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Global epidemiology and genotype distribution of the hepatitis C virus infection

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Summary

The treatment of chronic hepatitis C virus (HCV) infection has the potential to change significantly over the next few years as therapeutic regimens are rapidly evolving. However, the burden of chronic infection has not been quantified at the global level using the most recent data. Updated estimates of HCV prevalence, viremia and genotypes are critical for developing strategies to manage or eliminate HCV infection. To achieve this, a comprehensive literature search was conducted for anti-HCV prevalence, viraemic prevalence and genotypes for all countries. Studies were included based on how well they could be extrapolated to the general population, sample size and the age of the study. Available country estimates were used to develop regional and global estimates. Eighty-seven countries reported anti-HCV prevalence, while HCV viraemic rates were available for fifty-four countries. Total global viraemic HCV infections were estimated at 80 (64–103) million infections. Genotype distribution was available for ninety-eight countries. Globally, genotype 1 (G1) was the most common (46%), followed by G3 (22%), G2 (13%), and G4 (13%). In conclusion, the total number of HCV infections reported here are lower than previous estimates. The exclusion of data from earlier studies conducted at the peak of the HCV epidemic, along with adjustments for reduced prevalence among children, are likely contributors. The results highlight the need for more robust surveillance studies to quantify the HCV disease burden more accurately.

Introduction

The treatment of hepatitis C virus (HCV) infection has the potential to change significantly over the next few years as new all-oral treatment options become available with a shorter duration of treatment and more manageable side effects. With the advent of new antivirals, boasting improved sustained virologic response (SVR), HCV infection will be curable in nearly all patients. Previous studies have shown that HCV infection can be eliminated in the next 15–20 years with focused strategies to screen and cure current infections as well as prevent new infections [1,2]. However, a good understanding of the number of HCV infections is required to develop strategies to eliminate HCV.

A number of previous studies have reported global, regional and country level prevalence estimates of HCV infection. The original studies conducted by the World Health Organization (WHO) [3–7] outlined global and country level estimates. More recent analyses provided updated prevalence estimates, but were limited to select countries [1,8–13]. Finally, a recent study published a revised estimate of global HCV prevalence [14], but provided only regional estimates. Most previous global, regional and country level analyses have failed to reconcile estimates based on age-distribution and active infection. Most country-level studies were conducted in the adult population; however, when estimates were applied to a country's entire population, disease burden was likely overestimated. In addition, studies focused on anti-HCV (antibody positive) testing overestimated disease burden because they include those who have been cured, either spontaneously or through treatment.

Knowledge of the distribution of HCV genotypes has important clinical implications since the efficacy of current and new therapies differ by genotype. Until pan-genotypic therapies reach the market, SVR, duration of treatment and cost of treatment will be impacted by the genotype distribution. To date, there are no published studies assessing HCV genotype at the global level; however, it is understood that there are notable geographical differences.

The objective of the current study was to conduct a comprehensive review of recently published literature to estimate anti-HCV prevalence, viraemic (RNA positive) prevalence, number of anti-HCV and viraemic infections and genotype distribution. In addition, because more than half of the countries in the world do not have robust studies of the HCV infected population, a secondary objective of this analysis was to extrapolate available data to countries without prevalence estimates, to generate a global estimate of HCV disease burden.

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Abbreviations: HCV, hepatitis C virus; SVR, sustained viral response; WHO, World Health Organization; GBD, global burden of disease; PWID, people who inject drugs.

Key Points

Total HCV infections

- The total global prevalence of anti-HCV was estimated to be 1.6% (1.3-2.1%), corresponding to 115 (92-149) million past viraemic infections
- The majority of these infections, 104 (87-124) million, were among adults (defined as those older than 15 years old) with an anti-HCV infection rate of 2.0% (1.7-2.3%)
- The viraemic (RNA positive) prevalence was forecasted to be 1.1% (0.9-1.4%), corresponding to 80 (64-103) million viraemic infections
- Again, most of these viraemic infections were among adults who accounted for 75 (62-89) million viraemic infections or a viraemic prevalence of 1.4% (1.2-1.7%)

