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Patterns of Care Among Patients With Genotype 1 Hepatitis C Virus in Europe

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ABSTRACT

To assess clinical characteristics and patterns of care among patients with Genotype 1 (G1) Hepatitis C virus (HCV) in EU, a multi-center retrospective chart-review study of HCV patients was conducted in the EU (France/Germany/Italy/Spain/UK) in 2014 to collect de-identified data on diagnosis, clinical status, and treatment patterns. Physicians were screened for duration of practice (≥3yrs) and patient volume (≥15 HCV patients/month) and recruited from a large panel to be geographically representative. Medical charts of the next 10 consecutive HCV patients were abstracted. 2067 eligible G1 HCV patients were included in the final analysis (France: 374/Germany: 506/Italy: 412/Spain: 475/UK: 300). Patient characteristics included (France/Germany/Italy/Spain/UK) G1-subtype A (49%/38%/30%/31%/58%) or B (44%/47%/67%/61%/28%); current fibrosis scores: F0: 9%/15%/5%/7%/18%, F1: 18%/24%/24%/24%/29%, F2: 24%/23%/31%/23%/17%, F3: 20%/14%/17%/19%/10%, F4: 28%/5%/20%/22%/17%; latest mean alanine aminotransferase levels:58/90/95/62/73 IU/mL; patients with viral load >1Million IU/mL: 23%/12%/33%/27%/14%. Treatment patterns included (France/Germany/Italy/Spain/UK)- currently treated:23%/28%/20%/17%/20%, treatment naïve/never been treated:38%/40%/41%/41%/52%, not currently treated (previous treatment non-responder, discontinued or relapsed, or therapy complete and awaiting sustained viral response): 21%/20%/29%/30%/22%, not currently treated for other reasons: 19%/12%/11%/13%/6%. Disease burden was high in this cohort of G1 HCV patients and only a small proportion of patients were not treated owing to achieving sustained viral response.

KEYWORDS: HCV; Genotype 1; Europe; Burden; Treatments; SVR.

INTRODUCTION

Hepatitis C, caused by hepatitis C virus (HCV) is often asymptomatic and is characterized by slow disease progression. An estimated 160 million individuals may be infected with HCV globally and the corresponding estimate for Europe is approximately 5.5 million [1-3]. Globally, genotype 1 (G1) is estimated to account for 46.2% of all HCV cases. G1 is the most predominant genotype in Europe (estimated to be between 59% and 89% depending on the region); subtype 1a is most commonly associated with intravenous drug abuse and subtype 1b is typically observed in patients who have acquired HCV through a blood transfusion. In Europe, approximately 67% of HCV cases are acquired through IV drug use, and approximately 5% through blood and blood products [4-6].

Persistent HCV infection is associated with the development of liver cirrhosis, hepatocellular cancer, liver failure, and death, while HCV is a common cause of death in HIV-positive patients [7, 8]. As incidence of HCV infection decreases in the developed world, deaths from liver disease secondary to HCV infection are expected to increase over the next 20 years [5, 9]. Vaccination against hepatitis C is not yet available; however, current treatment options include antivirals and agents that stop the virus from replicating and may eliminate the infection altogether [5, 10-12]. There is evidence indicating that some patients do not receive treatments to manage their HCV infection. Research highlighting the current patterns of care in the key countries in Europe could help portray the current status of HCV management in that region, especially among the most prevalent HCV patients (i.e., G1 type).

MATERIALS AND METHODS

The study was a multi-country, multi-center retrospective medical chart review of adult (>18 years) HCV patients conducted in the big-5 European countries, namely, France, Germany, Italy, Spain & United Kingdom (UK)) in Oct-Dec 2014. Physicians were randomly sampled in each of the countries using online physician panels using geo-dispersion sampling

methods (whereby, stakeholders are recruited from a wide selection of clinics/hospitals in a given geography representing the modality of care delivery in HCV arena, with each institution contributing almost equal number of study-eligible patient charts); this sampling methodology ensures physician recruitment from diverse locations (urban, sub-urban and rural centers) and practice settings (hospitals and individual (community/private) clinics), and avoids physician sampling biases occasionally associated with selection/use of only limited set of sites, especially in research related to widely prevalent disease(s), thereby enabling the generalization of study findings in a given geography.

