

Hepatitis B and Delta Prevalence in an Immigrant Population in Italy

Giuseppe Colucci^{1*}, Massimo Colombo³, Patrizia Bono², Giovanna Lunghi² and Raffaella Romeo⁴

¹Division of Gastroenterology and Hepatology, Fondazione Ca'Granda, Policlinico, Milan, Italy

²Laboratory Medicine, Fondazione Ca'Granda, Policlinico, Milan, Italy

³Translational Research Center in Hepatology, Humanitas Research Hospital, Rozzano, Italy

⁴Servizio di Epatologia, Istituto Auxologico, Milan, Italy

*Corresponding Author: Giuseppe Colucci, Division of Gastroenterology and Hepatology, Fondazione Ca' Granda, Policlinico, Milan, Italy.

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Abstract

Objectives: The increasing flow of immigrants from hepatitis B (HBV) and hepatitis Delta (HDV) endemic countries to Europe may raise the prevalence of these infections that, due to their asymptomatic course, are likely to remain undiagnosed. We aimed at defining the actual prevalence of HBV and HDV in a representative population of migrant moving to Italy from high endemic countries and refer them to tertiary academic hospital for appropriate treatment. In addition, we intended to contribute to the ongoing debate on which public health initiatives may be implemented to better control these infections in high risk migrant populations.

Design: In this respect, we screened for the presence of HBsAg and anti-HDV a random population of primarily unregistered immigrants attending Non-Governmental Agency (NGO) clinics.

Settings: A consecutive population of unselected 213 individuals seen at the Opera San Francesco (OSF) and Fratelli di San Francesco clinics in Milan consent to participate to our screening program, independent of their specific medical needs. Patients positive for the presence of HBsAg and/or anti-HDV were further tested for HBV DNA and HDV RNA and offered appropriate counseling and treatment after receiving temporary enrollment into the national health insurance system.

Main Outcome Measures: The rate of migrants positive for HBsAg, anti-HDV, and their respective markers of active viral replication HBV DNA and HCV RNA, according to the country of origin.

Results: HBsAg was detected in 11.2% of our patients, 13% of whom were also anti-HDV positive. HBV DNA and HDV RNA were found, respectively, in 47.8% and 33.3% of them. HBsAg carriers as well as all HBV/HDV co-infected patients came mainly from Eastern Europe.

Conclusion: These data indicate a significant prevalence of undiagnosed HBV and HBV/HDV infection in a representative sample of primarily illegal, immigrants, emphasizing the need for more effective public health policies to manage this increasing and complex phenomenon.

Keywords: Hepatitis B; Hepatitis D; Immigrants; Italian Country

Introduction

Hepatitis delta virus (HDV), a defective agent co-infecting about 5% of chronic hepatitis B virus (HBV) carriers, has recently regained the interest of the scientific community because of its increasing prevalence and morbidity rates, particularly in developing countries [1-3]. The lack of adequate screening and diagnostic programs, the poor prognosis of cirrhotic cases, and the low

response rate to current anti-viral agents, make HDV infection a public health concern [4,5]. Based on an unprecedented number of immigrants reaching Italy from the poorest, least developed areas of Africa, former USSR and Latin America, we started a screening program at the Opera San Francesco (OSF), one of the largest NGO clinics in Milan, Italy, where more than 50 patients/day are seen by a team of multi-disciplinary clinicians [6,7]. The majority of these patients are illegal immigrants or refugees lacking health insurance coverage and adequate housing and potentially at risk for homelessness. To obtain an accurate estimate of the true prevalence of HBV and HDV infections in the immigrant population reaching our country, we conducted a screening program, which offered tests for HBV and HDV serological markers to a random population presenting at the OSF clinic, independent on their health status.

Materials and Methods

Serum/plasma samples were obtained from patients seen at the OSF Clinic (a minority of patients was also recruited at the Fratelli di San Francesco Clinic, Milan, Italy). 213 consecutive patients consented to participate to our HBV/HDV screening program with an adherence rate of about 15% over a 1 year period. Samples were analyzed for the presence of HBsAg and anti-HDV, both IgG and IgM, using commercially available ELISA tests (DAB, DIM, Diapro Srl, Sesto S. Giovanni, Italy). Positive patients underwent HBVDNA and HDV RNA testing, using real-time PCR kits (HBVDNAQT, HDVRNAQT, Diapro Srl, Sesto S. Giovanni, Italy) as well as HBsAg quantification (Architect HBsAg, Abbott Diagnostics SpA, Italy). Positive patients were referred to the OSF Clinic Liver Unit for clinical evaluation and then to the Division of Gastroenterology and Hepatology, Fondazione Ca' Granda, Policlinico or to the Division of Virology, Ospedale L. Sacco for specific treatment that in Italy can be prescribed only by accredited public hospitals.

