

## Hepatitis A virus infection in high-risk subjects

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### Article commented

Girardi E, Scognamiglio P, Sciarrone MR, Loffredo M, Gnesivo C, Noto P, Antonucci G, Capobianchi MR, Ippolito G; GEAS Group. High HIV prevalence in male patients with acute hepatitis A in the Rome metropolitan area, Italy 2002-2008. *J Hepatol* 2011; 54(6): 1102-6.

### Original abstract

**Background & Aims.** Several outbreaks of hepatitis A affecting homosexual men have been reported in Europe. However, the prevalence of HIV infection in patients affected by hepatitis A has not been extensively studied and hepatitis A is not considered as an indicator disease for routine HIV testing. **Methods.** We retrospectively analyzed all adult cases of acute hepatitis A, reported by the National Institute of Infectious Disease "L. Spallanzani", Rome-Italy, in 2002–2008. Data on HIV infection were obtained by chart review and cross-linkage with laboratory. Information on exposure to risk factors were collected from the standard questionnaire of the Local Health Unit. **Results.** We analyzed a total of 473 cases of hepatitis A, 368 (77.2%) males that accounted for 75% of all reported cases in Rome, aged 25–64 years (same gender distribution). During the study period, we diagnosed a high proportion of cases among male individuals (78%). Among the male patients, HIV serology was available for 203/368 (55.2%). The overall HIV prevalence was 15.2% (56/368); it was significantly associated

with same gender sex and was significantly higher than that observed among patients with hepatitis B (4.0%). **Conclusions.** We found a high HIV prevalence, associated with same gender sex, among adult male patients diagnosed with hepatitis A in the period 2002–2008, except for 2006. Our data suggest that in a low incidence area for hepatitis A, with a constant high proportion of cases among male individuals, all individuals with acute hepatitis A should be routinely offered an HIV test.

**Key words.** Hepatitis A. HIV infections/diagnosis. Prevalence. Sex factor. Homosexuality. Male.

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### Comment

Over the last decades, significant changes in the epidemiological profile of the hepatitis A virus (HAV) have followed to important economic, technological and social advances. While improvement in urbanization and sanitation helped to reduce HAV incidence in developing countries,<sup>1</sup> global commerce facilitated the transmission of endemic serotypes to other latitudes, producing important disease outbreaks around the world.<sup>2</sup> Technological advances, such as phylogenetic analysis, allows for a closer tracking and surveillance of the virus, increasing our understanding of infection pathways.<sup>3</sup> Vaccination has helped to reduce HAV incidence in children, bringing countries with traditionally medium and high prevalence to low-endemicity.<sup>1</sup> Finally, sex-related risk factors have become a fundamental piece of information to understand new patterns of infection and co-infection in the adult population.<sup>4</sup> For the public health and clinical practitioner, the previously trivial HAV infection is becoming an increasingly complex puzzle, requiring evidence to unveil its dynamics and to provide proper care and prevention.

A recent manuscript published by Girardi, *et al.*<sup>5</sup> adds an astonishing piece of information to the HAV

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puzzle, showing that 15.2% of adult HAV-infected male patients in a low-incidence area were co-infected with HIV. A strong statistical association with same-gender sex suggests that sexual behavior, perhaps mediated by oral-anal or digital-anal practices, could be an important risk factor for co-infection. This observation raises interesting questions; the most important being the natural history of disease in patients with both infections. Recently the TIM1/HAVCR1 polymorphism 157insMTTTPV has been associated with an aggressive course of HAV infection, with NKT-cell mediated liver damage.<sup>6</sup> Interestingly, this polymorphism has been also associated with progression to AIDS in HIV-positive patients. Although previous HIV infection produces changes in biochemical and virologic variables, no effect over HAV prognosis has been observed.<sup>7</sup>

If confirmed, Girardi's findings would imply deep changes for HIV testing protocols in adult patients. Some important lessons to further explore the association between hepatitis A and HIV must be learned from this seminal study. First, the HIV prevalence estimation must be confirmed in sample of community-based patients. Patients included in Girardi's study were treated at a highly specialized infectious disease center, excluding uncomplicated acute hepatitis cases, and increasing the likelihood of HIV infection and HIV risk factors. This possibility is reflected in an increased male to female ratio (3.4 for Girardi's study, 1.6 for a previous community-based Italian study<sup>8</sup>), a large prevalence of same gender sex (48% of those who provided information), and a large proportion of patients previously diagnosed with HIV (77% of those diagnosed in the study). Second, all participants must be subject to HIV testing. In Girardi's study, patients reporting same gender sex were more likely to be tested for HIV, increasing their likelihood of detection and the odds of observing an association between same-gender sex and HIV. Third, data should be prospectively acquired. Girardi's study found a lower prevalence of HIV amongst HBV and HCV patients, a rather unexpected finding considering their shared transmission pathway. Girardi proposes that such difference could be partially explained by increased hepatitis B vaccination among high HIV-risk population. However, it is unclear if such difference

could also be explained by a differential registry of cases in the Local Health Unit; for instance, that the primary cause of disease registered for HIV-positive HBV and HCV patients were HIV infection instead of hepatitis, excluding them by default from the analysis. Finally, the prospective design would allow for specific data gathering, since several important covariates, such as socioeconomic status must be taken into account.

The manuscript by Girardi, *et al.* unveils a potentially complex relationship between HAV and HIV, and suggests that, at least in the high-risk male adult population, the presence HAV could serve as an indicator for increased risk of HIV infection. Beyond the specific intervention that will be needed to reduce HAV/HIV comorbidity, this finding suggests that adult HAV infection could have deeper implications for other infectious diseases.

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