Invitations to participate in research were sent to a random set of physicians (hepatologists, gastroenterologists, hepato-gastroenterologists, internal medicine and infectious disease specialists) in the existing online physician panels. The physicians representing both hospital-based and private practices in each geography, personally responsible for managing at least 15 HCV patients per month and having >3 years of clinical practice experience were screened for study participation. Each physician reported de-identified anonymous data on 10 next consecutive patients they encountered in their practice within the study recruitment window. HCP patient charts were eligible for the study if the patient was being managed as part of usual care, without any participation in clinical trials.

An electronic data collection form was used to collect the following data elements from eligible HCV patient charts: patient demographics, clinical characteristics (incl. classification of liver histology per International Association for Study of the Liver (IASL)), comorbidities, laboratory values (e.g., Viral Load and alanine aminotransferase (ALT)) and HCV treatment patterns/dynamics. Only de-identified anonymous data was collected from the patient charts by the treating physicians. This mode of data collection method met the criteria for local ethics review exemption per the respective physician/site requirements in the respective countries. Study data analysis focused on G1 HCV patients. Descriptive statistics were utilized to analyze the data.

RESULTS AND DISCUSSION

Data corresponding to 2067 eligible medical charts of HCV patients with G1 genotype were included in the study analysis; 18% were from France, 24% from Germany, 20% from Italy, 23% from Spain and 15% from the UK. The mean age of patients was 51yrs. The cohort was predominantly male and caucasian; intravenous drug was the main route of infection reported across the studied countries, ranging from 17% (Germany) to 55% (UK). (Table 1).

Key comorbidities in the study cohort encompassed cardiovascular disease (12% (range: 3% (UK) – 20% (Germany))), Steatosis (12% (range: 5% (UK) – 17% (Italy))), HIV (11% (range: 4% (Germany) – 18% (France))), depression (11% (range: 5% (Italy) – 16% (UK))) and diabetes (11% (range: 8% (UK/Italy) – 13% (Germany))).

Table 1: Patient Demographic and Clinical Characteristics.

	France N=374	Germany N=506	Italy N=412	Spain N=475	UK N=300
Age:					
Mean, yrs	53	49	55	52	45
Missing data, %	1%	2%	0%	0%	0%
Gender:					
Male, %	61%	67%	61%	59%	69%
Female, %	39%	33%	39%	41%	31%
Race:					
Caucasian, %	84%	91%	95%	96%	92%
Other, %	15%	8%	5%	4%	8%
Missing data, %	1%	1%	0%	0%	0%
Weight:					
≤80 kg, %	78%	54%	79%	60%	61%
>80 kg, %	19%	27%	17%	21%	20%
Missing data, %	3%	19%	4%	19%	19%
Substance abuse:					
Alcohol, %	9%	9%	3%	12%	20%
Intravenous drug use, %	6%	8%	1%	1%	18%
Other, %	1%	2%	1%	2%	8%
None, %	70%	77%	86%	78%	50%
Missing data, %	15%	5%	8%	8%	4%
Route of Infection:					
Intravenous drug use, %	37%	17%	21%	27%	55%
Blood transfusion, %	12%	14%	14%	24%	5%
Homosexual contact, %	5%	7%	7%	4%	10%
Heterosexual contact, %	3%	6%	15%	7%	6%
Tattoo/body piercing, %	4%	4%	1%	1%	3%
Vertical transmission, %	2%	2%	2%	1%	1%
Other, %	3%	3%	7%	3%	0%
Missing data, %	34%	48%	32%	34%	21%
Genotype:					
Subtype 1a, %	49%	38%	30%	31%	58%
Subtype 1b, %	44%	47%	67%	61%	28%
Subtype 1c, %	0%	2%	1%	0%	0%
Missing data, %	7%	12%	2%	7%	14%
Alanine aminotransferase (ALT):					
Mean level, IU/L	58	90	95	62	73
Missing data, %	4%	17%	2%	2%	10%

