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Short Communication

Seroprevalence of hepatitis B virus and hepatitis C virus infections in elderly residents in nursing homes in southern Italy

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Background & aims. Epidemiological studies mainly performed in the '90s reported a high prevalence of hepatitis C virus (HCV) infections in Italian elderly subjects whereas HBV prevalence was generally below 1%, even in this age range. Moreover, during the last decades few studies were performed to investigate the seroprevalence of hepatitis B virus and hepatitis C virus infections in nursing homes. The aim of this study was to evaluate the current prevalence of HBV and HCV infections in a population of older residents in two nursing homes in a Sicilian urban area.

Methods. A total number of 316 male subjects [115 (36.4%), median age 84 years (range 65-101 years)] consecutively admitted to two nursing homes in Messina from January to December 2015, were tested for HBV surface antigen (HBsAg), anti-HBV and anti-HCV antibodies. Transaminase (AT) values were evaluated in all patients.

Results. Three/316 subjects(0.95%) tested HBsAg positive. Serological markers of previous HBV infection (HBsAg negative, anti-HBV positive) were found in 81/316 cases (25.6%). Nine/316 cases (2.8%) tested positive for anti-HCV. Neither HBsAg nor anti-HCV positive subjects had any laboratory or clinical evidence of liver disease. Only 2/316 patients (both HBV and HCV serum-marker negative) had AT values above the upper limit of the normal range.

Conclusions. Low HBV and HCV prevalence together with a lack of evidence of liver disease in both HBsAg and anti-HCV positive subjects suggest that the development of a virus-related hepatic illness is generally incompatible with reaching old age.

Key words: Elderly, Nursing home, Hepatitis B virus, Hepatitis C virus

INTRODUCTION

The epidemiology of Hepatitis B (HBV) and hepatitis C (HCV) virus infections is constantly changing, being influenced by several factors including population migrations, modification in the social and health-care systems in various geographic areas, availability of very efficient anti-HBV vaccine and efficacious therapies against both viruses. In this context, the persistent evidence of a higher morbidity and mortality rate related to one of both viruses amongst older people in several rich countries should be noted [1]. Infections are a major and persistent problem in Nursing Homes (NHs). Recently, an increase in the prevalence of viral hepatitis has been demonstrated in NHs residents in the United States [2].

Studies carried out mainly in Italy (including Sicily) in the 1990s and at the beginning of the current century reported an HBV surface antigen (HBsAg) prevalence

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ranging between 0.6 and 1%, whereas the HCV infection prevalence was very high, ranging between 5.2 and 42.2% in elderly subjects [3]. Additional Italian studies carried out in the late '90s reported 0.6% of HBsAg prevalence in subjects resident in NHs, whereas more than one third of residents had evidence of previously productive HBV infection since they were positive for the antibody to HBsAg (anti-HBs) and/or to the HBV "core" antigen (anti-HBc) [4]. In similar subsets of NH residents,anti-HCV seroprevalence appeared to have increased from 2.2 to 11.8% in two studies performed, respectively, in the early and the late '90s by the same group in the North of Italy [5 6].

More than 10 years after these studies and considering the data they produced altogether, it would be reasonable to expect a persistent, high prevalence of HCV infection (as well as of HCV-related morbidity) in elderly southern Italian people, and at the same time a further decline of the HBsAg prevalence in that population.

The aim of our study was: to evaluate the serum-prevalence of HBV and HCV infection markers in elderly subjects admitted to two national healthcare NH in a Sicilian city, and to compare the results with those present in the literature.

MATERIALS AND METHODS

Three-hundred-sixteen subjects [115 males (36.4%), median age 84 years (range 65-101 years)] consecutively admitted from January to December 2015 to two national healthcare NH in the Sicilian city of Messina were included in the study.

All subjects were tested for HBsAg, anti-HBs, anti-HBc, and for the anti-HCV antibody. Serum samples testing HBsAg positive were subsequently examined for the HBV "e" antigen and the corresponding antibody (HBeAg and anti-HBe, respectively). Patients who tested anti-HCV positive were considered for subsequent HCV RNA analysis.

Aspartate- and alanine-aminotransferase (AST and ALT, respectively) levels were dosed at the time of the viral marker screening in all residents.

HBV serum markers and anti-HCV were tested by chemiluminescent enzyme immunoassay (Abbott, Chicago, IL). HCV RNA was determinedby a real time polymerase chain reactionassay(rtPCR – CobasAmpliprepTaqMan 2.0 detection limit: 15 IU/ml; RocheDiagnostics, Branchburg, NJ).

χ^2 test was applied with reference to categorical variables for statistical analyses. A p-value < 0.05 was considered to be statistically significant.

The study was performed in accordance with the ethical standards established in the Declaration of Helsinki and its later amendments, and the Ethics Committee of the University Hospital of Messina approved it.

