RESEARCH PAPER | Medical Science | Volume : 4 | Issue : 5 | May 2014 | ISSN - 2249-555X

Risk of Developing Specific Aids-Defining Illnesses and Opportunistic Infections in Romanian Coinfected Patients with HIV and Hepatitis B Virus

KEYWORDS

*** Gabriela Juganariu**

Assistant Professor, University of Medicine and Pharmacy "Grigore T. Popa"-Iasi, Faculty of Medicine Department of Infectious Diseases ,Iasi
*Corresponding Author

Egidia Miftode

Professor Associate, University of Medicine and Pharmacy "Grigore T. Popa"-Iasi, Faculty of Medicine Department of Infectious Diseases,Iasi

ABSTRACT *Objectives: To assess the influence of HIV/HBV coinfection on the risk of opportunistic infections and AIDS-defining illnesses in HIV-infected patients in Northeastern Romania. Material and Methods: Retrospective study included 466 patients with HIV infection assessed at the Iasi HIV-AIDS Regional Center during 2000-2013 stratified into two groups according to the presence of HBV coinfection. Results: The prevalence of HIV/HBV coinfection was 19.9%. Coinfection was more frequent in the age group 20-29 years (86.5%). HIV infection was predominantly transmitted through parenteral routes (58.5% vs. 61.5%). In the coinfected group, lower CD4 counts (246.20 vs 296.86 cel/mm3) and higher mean HIV RNA levels (142,906 copies/ml) were found. A CD4 count <200/ml and HIV RNA > 100,000 copies/ml were strong predictors for most opportunistic infections. Conclusions: HIV -HBV coinfected patients in our cohort had a 3.87 times higher risk of developing opportunistic infections and AIDS-defining illnesses. Keywords: coinfection HIV-HBV, opportunistic infections.*

INTRODUCTION

Since the advent of effective antiretroviral therapy (ART) for human immunodeficiency virus-1 (HIV), there has been a substantial decrease in deaths related to acquired immunodeficiency syndrome (AIDS). However, in the ART-era liver disease is now the most common non-AIDS related cause of death among HIV-infected patients.

Having common routes of transmission, coinfection with hepatitis B virus (HBV) is common among HIV-infected individuals, its prevalence among this patient category being higher than in general population. Worldwide, hepatitis B virus infection affects 10% of the 40 million HIV-infected individuals (1,2,3). HBV tends to be more aggressive in HIV-positive individuals than in monoinfected individuals, with higher levels of HBV viremia, more frequent episodes of activation and faster progression to cirrhosis. (4,5,6,7,).

The aim of this study was to estimate the prevalence of chronic HBV infection in HIV infected patients in Northeastern Romania and to assess the risk of opportunistic infections and AIDS-defining diseases in relation to its presence.

MATERIALS AND METHODS

This retrospective study included 466 patients cared at the Iasi Regional HIV-AIDS Centre during 2000-2013. The patients were stratified into two groups: HBV group - 252 patients with HIV/HBV coinfection and nonVHB group - 214 HIV patients without HBV coinfection, which served as control group.

The participants in this study were defined as positive for HBV if HBsAg was persistently positive for > 6 months; the patients with HCV infection or HBV-HCV and HBV-HDV coinfections were excluded from the study.

The epidemiological, clinical and viroimmunological data were obtained from patients monitoring sheets and medical records.

The incidence of various opportunistic infections and AIDS-defining illnesses in the 2 groups, classified according to CDC criteria into 6 groups according to etiology, was determined.

Statistical analysis

The results were interpreted based on frequency and structure indicators, processed with SPSS statistical functions using Student t-test, χ^2 test, Pearson correlation coefficient and the linear trend. P values < 0.05 were considered significant.

RESULTS

1. Cohort characteristics

Of the 1,358 patients cared at the Iasi HIV-AIDS Centre we studied 466 HIV-infected patients who underwent at least one serologic test for HBV, the incidence of chronic HBV hepatitis being 19.19%.

HBV coinfection was more common among males than females, but the difference was not statistically significant (53.2 % vs. 48.13 %) (p = 0.321). Most patients in both groups belonged to the age group 20-29 years (86.5 % vs. 72.4 %), the mean age of patients in the HBV group being significantly lower (25.56 vs. 27.14 years) (p = 0.025). In more than half of the subjects (58.5 %) HIV infection was transmitted nosocomially. Heterosexual route of transmission was more common among HBV group (40.1 % vs. 35 %), and homosexual mode of transmission was identified in a minority of cases (2.4% vs. 3.3%) (Table 1).

The time from HIV diagnosis until the occurrence of opportunistic infection in the HBV-coinfected group was significantly longer than in controls (mean, 9.27 vs. 7.99 years) (p = 0.001).