Forty percentage (range: 30% (Italy) – 58% (UK)) of G1 patients in the study had a documented diagnosis of genotype subtype 1a, and 51% (range: 28% (UK) – 67% (Italy)) had

subtype 1b and 1% (range: 0% (France/Spain/UK) – 2% (Germany)) had subtype 1c. Mean alanine aminotransferase (ALT) level of patients across the countries was 76 IU/L, and this varied across the countries (Table 1). Distribution of fibrosis scores (per IASL) documented in the patient charts indicated 10% (range: 5% (Italy) – 18% (UK)) had F0 (no liver damage), 24% (range: 18% (France) – 29% (UK)) had F1 (minimal liver damage), 24% (range: 17% (UK) – 31% (Italy)) had F2 (moderate liver damage), 16% (range: 10% (UK) – 20% (France)) had F3 (advanced liver damage) and 18% (range: 5% (Germany) – 28% (France)) had F4 (cirrhosis) [Figure 1] Distribution of viral load count (IU/mL) documented in patient charts within the past 3 months varied widely across the studied countries; 5% (range: <1% (UK) – 21% (Italy)) had an undetectable viral load (<500 IU/mL); 35% (range: 32% (Italy) – 42% (UK)) had a viral load count of 5001 to <1 Million IU/mL; 22% (range: 12% (Germany) – 33% (Italy)) had a viral count of >1 Million IU/mL; 37% however had missing data (range: 14% (Italy) – 52% (Germany)) (Figure 2).

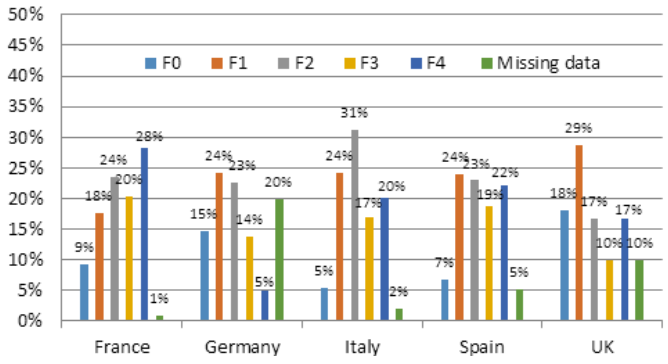

Figure 1: Distribution of Current Fibrosis Score: Percentage of Patients.

Note: Classification of liver histology per International Association for Study of the Liver (IASL): fibrosis score of F0 indicates no liver damage / no fibrosis; F1 indicates minimal liver damage / mild fibrosis; F2 indicates moderate liver damage / moderate fibrosis; F3 indicates advanced liver damage / severe fibrosis; F4 indicates cirrhosis.

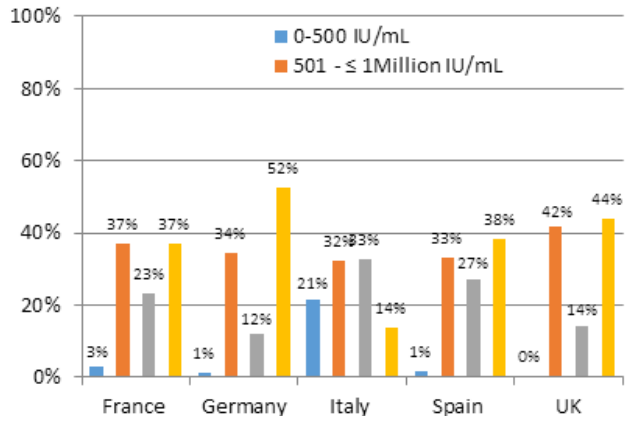

Figure 2: Distribution of Viral Load Count: Percentage of Patients.