Results

213 consecutive, unselected patients presenting at the OSF NGO Clinic agreed to participate to our epidemiological study, with an adherence rate of about 15% over a 1 year period. They originated from South America, Eastern Europe and North Africa (Figure 1), coming mainly from El Salvador, Peru, Bolivia, Romania, Ukraine and Egypt, as expected given the current flow of immigrants reaching our country (Figure 2). Men and women were equally distributed, 54% vs 46%, with 1 transgender patient and a mean age of 46 and 44 years, respectively.

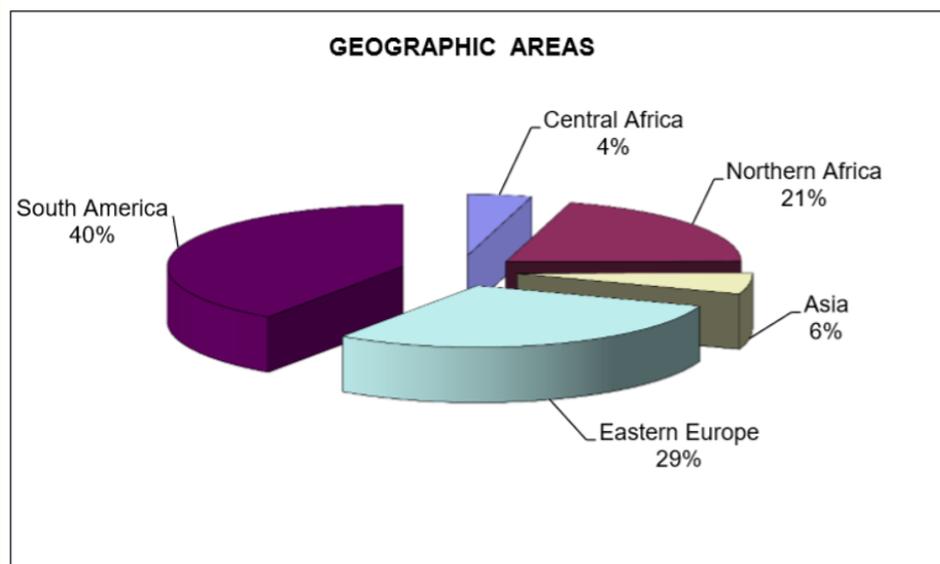


Figure 1: Geographic origin of enrolled immigrants.

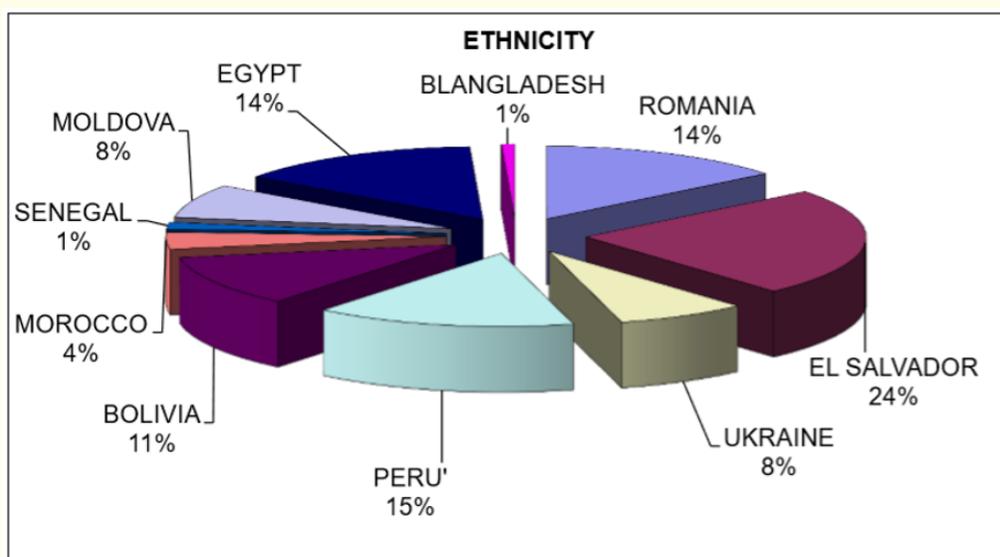


Figure 2: Ethnic origin of recruited immigrants.

