BACKGROUND

• Chronic infection with the hepatitis C virus (HCV) is a major cause of chronic liver disease, which may lead to cirrhosis and predispose patients to the development of liver cancer.

• The long-term impact of chronic HCV infection on the liver is highly variable, ranging from minimal liver damage to extensive fibrosis, and decompensated cirrhosis with or without hepatocellular carcinoma (HCC).

• HCV is spread primarily through direct contact with human blood, including via blood transfusions in settings in which the blood supply is not suitably screened, reuse of needles and syringes that have been inadequately sterilized, and sexual contact with infected persons.

• Due to slow disease progression, symptoms of HCV often appear late after exposure, and many individuals have no knowledge of their infection or of the hepatic diseases that may follow. Consequently, the virus is underdiagnosed and underreported, and it is estimated that the number of chronically infected persons worldwide may exceed 200 million.

• HCV genotypes, numbered 1 to 6, and many subtypes have been described.

• The diverse genotype and subtypes originate from different areas in Africa, Asia, and the Americas throughout the world.

• Genotype 1 (GT1) (subtypes 1a and 1b) is the most prevalent genotype worldwide, with a higher prevalence of 1a in the United States (US) and some areas of Southern Europe.

• GT-1 is associated with more aggressive disease, with increased insulin resistance, worse response to therapy, and higher risk of developing cirrhosis and HCC.

• GT-3 is associated with increased steatosis (up to 73% of patients vs. 10% of patients with other genotypes) and fibrosis.3

• The primary goal of HCV therapy is to cure the infection by eliminating detectable circulating HCV. The combination of pegylated interferon (PEG-IFN) alfa and ribavirin is the approved and well-accepted standard of care for chronic HCV.

• Many drugs for HCV are at various stages of preclinical and clinical development. New therapeutic strategies aim toward treating specific genotypes, increasing efficacy, shortening treatment, simplifying administration, and improving tolerability and patient adherence.

OBJECTIVE

• To identify and understand HCV prevalence and mortality rates, disease course, and the availability of data on patient and viral characteristics that may affect treatment and outcomes.

METHODS

• A targeted review was undertaken in Medline, using a predefined search strategy, to update a review conducted in 2009 and to identify studies describing HCV burden.

• Additional searches were performed on the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) conference and key epidemiological websites.

• The focus for this research was studies conducted in Australia, Brazil, Canada, China, France, Germany, Italy, Japan, Mexico, the Netherlands, South Korea, Spain, Sweden, the United Kingdom (UK), and the US.

RESULTS

• The targeted review identified 1,773 references.

• Results indicated that between 1990 and 2005 globally, the number of people with HCV increased from more than 122 million to more than 185 million, and HCV prevalence increased from 2.3% to 2.8%.4

• Asia-Pacific, Tropical Latin America, and North America were estimated to have the highest prevalence levels (6.5%).

• Australia, Western Europe, and Central Latin America were estimated to have moderate prevalence (1.5%-3%).

• East Asia was estimated to have the highest prevalence (6.5%).

• Data for most regions showed an increase in prevalence as a function of age, followed by a gradual decrease after peak prevalence was reached in the group aged 55 to 64 years.

• A more recent estimate suggested a total global prevalence of 2.95%, with 159 million HCV-infected individuals in 2010 (Table 1).5

• Differences between the two estimates may be explained by the methodology used to calculate the estimate, differing definitions and regions of the disease, and the year for which the prevalence estimates are given.

• Figure 1 presents the identified HCV prevalence results by country.

• HCV screening programmes and mandatory reporting are present in only a few countries, so actual prevalence is likely to be even greater.

• The increasing prevalence of HCV over time is mirrored by an increase in the number of deaths due to HCV infection. HCV, combined with diseases secondary to HCV, is ranked as the 25th most common cause of death in the US between 1999 and 2007.

• The diverse genotype and subtypes originated from different areas in Africa and Asia, and some have spread throughout the world.

• In 2010, there were estimated to be 499,000 deaths globally – 9% of deaths from HCV (from 1 13,000 to 195,700 deaths).

• HCV infection now has a higher mortality rate than HIV (Figure 2).

