Hepatitis C Epidemiology in Belgium

P. Van Damme¹, W. Laleman², P. Stärkel³, H. Van Vlierberghe⁴, D. Vandijck^{5,6}, S.J. Hindman⁷, H. Razavi⁷, C. Moreno⁸

(1) Universiteit Antwerpen, Antwerpen, Belgium; (2) University Hospitals Leuven, KU Leuven, Leuven, Belgium; (3) Cliniques Universitaires Saint-Luc, Université Catholique de Louvain (UCL), Brussel, Belgium; (4) Ghent University Hospital, Ghent, Belgium; (5) Ghent University, Ghent, Belgium; (6) Hasselt University, Dept. of Health Economics & Patient Safety, Diepenbeek, Belgium; (7) Center for Disease Analysis (CDA), Louisville, Colorado, USA; (8) Erasme University Hospital, Université Libre de Bruxelles, Brussels, Belgium.

Abstract

Background : The burden of hepatitis C virus (HCV) infection is significant and is increasing with the aging population. The results of a modeling study that included Belgium, along with many other countries, was published in April 2014. An in depth discussion surrounding the epidemiology of HCV in Belgium will be presented here.

Methods : A systematic literature review was conducted to assess the historical and current clinical burden of HCV in Belgium. Two expert panels were convened to discuss the strengths and limitations surrounding the available data and to generate consensus regarding the best estimates for total number of HCV cases, number of cases diagnosed, and the number of patients treated and cured, including potential HCV control strategies.

Results: Although no national studies exist, there were an estimated 70,000 (10,000-91,000) viremic HCV infections in 1994. By 2010 there were an estimated 22,900 individuals diagnosed with viremic HCV, and in 2011 approximately 710 patients were treated annually. An estimated 13% of liver transplants were attributable to HCV in 2011. Genotype 1 predominated (59%), followed by genotypes 3 (19%) and 4 (14%).

Conclusions : Estimates of HCV prevalence, diagnosed cases and liver transplants due to HCV were available through published studies. However these publications were subject to bias and were occasionally outdated. Improved estimates of HCV prevalence would be useful for informing treatment, prevention and policy efforts in Belgium. (Acta gastroenterol. belg., 2014, 77, 277-279).

Background

Chronic hepatitis C has an estimated prevalence of 0.87% in Belgium and is the primary viral etiology for liver transplantation. Moreover in 2000, Belgium was confronted with a HCV contaminated Cidex® (Johnson & Johnson Medical, UK) disinfection solution, causing several iatrogenic HCV infections after invasive medical procedures were performed at 60 hospitals across the country. A study based on the recall of patients with known exposure estimated that 99 of the 265 (37%) positive patients were aware of their status. This estimated screening rate is low compared to France. Currently no formal screening strategy exists in Belgium. However, the Belgian Association for the Study of the Liver (BASL) recommends targeted HCV screening for high risk populations (including individuals with a blood transfusion or major medical event prior to July 1, 1990, intranasal or intravenous drug users, and dialysis patients) in addition to non-systematic screening of preoperative patients and pregnant women (1). On average an estimated 345,000 anti-HCV tests are performed annually (1). Despite inadequate screening and dated

prevalence estimates, efforts to improve screening and HCV data quality have not been initiated. Moreover, following a diagnosis the likelihood of initiating treatment in Belgium is low compared with other European countries (2). Treatment guidelines, including mandatory liver biopsy prior to treatment initiation, may explain low treatment rates.

Methods

Published literature and Belgian government reports were scanned for recent data describing the total population as well as the HCV prevalent population within Belgium. Belgian population data were obtained by 5 year age and gender cohorts from the United Nations population database (3). Following the initial literature review, an expert panel was convened and met twice to discuss the merits and limitations of the available data. The study methodology has been published in more detail elsewhere (4).

Baseline characteristics of the HCV population

Recent population-based studies of the anti-HCV prevalence in Belgium are scarce and subject to selection bias. A 2003 mail-based study in the Flanders region measured HCV antibodies in oral fluid, resulting in a prevalence estimate of 0.12% (0.09%-0.39%) (5). This single region study had a 30% response rate and likely under-sampled high risk populations (1,5). By contrast a 2012 report by the Belgian Health Care Knowledge Center (KCE) estimates an anti-HCV positivity rate of 1.23% among patients with a test funded by one of the seven national sickness funds (1). This estimate was generated through a review of the total number of anti-HCV and confirmatory HCV tests reimbursed from 2002-2007, and may exclude tests ordered for high risk groups, or prior to blood donation (1). Furthermore regional estimates suggest that the prevalence in Flanders ($\sim 0.4\%$) is lower than in the Walloon region ($\sim 1\%$), and that both