RESULTS

Three/316 (0.95%) patients (all males, 69-, 82- and 83-years old, respectively) were HBsAg positive. All these subjects tested anti-HBe positive. Eighty-one/316 (25.6%) patients, (median age 84 years, range 65-101) were positive for anti-HBV antibodies, 11 of whom were positive for anti-HBs alone, 18 for anti-HBc alone, and 52 were positive for both antibodies. None of the patients had been vaccinated against HBV infection (Tab. I).

Anti-HCV was detected in 9/316 (2.8%) subjects (3 males, median age 88.8 years, range 69-99) (Tab. I). HCV RNA was tested only in two cases, proving positive in one ($2x10^6$ IU/ml viral load)and undetectable in the other. In the remaining seven cases, HCV RNA was not examined because the patients had been discharged (4 cases) or died (2 cases) before the result of the anti-HCV test was available. One additional subject refused further analyses. Two of the nine anti-HCV positive subjects were also antiHBs/antiHBc positive. No statistically significant difference was observed in terms of HBV and HCV positive/negative serum marker distribution between sexes and after stratifying subjects by age.

Mean ± SD and median transaminase values were 20.34 ± 11.56U/L and 18U/L for AST, and 17.08 ± 15.85U/L and 13U/L for ALT, respectively.

All 316 subjects, except 2, had ALT and AST values within the normal range. Two cases had a slight/moderate (1-3 times the normal values) increase of both amino transferases, and none of them showed any viral marker positivity or additional clinical/biochemical signs of liver disease.

DISCUSSION

In the decades following the Second World War, Italy was one of the European countries with the highest HBV and HCV endemicity, with a general prevalence of both viral infections reaching percentages higher than 10% in some areas of the South [3 7]. This was essentially related to the perinatal transmission from infected mothers to new-borns (mainly for HBV) and to the widespread use of injections with non-sterile needles and syringes (mainly for HCV) [5]. Improvement of socio-economic conditions and introduction of effective public health measures as well asthe HBV universal vaccination programme of newborns and 12-year-old

Table I. Distribution of HBs Ag, anti-HBV antibody, and anti-HCV by sex and age in nursing homes residents.

	Number of cases	Anti-HCV positive n. (%)	HBs Ag positive n. (%)	Anti -HBs and/or anti- HBc positive n. (%)
Study population*	316	9 (2.8)	3 (0.9)	81 (25.6)
Age: 65-74 years	56	0†	1 (1.8) †	11 (19.6) †
75-84 years	131	4 (5.9)†	2 (1.5) †	31 (23.7) †
≥ 85 years	129	5 (3.9)†	0†	39 (30.2)†
Male	115	3 (2.6) ‡	2 (1.7) ‡	35 (30.4) ‡
Female	201	6 (2.9) ‡	1 (0.5) ‡	46 (22.8) ‡

* median age 84 years, range 65-101; † p = 0.4; ‡ p = 0.6

adolescents started in 1991 brought about significant changes in the epidemiology of the two viruses and a considerable reduction of their spread. Because of this progressive and irreversible improvement of general living conditions, the chronic HBV and/or HCV carrier state appeared to be essentially confined to the elderly subjects who had contracted the life-long infections in their youth. Indeed,a number of epidemiological studies performed in the last decade of the past century indicated a high prevalence (range 5-42%) of HCV infection among subjects 55 years and older [3 8] whereas HBV prevalence was generally below 1% even this age range. On these bases, one might expect that – 15-20 years after those epidemiological studies – a large number of subjects aged 75-90 years should be HCV infected whereas the total number of HBsAg carriers should have subsequently decreased in our area. Thus, we approached this study in the attempt to verify the prevalence of HBV and HCV infection as well as of the virus-related liver diseases in a quite large number of NH residents in a metropolitan area of Southern Italy.

During the last decades few studies were performed to investigate the seroprevalence of hepatitis B virus and hepatitis C virus infections in Nursing Homes.

Comparing the results of the present study with the few studies investigating the viral hepatitis prevalence in nursing home residents performed over time in various countries, we observed that both HBsAg and anti-HBV antibody seroprevalence was similar to that observed in the '90s in North Italy and in some (even if not in all) other countries [4 9-14] (Tab. II).

The anti-HCV prevalence found in our study was similar to previous data obtained in NH from various countries [4,9,12-15] (Tab. III), except for the previously reported study performed in the late '90s in northern Italy and showing an HCV prevalence of 11.8% [6]. It should be stressed that there is paucity of data on prevalence of HCV infection among older adults in long-term care setting, as confirmed by a recent systematic review of the literature [16].

