Report Title: The burden of liver disease in Europe: a review of available epidemiological data

Authors : Martin Blachier, Henri Leleu, Markus Peck-Radosavljevic, Dominique-Charles Valla and Françoise Roudot-Thoraval Release date : 20th February 2013 ISBN No. 978-2-8399-1176-4

Summary

The past 30 years have witnessed major progress in the knowledge and management of liver disease, yet approximately 29 million people in the European Union still suffer from a chronic liver condition [1]. Difficulties in accessing data from individual countries hinder global evaluation of liver disease in Europe. *The Burden of Liver Disease in Europe: A Review of Available Epidemiological Date* reviews 260 epidemiological studies published in the last five years to survey the current state of evidence on the burden of liver disease in Europe and its causes.

The incidence and prevalence of two conditions, cirrhosis and primary liver cancer, are key to understanding the burden of liver disease. They represent the end-stage of liver pathology and thus are indicative of the associated mortality. Literature on the prevalence and incidence of cirrhosis is scarce, but available data suggest this disease is responsible for an estimated 170,000 deaths per year in Europe [2]. There are, however, large intra-European variations. About 0.1% of Hungarian males will die of cirrhosis every year compared with 0.001% of Greek females [2].

Hepatocellular carcinoma (constituting 70–90% of cases of primary liver cancer) is the fifth most common cause of cancer in Europe and one of the most serious outcomes of cirrhosis [3]. European epidemiological data show that there are 1-13 new cases of hepatocellular carcinoma and 1-10 deaths per 100,000 inhabitants per year. WHO estimate that liver cancer is responsible for around 47,000 deaths per year in the EU.

Alcohol consumption, viral hepatitis B and C and metabolic syndromes related to overweight and obesity are the leading causes of cirrhosis and primary liver cancer in Europe.

Alcohol is the main cause of liver disease, including liver cirrhosis. Alcohol consumption in Europe decreased during the 1990s, but increased and stabilized at a higher level between 2004 and 2006, with huge variations among European countries [4].

Chronic viral hepatitis B is the second major cause of both cirrhosis and liver cancer. Between 0.5% and 0.7% of the European population is affected by chronic hepatitis B, with the highest prevalence being recorded in Romania (5.6%) and Greece (3.4%) [5-12]. Throughout Europe, an average of only 23% of patients knew of hepatitis B at the time of their diagnosis [13]. Data suggest there has been a reduction in the yearly incidence of HBV, accompanied by a decline in prevalence related to the vaccination campaigns that have been mounted throughout Europe [12, 14].

Chronic hepatitis C is an important risk factor for hepatocellular carcinoma, which develops several decades after infection. Since the discovery of the virus in the late eighties, the number of new cases of infection has dropped substantially. Prevalence rates of hepatitis C virus (HCV) infection in the last

decade in the European population were between 0.13 and 3.26 %, the highest rates being found in Italy and Romania [5-7, 9, 15-17]. These HCV-infected populations will develop complications in the years to come, leading to a substantial increase in the burden of disease. It is of great concern that about 90% of people in Europe infected by viral hepatitis are unaware of their status [13].

Non-alcohol fatty liver disease (NAFLD) is becoming a major concern with the increasing incidence of obesity in Europe. In this condition, accumulation of fat in the liver leads to chronic liver disease. Available data suggest the prevalence rate of NAFLD is 2–44% in the general European population (including obese children) and 42.6–69.5% in people with type 2 diabetes [18-28].

Each of these four major causes of liver disease is amenable to prevention and treatment, reducing the burden of liver disease in Europe and saving lives. However, epidemiological data are scarce. Additional surveys are urgently needed to provide reliable information, without which it will not be possible to implement cost-effective prevention programmes and novel treatments to tackle liver disease and avoidable deaths in Europe.

A limited number of hard copies of the report are available. The report can also be found online at http://www.easl.eu/_eu-policy/eu-literature-review

For further information please contact Margaret Walker, EASL Director of EU Public Affairs at <u>margaret.walker@easloffice.eu</u>

References

European Liver Patients Association. 2005 [cited; Available from: <u>http://www.elpa-info.org/</u>
 Zatonski WA, Sulkowska U, Manczuk M, Rehm J, Boffetta P, Lowenfels AB, et al. Liver
 cirrhosis mortality in Europe, with special attention to Central and Eastern Europe. Eur Addict Res

2010;16:193-201.[3] Ferlay J, Parkin DM, Steliarova-Foucher E. Estimates of cancer incidence and mortality in

Europe in 2008. Eur J Cancer 2010;46:765-781.
[4] WHO. European Status Report on Alcohol and Health: World Health Organization. Regional Office for Europe; 2010.

[5] Baaten GG, Sonder GJ, Dukers NH, Coutinho RA, Van den Hoek JA. Population-based study on the seroprevalence of hepatitis A, B, and C virus infection in Amsterdam, 2004. J Med Virol 2007;79:1802-1810.

[6] Fabris P, Baldo V, Baldovin T, Bellotto E, Rassu M, Trivello R, et al. Changing epidemiology of HCV and HBV infections in Northern Italy: a survey in the general population. J Clin Gastroenterol 2008;42:527-532.

[7] Meffre C, Le Strat Y, Delarocque-Astagneau E, Dubois F, Antona D, Lemasson JM, et al. Prevalence of hepatitis B and hepatitis C virus infections in France in 2004: social factors are important predictors after adjusting for known risk factors. J Med Virol 2010;82:546-555.