HBsAg was detected in 24 patients (10 males, 14 females), with a prevalence of 11.2% and anti-HDV antibodies in 3 (12,5%) of them (all males). These prevalence rates are higher than those reported for the general Italian population (Figure 3). Among HBsAg carriers, 49% come from Eastern Europe, mainly Romania, 37% from Northern and Central Africa and only 1 from Bangladesh (Figure 4). All HBV/HDV co-infected patients were of Eastern Europe descent.

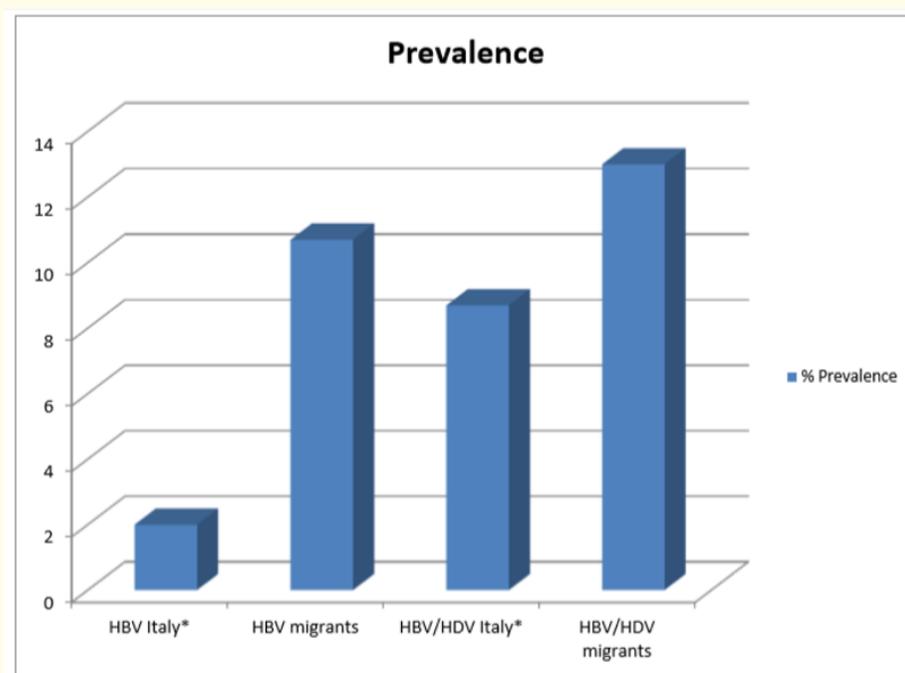


Figure 3: Prevalence of HBV and HDV infection in the study immigrant population as compared to that reported in Italian blood donors.

*ISS data on file; Sagnelli E., et al. Epidemiology of acute and chronic hepatitis B and delta over the last 5 decades in Italy. World J Gastroenterol. 20 (2014): 7635-7643.