Genotype distribution

- Globally, genotype 1 was most common, accounting for 46% of all infections, followed by genotypes 3 (22%), and genotypes 2 and 4 (13% each). Subtype 1b accounted for 22% of all infections at the global level
- There were significant variations across regions with genotype 1 dominating in Australasia, Europe, Latin America and North America (53-71% of all cases) and G3 accounting for 40% of all infections in Asia
- Genotype 4 was most common (71%) in North Africa and the Middle East, but when Egypt was excluded, it accounted for 34% while genotype 1 accounted for 46% of infections across the same region

Methodology

HCV prevalence

A comprehensive literature search was conducted in PubMed and EMBASE, using the following search terms, respectively: "[Country Name] and [hepatitis c or hcv] and [prevalence]" and "['hepatitis c or hcv] and [prevalence]". Additional studies were identified through manual searches of references noted in the publications. Non-indexed government reports and personal communication with experts within countries were also included. Regions included in the analysis were those defined by the Global Burden of Diseases, Injuries, and Risk Factors 2010 (GBD) study [15,16].

Article titles and abstracts were reviewed for relevance and the following data were extracted from full articles or abstracts: anti-HCV prevalence, viraemic prevalence, studied population (e.g., pregnant women, health care patients, screening participants, military recruits, blood donors, etc.), sample size, data collection/analysis date, analysis scope (urban, rural, both and unknown), region(s) studied (one hospital/clinic, multi hospitals/clinics, city, multi city, region, multi region, national, other and unknown) and analysis type (meta-analysis, modelling, review article, surveillance study and other/unknown).

Exclusion criteria

Studies in non-representative populations, (e.g., people who inject drugs (PWID's), haemophiliacs, minority ethnic groups, refugees, etc.), studies with a sample size of less than 1000 and studies published prior to 2000 were excluded from the analysis.

Quality score

A multi-objective decision analysis approach [17–20] was used to derive a score of 0–10 for each study, using three measures: how well the reported data could be extrapolated to the general population, sample size and year of analysis. Supplementary Table 1 shows the 0–10 scoring system used to determine how well the reported data could be extrapolated to the general population. The log of the sample size was scaled as 0–10 where all studies with a sample size greater than 10,000 received a score of 10. Analyses conducted from 2000 to 2003 received a score of 6, 2004–2010 a score of 8 and >2010 a score of 10. A final score was calculated using a weighting of 60% for the extrapolation score and 20% each for sample size and study year. For simplicity, the 0–10 scores were converted to a data quality scale of 1–3 (study score of 0.0–<4.0 received a data quality score of 1, 4.0–<8.0 = 2, and 8.0–10.0 = 3). Modelling studies were automatically given a data quality score of 2. Studies without a formal assessment, but deemed to be of quality for inclusion, were given a score of 1.

Studies with the highest score were considered for the base assumption with the exception of China, India and Nigeria where a meta-analysis of all studies after 2000, which were representative of the general population, were used to develop a base estimate (see Supplementary Table 2). Blood donor studies were excluded from base estimates because they represent healthy screened adults, but were used for low prevalence estimates when applicable. When insufficient data was available to determine a range in a country, data from neighboring countries (or countries in the region) were used. When applicable, a wide range was used for countries with a high level of uncertainty.

The UN population database was used for the 2013 country population by five-year age cohort [21]. The number of anti-HCV and viraemic HCV infections was calculated by multiplying the country's population and the appropriate HCV prevalence.

HCV prevalence in adults

Most studies reported HCV prevalence in the adult population. For the purpose of this exercise, the definition of adults was assumed to include all individuals aged $\geqslant$15 years. When a study included data in children, prevalence in adults was calculated using the reported prevalence by age groups. In addition, when studies that calculated HCV prevalence in 2013 by age group were available [1,8,13], the adult prevalence from those studies was considered. Countries where adjustments were made to capture only the adult population and/or HCV infection in 2013 included: Australia, Bangladesh, Belgium, Brazil, Cameroon, Canada, Czech Republic, Denmark, Ethiopia, Finland, France, Germany, Ireland, Luxembourg, New Zealand, Pakistan, Portugal, Slovakia, Spain, Sweden, Switzerland, Thailand, Tunisia, United Kingdom and Yemen.