Correspondence to : Pierre Van Damme, Centre for the Evaluation of Vaccination, Vaccine & Infectious Disease Institute, Faculty of Medicine and Health Sciences, University of Antwerp, Campus Drie Eiken, Universiteitsplein 1, 2610 Wilrijk, Belgium. E-mail : pierre.vandamme@uantwerp.be

Submission date : 21/05/2014 Acceptance date : 22/05/2014



Fig. 1. - Age and gender distribution of anti-HCV prevalence, Belgium, 2004

are lower than the prevalence in Brussels ($\sim 1.5\%$) (6). Finally the most commonly cited estimate of the anti-HCV prevalence in Belgium comes from Beutels et al, published in 1997, which estimates an anti-HCV prevalence of 0.87% (7). This data was based on residual samples from 10 laboratory hospitals in Flanders. However, it was collected in 1994 (7).

An expert panel met to discuss the study's strengths and limitations and agreed that the most representative anti-HCV prevalence estimate for the Belgian general population was 0.87% in 1994, with a range of 0.12%-1.1% (1,5,7). The age and gender distribution of the anti-HCV cases in Belgium (Fig. 1) came from an observational survey conducted with the support of BASL (8,9).

For the purposes of the model, only viremic cases were tracked, and a rate of 80% was used to adjust for viremia (10). Inputs prior to 2004 were adjusted using only the spontaneous clearance rate, since treatment was not available prior to this time. Accounting for spontaneous clearance, the total number of viremic cases in 1994 is estimated to be 76,100 (10,830-99,230) (1,5,7,10).

The annual number of new cases in Belgium is considered to have peaked in 1989 due to high risk behaviors and a contaminated blood supply and then to have decreased sharply following blood screening and harm reduction efforts. In 2010 it was estimated that 22,900 viremic individuals were diagnosed in Belgium, with approximately 2,800 new anti-HCV diagnoses annually (1). This value was adjusted for spontaneous clearance resulting in 2,140 viremic individuals diagnosed annually (1,10). The leading causes of HCV transmission were found to be IV drug use (27%), blood transfusion (23%), and invasive medical procedure (11%) (8). The genotype distribution (Table 1) in Belgium is predominantly genotype 1 of 61% followed by genotype 3 (19%), genotype 4 (14%), and genotype 2 (6%) (8).

| Table 1 | Genotype | Distribution, | Belgium, | 2004 | (8) |
|---------|----------|---------------|----------|------|-----|
|---------|----------|---------------|----------|------|-----|

| | | , | 8 / | · · · |
|----------|-------|------|-------|-------|
| Genotype | 1 | 2 | 3 | 4 |
| Percent | 61.0% | 6.0% | 19.0% | 14.0% |
| | | | | |

In 2010 it was estimated that 710 patients were treated in Belgium. This value was calculated using IMS data for the standard units of Peg-IFN sold in Belgium, discounted 5% for Peg-IFN used for other indications (11). The genotype distribution, as well as estimates of compliance and persistence, was used to estimate the average number of weeks of treatment per patient.

From 2008-2012 1,159 liver transplants were performed, of which, 146 (12.6%) were attributable to HCV infection (12). A panel of experts from centers in Ghent and Leuven reported 10-15% transplant rates due to HCV, whereas those from Liège and Brussels report rates closer to 25% but also note a lower rate of transplantation in these centers.

Background mortality was estimated by five year age and gender cohorts using the Max Planck Institute for Demographic Research, housed at the University of California Berkeley (13).

Discussion

There are limitations surrounding the historical inputs used in the model. First, a recent and well adopted prevalence estimate is not currently available for Belgium. Beutels 1997 is commonly cited for the prevalence estimate in Belgium ; however, it is based on data from 1994, in one region of Belgium and may not be representative of the general population. Additionally an age distribution from 2004 was chosen, requiring the datasets be matched with ten years of lag time. The model's functionality allows for this type of data matching, how-

| | Historical (Min-Max) | Year | 2013 estimate (Uncertainty Interval) |
|-------------------------------|----------------------------|------|---|
| HCV Infected Cases | 87,500 (12,400-114,100) | 1994 | |
| Anti-HCV Prevalence | 0.9% (0.1%-1.1%) | | |
| Total Viremic Cases | 70,000 (10,000-91,200) | 1994 | 67,100 (24,800-78,600) |
| Viremic Prevalence | 0.7% (0.1%-0.9%) | | 0.6% (0.3%-0.8%) |
| Viremic Rate | 80.0% | | 80.0% |
| HCV Diagnosed (Viremic) | 22,900 | 2010 | 28,600 |
| Viremic Diagnosis Rate | 32.7% | | 42.6% |
| Annual Newly Diagnosed | 2,850 | 2010 | 2,850 |
| New Infections | | | 910 |
| New Infection Rate (per 100K) | | | 8 |
| Treated | | | |
| Number Treated | 710 | 2011 | 710 |
| Annual Treatment Rate | 1.0% | | 1.1% |
| Risk Factors | | | |
| Number of Active IDU with HCV | | | 18,100 |
| Percent Active IDU | 27.0% | 2004 | 27.0% |
| Previous Blood Transfusion | | | 10,100 |
| Percent Previous Blood | 23.0% | 2004 | 15.0% |