[8] Papaevangelou V, Hadjichristodoulou C, Cassimos DC, Pantelaki K, Tzivaras A, Hatzimichael A, et al. Seroepidemiology of hepatitis B in Greek children 6 years after the implementation of universal vaccination. Infection 2008;36:135-139.

[9] Quoilin S, Hutse V, Vandenberghe H, Claeys F, Verhaegen E, De Cock L, et al. A populationbased prevalence study of hepatitis A, B and C virus using oral fluid in Flanders, Belgium. Eur J Epidemiol 2007;22:195-202.

[10] Salleras L, Dominguez A, Bruguera M, Plans P, Costa J, Cardenosa N, et al. Declining prevalence of hepatitis B virus infection in Catalonia (Spain) 12 years after the introduction of universal vaccination. Vaccine 2007;25:8726-8731.

[11] Voiculescu M, Iliescu L, Ionescu C, Micu L, Ismail G, Zilisteanu D, et al. A cross-sectional epidemiological study of HBV, HCV, HDV and HEV prevalence in the SubCarpathian and South-Eastern regions of Romania. J Gastrointestin Liver Dis 2010;19:43-48.

[12] Zacharakis G, Kotsiou S, Papoutselis M, Vafiadis N, Tzara F, Pouliou E, et al. Changes in the epidemiology of hepatitis B virus infection following the implementation of immunisation programmes in northeastern Greece. Euro Surveill 2009;14.

[13] European Liver Patients Association. Report on hepatitis patient self-help in Europe; 2010. http://www.hepbcppa.org/wp-content/uploads/2011/11/Report-on-Patient-Self-Help.pdf

[14] Salleras L, Dominguez A, Bruguera M, Plans P, Espunes J, Costa J, et al. Seroepidemiology of hepatitis B virus infection in pregnant women in Catalonia (Spain). J Clin Virol 2009;44:329-332.

[15] Cozzolongo R, Osella AR, Elba S, Petruzzi J, Buongiorno G, Giannuzzi V, et al. Epidemiology of HCV infection in the general population: a survey in a southern Italian town. Am J Gastroenterol 2009;104:2740-2746.

[16] Delarocque-Astagneau E, Meffre C, Dubois F, Pioche C, Le Strat Y, Roudot-Thoraval F, et al. The impact of the prevention programme of hepatitis C over more than a decade: the French experience. J Viral Hepat 2010;17:435-443.

[17] Gheorghe L, Csiki IE, Iacob S, Gheorghe C, Smira G, Regep L. The prevalence and risk factors of hepatitis C virus infection in adult population in Romania: a nationwide survey 2006 - 2008. J Gastrointestin Liver Dis 2010;19:373-379.

[18] Bedogni G, Miglioli L, Masutti F, Castiglione A, Croce LS, Tiribelli C, et al. Incidence and natural course of fatty liver in the general population: the Dionysos study. Hepatology 2007;46:1387-1391.

[19] Caballeria L, Pera G, Auladell MA, Toran P, Munoz L, Miranda D, et al. Prevalence and factors associated with the presence of nonalcoholic fatty liver disease in an adult population in Spain. Eur J Gastroenterol Hepatol 2010;22:24-32.

[20] Caserta CA, Pendino GM, Amante A, Vacalebre C, Fiorillo MT, Surace P, et al. Cardiovascular risk factors, nonalcoholic fatty liver disease, and carotid artery intima-media thickness in an adolescent population in southern Italy. Am J Epidemiol 2010;171:1195-1202.

[21] Gastaldelli A, Kozakova M, Hojlund K, Flyvbjerg A, Favuzzi A, Mitrakou A, et al. Fatty liver is associated with insulin resistance, risk of coronary heart disease, and early atherosclerosis in a large European population. Hepatology 2009;49:1537-1544.

[22] Haring R, Wallaschofski H, Nauck M, Dorr M, Baumeister SE, Volzke H. Ultrasonographic hepatic steatosis increases prediction of mortality risk from elevated serum gamma-glutamyl transpeptidase levels. Hepatology 2009;50:1403-1411.

[23] Imhof A, Kratzer W, Boehm B, Meitinger K, Trischler G, Steinbach G, et al. Prevalence of nonalcoholic fatty liver and characteristics in overweight adolescents in the general population. Eur J Epidemiol 2007;22:889-897.

[24] Radu C, Grigorescu M, Crisan D, Lupsor M, Constantin D, Dina L. Prevalence and associated risk factors of non-alcoholic fatty liver disease in hospitalized patients. J Gastrointestin Liver Dis 2008;17:255-260.

[25] Sartorio A, Del Col A, Agosti F, Mazzilli G, Bellentani S, Tiribelli C, et al. Predictors of nonalcoholic fatty liver disease in obese children. Eur J Clin Nutr 2007;61:877-883.

[26] Targher G, Bertolini L, Padovani R, Rodella S, Tessari R, Zenari L, et al. Prevalence of nonalcoholic fatty liver disease and its association with cardiovascular disease among type 2 diabetic patients. Diabetes Care 2007;30:1212-1218.

[27] Williamson RM, Price JF, Glancy S, Perry E, Nee LD, Hayes PC, et al. Prevalence of and risk factors for hepatic steatosis and nonalcoholic Fatty liver disease in people with type 2 diabetes: the Edinburgh Type 2 Diabetes Study. Diabetes Care 2011;34:1139-1144.

[28] Zois CD, Baltayiannis GH, Bekiari A, Goussia A, Karayiannis P, Doukas M, et al. Steatosis and steatohepatitis in postmortem material from Northwestern Greece. World J Gastroenterol 2010;16:3944-3949.