowledged drug use (44.0% and 32.0% respectively in 2007)
- HBs antigen and anti-HIV seropositivity proportions remained constant over the period (3.8% and 6.6% in 2007, respectively)
- The proportion of severe liver disease at first referral in HRC increased from 10.9 % in 2001 to 13.8% in 2007 (table 2)

**Table 2** Distribution of clinical stage of the disease at clinical evaluation in anti-HCV patients newly referred to HRC, France, 2001-2007

| | 2001 n=3,336 | 2004 n=2,791 | 2007 n=2,423 |
|---|---|---|---|
| Information available | 87.0% | 93.1% | 89.4% |
| Acute hepatitis | 0.4% | 0.8% | 0.4% |
| Chronic hepatitis with normal ALT | 17.2% | 17.1% | 17.5% |
| Chronic hepatitis | 71.5% | 69.8% | 68.3% |
| Cirrhosis (compensated or not) | 10.2% | 11.2% | 11.5% |
| Hepatocellular carcinoma | 0.7% | 1.1% | 2.3% |

*For patients for whom clinical stage was different from recovering.*
*Chronic hepatitis with normal ALT: repeated ALT values. Chronic hepatitis: elevated ALT value, no clinical, morphological or biological signs of cirrhosis or hepatocellular carcinoma. Cirrhosis / hepatocellular carcinoma: diagnosis based on clinical, morphological and biochemical criteria.*

## Discussion

- High and increasing proportion of systematic screening among circumstances of HCV testing ➔ suggests a crucial need for optimizing hepatitis C screening in France
- Increasing proportion of severe liver disease at first referral:
  - may be related to:
    . a longer history of HCV-infection at first referral suggested by the rising age of patients
    . a remaining high proportion of past excessive alcohol intake
    . a modification of the patients' recruitment in the HRC, patients with less severe liver disease being referred to private sector preferentially
  - indicates that early screening and medical follow-up is still warranted for at-risk patients
- High remaining stable proportion of patients reporting excessive alcohol consumption reinforces the need to integrate the management of alcohol dependence among HCV-infected patients, especially among drug users

## Conclusion

In the context of ongoing preparation of harmonization and strengthening of HCV surveillance in Europe, we demonstrate that our system allowed the monitoring of changes in epidemiological and clinical characteristics of HCV-infected patients newly referred to HRC.

Associated with other systems (anti-HCV screening: blood donors, laboratories, anonymous testing sites) and cross-sectionnal studies (*e.g.* seroprevalence studies), it enables the description of HCV testing, care and treatment trends.

Complementary and flexible systems might be an interesting approach for harmonization of EU-wide surveillance.

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