| Table 2. – | Model | inputs | and | 2013 | estimations |
|------------|-------|--------|-----|------|-------------|
|------------|-------|--------|-----|------|-------------|

ever, more recent and representative data would allow for more reliable estimations. Finally, although HCV requires mandatory reporting in Belgium, in 2009 treating physicians in Flanders were no longer required to report cases, suggesting an underreporting of new diagnoses (1).

There are no formal HCV screening strategies in Belgium, however, a 2012 KCE Report estimates that nearly 50% of the 1945-1965 birth cohort has received an HCV test, (29% during 2002-2009 and 21% estimated to have been tested before or after this time) (1). Birth cohort screening among individuals born between 1945 and 1965 has proven effective in the United States (US) (14). The Belgian HCV epidemic is younger than that of the US, with 70% of the viremic population born between 1950 and 1975. Screening programs targeting this population are estimated to have the greatest success in identifying new cases.

This review aims to present and synthesize the best available epidemiologic HCV data in Belgium, as identified through literature review and expert consensus. The data presented here were compiled for use in modeling efforts to forecast the future burden of HCV in Belgium, but also to identify areas in need of further epidemiologic study.

References

 GERKENS S., MARTIN N., THIRY N., HULSTAERT F. [Hepatitis C : Screening and Prevention] HEPATITIS C : SCREENING EN PREVENTIE. Belgian Health Care Knowledge Center (KCE), 2012.

- DEUFFIC-BURBAN S., DELTENRE P., BUTI M. et al. Predicted effects of treatment for HCV infection vary among European countries. Gastroenterology, 2012, 143: 974-85.
- United Nations.Dept.of Economic and Social Affairs.Population Division (2011). World population prospects: The 2010 revision, Volume I: Comprehensive tables. ST/ESA/SER.A/313.2011 Available from: URL: http://esa.un.org/wpp/Documentation/pdf/WPP2010_Volume-I_ Comprehensive-Tables.pdf
- BRUGGMANN P., BERG T., OVREHUS A.L. et al. Historical epidemiology of hepatitis C virus (HCV) in selected countries. J. Viral. Hepat., 2014, 21 Suppl 1: 5-33.
- QUOILIN S., HUTSE V., VANDENBERGHE H. et al. A population-based prevalence study of hepatitis A, B and C virus using oral fluid in Flanders, Belgium. Eur. J. Epidemiol., 2007, 22: 195-202.
- VAN DAMME P., THYSSEN A., VAN L.F. Epidemiology of hepatitis C in Belgium : present and future. *Acta Gastroenterol. Belg.*, 2002, 65 : 78-9.
- BEUTELS M., VAN DAMME P., AELVOET W. et al. Prevalence of hepatitis A, B and C in the Flemish population. Eur. J. Epidemiol., 1997, 13: 275-80.
- DE MAEGHT S., HENRION J., BOURGEOIS N. et al. A pilot observational survey of hepatitis C in Belgium. Acta Gastroenterol. Belg., 2008, 71: 4-8.
- 9. Scientific Institute of Public Health. Hepatitis C, 2010.
- DELTENRE P., MORENO C., MATHURIN P. et al. Impact of current treatment practice and different scenarios improving screening, access to treatment and treatment efficacy on HCV-related mortality in Belgium : A mathematical modeling approach. XXIIth BelgianWeek of Gastroenterology, 2010.
- RAZAVI H., WAKED I., SARRAZIN C. *et al.* The present and future disease burden of hepatitis C virus (HCV) infection with today's treatment paradigm. *J. Viral. Hepat.*, 2014, **21** Suppl 1 : 34-59.
- 12. Eurotransplant. Eurotransplant Data Request-Belgium, 2013.
- University of California, B, Mack Planck Institute for Demographic Research. Human Mortality Database Jun 14, 2013 [cited : Feb 1 2013] Available from : URL: www.mortality.org
- SMITH B.D., MORGAN R.L., BECKETT G.A. *et al.* Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945-1965. *MMWR Recomm. Rep.*, 2012, **61**: 1-32.