• The breakdown of all-ages deaths attributable to HCV demonstrated an increase in the number of deaths from 1990 to 2010:

  - 9.2% increase in deaths due to acute HCV (from 8,110 to 10,000 deaths)
  - 73.3% increase in deaths due to liver cancer secondary to HCV (from 113,000 to 185,700 deaths)
  - 30.5% increase in deaths due to cirrhosis of the liver secondary to HCV (from 273,900 to 284,400 deaths).

• The prevalence of HCV genotypes varies geographically.

• GT-1 is the most prevalent genotype in North and South America (50%-60%), Europe (46%-59%), and the Asia-Pacific region (48%-68%).

• GT-3 is most prevalent in South Asia (Pakistan, India, and Thailand) (52%-67%).

• GT-4 is most prevalent in the Middle East (Egypt, Syria, and Saudi Arabia) (50%-63%).

• Figure 3 shows HCV prevalence and genotype distribution by key countries and region.

• There is a lack of detailed data on genotype distribution for the majority of African and some Middle Eastern countries; however, recent data6 suggest the following:

  - GT-1 is most prevalent in West Africa and some East African countries (Ethiopia, Eritrea, and Kenya).
  - GT-2 is most prevalent in Tunisia and Morocco.
  - GT-4 is most prevalent in Central Africa and some North African countries (Egypt, Sudan, Libya).

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• GT-5 is most prevalent in South and East Africa, including South Africa, Tanzania, and Zambia.

DISCUSSION

• HCV infection shows a high degree of interindividual variability, and the risk of HCV-related liver morbidity and mortality depends on a number of factors, including the duration of HCV infection, HCV, prevalence of cofactors for liver fibrosis, access to treatments, and competing mortality risks from factors such as intravenous drug use.

• The global prevalence of HCV increased from 2.3% to 2.8% between 1990 and 2005, which equates to an additional 63 million people living with HCV.7 Further, HCV screening programmes and mandatory reporting are present in only a few countries, so actual prevalence is likely to be even greater.

• Since the burden of disease for HCV infection and the subsequent hepatic diseases continue to increase.

• The increasing prevalence of HCV over time is mirrored by an increase in the number of deaths due to HCV infection. HCV, combined with diseases secondary to HCV, is ranked as the 25th most common cause of death if these deaths were counted in the main global burden of disease cause list.8,9 HCV infection poses a significant global health problem.

• Across countries, it is recommended that HCV genotype should be considered when selecting therapy.

• The recommended treatment regimen of therapy for GT-1 HCV is PEG-IFN alfa plus ribavirin, with directly acting antivirals now being recommended, particularly in the US and the UK.

• In many markets, tailoring length of treatment according to the patients’ response is recommended. Doing so has the benefit of reducing the cost of therapy while minimizing the risk of adverse events to treatment in patients with HCV infection.

• New drugs in development target specific HCV genotypes; as such, it is important to know patients’ genotypes prior to treatment.

• Epidemiological data on genotype distributions may help ensure appropriate therapy for patients in different parts of the world.

CONCLUSION

• In light of upcoming treatment alternatives, detailed epidemiological studies will help ascertain more accurately the prevalence of each HCV genotype and subtypes, so that the true burden of HCV can be understood and treatments targeted appropriately.

REFERENCES

Please see handout for complete reference list.

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Presented at: ISPOR 16th Annual European Congress
November 24, 2013
Dublin, Ireland

Table 1. Regional Prevalence of HCV in 2010

<table>
<thead>
<tr>
<th>Region</th>
<th>HCV Prevalence (%)</th>
<th>No. of HCV-infected Individuals</th>
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</thead>
<tbody>
<tr>
<td>Africa</td>
<td>3.2</td>
<td>38.1 million</td>
</tr>
<tr>
<td>Americas</td>
<td>1.5</td>
<td>14 million</td>
</tr>
<tr>
<td>Asia</td>
<td>2.1</td>
<td>62 million</td>
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<tr>
<td>Australia and Oceania</td>
<td>1.2</td>
<td>8.4 million</td>
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<td>Europe</td>
<td>2.3</td>
<td>17.4 million</td>
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<tr>
<td>Middle East</td>
<td>4.7</td>
<td>16 million</td>
</tr>
<tr>
<td>Total</td>
<td>2.95</td>
<td>159 million</td>
</tr>
</tbody>
</table>

Source: CDC, 2010; Zerbo et al., 2011; Ekström et al., 2011; Kehan et al., 2011; Logan and Dikri, 2011; Pollicino et al., 2011; Vriend et al., 2012; World Health Organization, 2011.