Surprisingly, we found that less than 3% of the study population were positive for anti-HCV antibody, thus a much lower prevalence than expected based on the previous epidemiological studies mentioned above. Furthermore, HCV RNA was undetected in one of the two subjects tested, thus suggesting that the prevalence of productive HCV infection is even lower than that indicated by anti-HCV testing. A possible explanation of these results, apparently not in agreement with expected data, is that although HCV-related liver injury is usually a slowly progressing disease, it is in any case a cause of death that stops patients reaching very old age (of note, the

Table II. Reported HBV serum marker prevalence in nursing homes residents in comparison with previous studies.

Author	Country	Study period	Number of cases	Age, years (± SD)	HBsAg n. (%)	Anti-HBs n. (%)	Anti-HBc n. (%)
Braconier	Netherlands	1972	59	n.a.	6 (10.1%)	n.a.	n.a.
Chiaramonte	North Italy	1982	108	n.a.	9 (8.3%)	55 (50.9%)	14 (12.9%)
Simor	Toronto	1992	508	83	3 (0.6%)	n.a.	n.a.
Floreani	Italy	1992	315	n.a.	2 (0.6%)	116 (36.8%)	n.a.
Chien	Missouri	1999	199	79	0	39 (19.5%)	48 (24.1%)
Sugauchi	Japan	1999	119	82.8 ± 7.3	6 (5.0%)	17 (14.3%)	6 (5.0%)
Ganaei	Iran	2007	383	58.4 ± 21.9	2 (0.6%)	n.a.	1 (0.3%)
Maral	Turkey	2009	227	76.1 ± 8.5	27 (11.9%)	109 (48.0%)	57 (25.1%)
Present study	South Italy	2015	316	83.5 ± 7.5	3 (0.9%)	63 (19.9%)	70(22.1%)

n.a.= not available; SD= standard deviation

Table III. Reported anti-HCV prevalencein Nursing Homes residents in comparison with previous studies.

Author	Country	Study period	Number of cases	Age, years (± SD)	Anti-HCV n. (%)
Simor	Toronto	1992	508	83	7 (1.4%)
Floreani	North Italy	1992	315	n.a.	7 (2.2%)
Chien	Missouri	1999	199	79	9 (4.5%)
Baldo	Italy	2000	288	79.3 ± 8.9	34 (11.8%)
Ganaei	Iran	2007	383	58.4 ± 21.9	9 (2.3%)
Maral	Turkey	2009	227	76.1 ± 8.5	6 (2.5%)
Present study	South Italy	2015	316	83.5 ± 7.5	9 (2.8%)

n.a.= not available; SD= standard deviation

median age of our study population was 84 years).On the contrary, the HBV prevalence appears to be stable over time and comparable to that detected in studies performed even twenty years ago in North Italy [4], since one percent of subjects included in this study tested positive for HBsAg and more than 20% for anti-HBV antibodies. Of course, the normal AT values and the absence of any clinical sign of liver disease clearly indicate that the HBsAg positive subjects were long-term inactive HBV carriers who have a survival expectancy comparable to that of the general, HBV-uninfected population, at least in the western world [17].

Summarizing, our data seem to indicate that active, chronic HBV and HCV infections are incompatible with long-term survival and are largely uncommon in the very old, among residents in NH. In this context, it appears to be of particular interest that only two out of 316 (0.6%) of our NH residents had biochemical evidence of liver damage, and this tempts us to speculate that chronic liver injury is in itself a factor that reduces the chance of reaching very old age, even regardless of the viral etiology of the disease.

On the basis of our findings, a major question that may arise is whether it makes sense to screen NH residents for HBV and HCV, and whether it is worth administering specific anti-viral therapy in those subjects found (or already known) to be actively infected. This important question also has evident ethical implications that are not dealt with here since they are not the objectives of this study. From the point of view of clinical practice, one should consider that NHs are restricted communities where quite large numbers of subjects live very close to each other and share spaces and objects such as cutlery. Consequently, the risk of infection spread is high, and indeed various hepatitis B and C epidemics have been reported in NHs of various European countries [18-20]. In this context, it is noteworthy to consider that an acute hepatitis infection developing in an old person may easily cause clinical decompensation, thus being potentially lethal. Consequently, we do believe that HBV and HCV screening of subjects on admission to an NH is a useful way of identifying subjects who are potentially a source of infection transmission to the other members of the community. Those found to be infected and viremic should be treated with antivirals to avoid the transmission of the infection to other residents (and also to health workers). Furthermore, considering that there are very few of these subjects, the excellent tolerability of both anti-HBV and anti-HCV drugs, the low cost of anti-HBV antivirals also due to the expiry of patents, the continuing decrease in price of direct acting anti-HCV antivirals might suggest the cost-effectiveness of this procedure.

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Conflict of interest

On behalf of all Authors, the corresponding author states that there is no conflict of interest.

Ethical approval

The study was approved by the Ethics Committee of the University of Messina (prot. Number 36/17). The study have been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

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