Forty two percentage of patients (range: 38% (France) – 52% (UK)) had never been treated; 21% (range: 17% (Spain) – 28% (Germany)) were currently treated; 25% (range: 20% (Germany) – 30% (Spain)) were not currently treated (but had prior treatment experience and were either non-responders or discontinued or relapsed or therapy competed and awaiting sustained viral response (SVR)); 13% (range: 6% (UK) – 19% (France)) were not currently treated as they had achieved SVR. The distribution of patient treatment status is depicted in Table 2.

Table 2: Patient's Current Treatment Status.

	France N=374	Germany N=506	Italy N=412	Spain N=475	UK N=300
Never been treated, naive	38%	40%	41%	41%	52%
Currently treated: Previously treatment naïve	14%	23%	15%	13%	19%
Currently treated: Previous treatment non-responder, discontinued / relapsed	9%	5%	5%	4%	1%
Not currently treated: Previous treatment non-responder/ discontinued/ relapsed	17%	14%	27%	26%	19%
Not currently treated: Therapy completed and awaiting SVR	4%	6%	2%	4%	3%
Not currently treated: SVR achieved	19%	12%	11%	13%	6%

Note: SVR is Sustained Viral Response.

Telaprevir (TVR) plus peginterferon-α2a (IFN) and ribavirin (RBV) was the most frequently used HCV regimen used among those currently being treated (19%; range: 5% (France) – 43% (UK)), followed by IFN+RBV (19%; range: 1% (France) – 50% (Italy)), sofosbuvir plus daclatasvir (SOF+DCV; 13% (range: 1% (Italy) – 36% (France))), SOF+IFN+RBV (12% (range: 1% (UK/Italy/Spain) – 34% (Germany))), boceprevir plus IFN+RBV (12% (range: 4% (France) – 21% (Spain))) and SOF + simeprevir + RBV (9% (range: 0% (Italy) – 31% (France))).

This research found that more than half of the HCV patients had moderate/severe liver damage or cirrhosis and only 13% of the patients had achieved SVR (and hence not treated), indicating high disease burden among this cohort of G1 patients in Europe. Compounding this burden is the observation that 42% remained treatment-naïve, and another 25% were not currently treated for other reasons. These observed rates of non-treatment varied by country. Papatheodoridis et al. [2014] had reported the proportion of untreated HCV patients across Europe to be 57% (range: 45-89%; notably, France had a non-treatment rate of 79%), while other studies have reported similar or even higher rate of non-treatment [13-16]. Our study results are directionally consistent with the past reports.

Slow progressive nature of HCV infection may imply a potential public health risk of increasing late stage complications in the future unless those infected are successfully treated, as determined by the achievement of a SVR [17-19]. Sub-optimally managed (incl. lack of achievement of SVR) or untreated HCV may result in high morbidity and mortality [7, 8, 12, 19-22]. EASL guidelines recommend the primary goal of HCV therapy to be the cure of infection, associated with resolution of liver disease in patients without cirrhosis [1]. Results from this study denoting the potential suboptimal management of HCV in the studied countries in Europe hence assumes importance.

Newer potent direct acting antivirals (DAAs) such as daclatasvir, sofosbuvir and simeprevir are now available to manage HCV aggressively, and several national and international guidelines recommend their use in certain situations [1, 23-29]. While these therapies are associated with higher SVRs, healthcare systems are concerned about their widespread use on their national/regional budget and thus, the economic sustainability of their policies in HCV arena, owing to the high costs of these drugs [12, 19, 23, 24, 30]. The sporadic use of DAAs observed in this study cohort may have been influenced by these economic and access issues, besides patient characteristics (such as comorbidities, substance abuse, etc.). Further research is warranted to determine the comparative effectiveness of the observed treatments, as a means to discriminate therapeutic choices for optimal patient outcomes and foster best practices amidst a cost-conscious environment.

Although physicians were randomly recruited for this study in respective geographies, the findings may represent only the participating physician practices, and may vary from those of non-participating physician practices.

CONCLUSIONS

In this cohort of G1 HCV patients, treatment rates were low and disease burden was high, and they varied among studied countries in EU; only a small proportion of patients were not treated owing to achieving sustained viral response. Further research is warranted to assess the factors influencing the current patient management strategies to alleviate disease burden in this patient population.

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