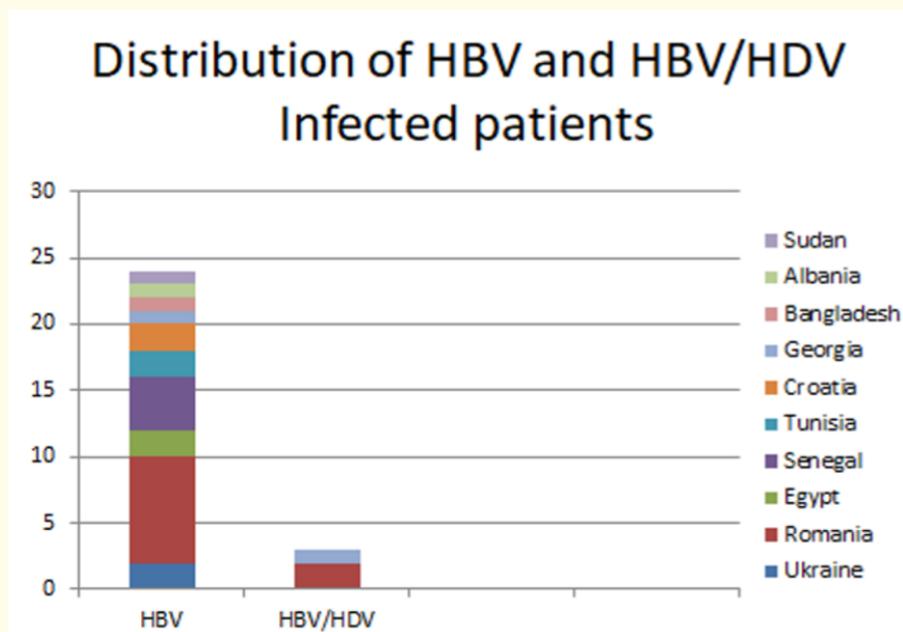


Figure 4: Distribution of HBV and HBV/HDV infected patients.

HBV DNA was detected in 11 of the HBsAg carriers, including 2 of the co-infected patients, while HDVRNA was found in 1 of the anti-HDV positive individuals who was HBVDNA negative. When quantitatively assessed, HBsAg had a mean concentration of 11496,5 IU/ml and a median value of 1217 IU/ml. No patient was symptomatic or aware of being infected at the time they were screened except 2 of the 3 HDV co-infected patients, who presented evidence of compensated cirrhosis as assessed by liver histological examination, previously performed at other institutions in their countries of origin. They, both HBV and HDV viremic, were already on treatment with Entecavir. The third patient was lost to follow-up.

Discussion

The increasing flow of immigrants from less developed countries with high endemicity for hepatitis B and Delta virus infections is a public health concern, which deserves careful assessment of the risk of transmission and makes it important to devise surveillance and control strategies [8-11]. In this respect, several NGOs are at the forefront of assisting and providing basic health care services to immigrants and can help assess the real burden of diseases in these populations [12-14]. In the current study we report the results of a screening program we conducted at a major confessional NGO clinic in Milan, the Opera San Francesco (OSF), where illegal immigrants without health insurance are taken care of [6]. A minority of patients were also enrolled at the Fratelli di San Francesco clinic. We offered tests for HBV and HDV infections, analyzing the presence of HBsAg/anti-HBs and anti-HDV IgG/IgM, to any patients who presented at the clinic regardless their complains and with no selection criteria. With an adhesion rate of about 15%, we recruited 213 individuals of whom the majority had no relevant medical history or liver disease. Most of them originated from Eastern Europe, South America and North Africa. As expected we observed high prevalence rates for both virus, significantly higher than those reported from both the Italian and the average European populations by about 5 and 1.5 fold for HBV and HDV respectively [4,15]. Moreover, half of the HBsAg carriers and 30% of those positive for anti-HDV antibody had signs of ongoing virus replication as indicated by detectable viremia. Interestingly, only 2 of the 3 HBV/HDV coinfecting patients admitted previous HBsAg testing and presented with chronic hepatitis and cirrhosis, while the others

were all asymptomatic carriers. For most of the positive individuals no clear source of the infection or risk factors could be identified, except for approximately 30% of them who had undergone surgical procedures and reported previous hospitalization. Positive patients were offered the opportunity to screen their household contacts and were provided with STP certificates (Straniero Temporaneamente Presente), which allows temporary enrollment in the national health insurance system (SSN, Servizio Sanitario Nazionale) [16]. This is the only opportunity to provide illegal or unemployed immigrants with the necessary treatment but its access is limited and restricted to urgent cases. In addition, it is not available to EU citizens, including Rumanians, who represent a significant proportion of immigrants in need of social and health care services and support [17]. These data suggest the need to vaccinate against HBV infection all negative family members or household contacts of positive immigrants as well as the need to introduce reflex HDV screening for HBsAg carriers as an early diagnosis of coinfection may help implementing appropriate treatment interventions [18]. This could also prevent super-infection by sexual transmission when both partners are HBsAg carriers. Indeed, recent epidemiological studies showed different age specific prevalence with higher rates in sexually active populations [3]. In this respect specific education programs should be developed for the most at risk categories.

Conclusion

In conclusion, our data confirm a high prevalence of HBV and HDV infection in immigrants from endemic countries with rates even higher than expected but probably more accurately reflecting the true dimension of the problem. This calls for urgent public health interventions that could provide carriers with the appropriate treatment and prevent further spread of the infection. Screening programs at the port of entry for illegal immigrants, and for all HBsAg carriers at risk of HDV superinfection, could be effective if organized by the SSN in close coordination with the EU.

Conflict of Interest

Authors have no conflicts of interest to disclose.

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