Table-1: Patient characteristics by study groups

Parameter	HBV group (n=252)	NonHBV group (n=214)	P
Male gender no (%)	134 (53.2%)	103 (48.1%)	0.321
Mean age (years)	25.56±6.33	27.14±8.75	0.025
Sexual transmission no (%)	107 (42.5%)	82 (38.3%)	0.416
Average time from HIV infection diagnosis (years)	9.27±2.76	7.99±3.46	0.001
Mean CD4 level (cells/ml)	246.20± 185.04	296.86± 220.06	0.007

Volume : 4 | Issue : 5 | May 2014 | ISSN - 2249-555X

CD4 nadir (cells/ml)	113.34± 124,41	166,74± 186,65	0.001
HIV RNA (copies/ml) - Undetectable no (%) - Mean value	46 (18.3%) 142,906± 27519	41 (19.2%) 110,844± 23212	0.896 0.383
Alanine transaminase (UI/l)	49.90±38.00	32.93±30.72	0.001

CD4 nadir: lowest ever CD4 count

Significant differences in mean CD4 counts (p = 0.007) between the study groups were found. The average level in the coinfected group (246,20 cells/ml) was lower than in the HBV-noninfected group (296.86 cells/ml). During disease progression the mean CD4 nadir count was significantly lower in the HBVgroup (113.34 vs. 166.74 cells/ml) (p = 0.001). Mean plasma viremia was slightly higher in patients with HIV/HBV coinfection (142,906 versus 110,844 copies/ml) (p = 0.383).

The HIV/HBV coinfected patients had a mean ALT level significantly higher than that recorded in the nonHBV group (49.90 vs. 32.93IU/l) (p = 0.001). For elevated ALT levels, the relative risk induced by HBV coinfection was over two times higher (RR = 2.19).

2. Opportunistic infections

In the study population we found a total of 375 opportunistic infections and AIDS-defining illnesses, their classification according to cause being presented in table II. which shows their higher incidence in the HBV group which included patients with two or more opportunistic infections.

Table-2: Classification of opportunistic infections by study groups

Infections	HBV group (no=252)		NonHBV group (no=214)		P	RR	IC95%
	No.	%	No.	%			
Mycotic							
Pneumocystis jirovecii	4	1.6	3	1.4	0.827	1.13	0.26÷ 5.00
Oropharyngeal candidiasis	56	22.2	24	11.2	0.003	1.98	1.27÷ 3.08
Cryptococcus neoformans	4	1.6	2	0.9	0.833	1.70	0.31÷ 9.18
Cryptosporidium	1	0.4	-	-	0.935	-	-
Bacterial							
Mycobacterium tuberculosis	69	27.4	43	20.1	0.096	0.69	0.46÷ 1.04
Recurrent pneumonia	52	20.6	11	5.1	0.001	4.01	2.15÷ 7.50
Sepsis	15	6.0	1	0.5	0.003	12.74	1.70÷ 95.65
Viral							
Kaposi sarcoma	1	0.4	-	-	0.935	-	-
Cytomegalovirus	7	2.8	1	0.5	0.120	5.94	0.74÷ 47.94
Herpes zoster	27	10.7	9	4.2	0.014	2.55	1.23÷ 5.30
Progressive multifocal encephalopathy (PML)	1	0.4	1	0.5	0.552	0.85	0.05÷ 13.50
Parasitic							
Cerebral toxoplasmosis	3	1.2	5	2.3	0.554	0.51	0.12÷ 2.11
Other HIV-related diseases							
Wasting syndrome	52	20.6	14	6.5	0.001	3.15	1.80÷ 5.53
AIDS dementia complex	1	0.4	-	-	0.935	-	-
Neoplasms							
Hodgkin lymphoma	3	1.2	2	0.9	0.854	1.27	0.21÷ 7.55
Neoplasms	2	0.8	1	0.5	0.887	1.70	0.16÷ 18.60
TOTAL	298		77				

HBV-HIV coinfection was associated with a 2 to 5 times higher risk of bacterial, viral (CMV, HSV), and mycotic (Candida albicans) infections and wasting syndrome, but not of protozoan infections or neoplasms, with the highest value for the relative risk of sepsis (RR = 12.74) and CMV infection (RR = 5.94) (Table 2).

An average CD4 count of <200/ml was a strong predictor for all opportunistic infections except herpes zoster, sepsis episodes, oropharyngeal candidiasis, and AIDS dementia complex (Fig. 1). In this regard, there were significant differences between the 2 groups for CMV (p =0,049) and Pneumocystis jirovecii (p =0,016) infections.

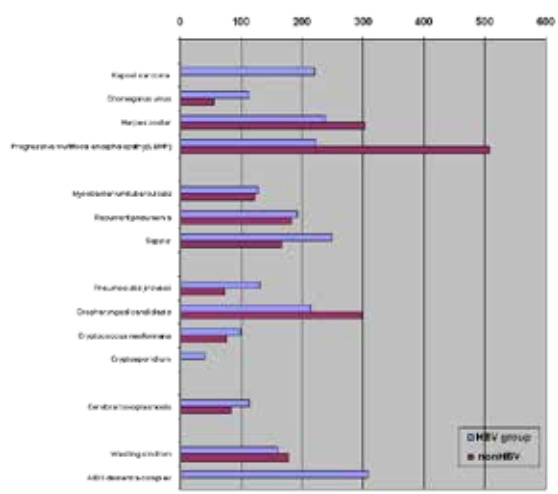

Fig. 1: Mean CD4 counts (cells/mm³) for opportunistic infections

The small number of cancer cases did not allow statistically reliable conclusions even though in the HBV group a slightly higher relative risk of Hodgkin lymphoma (RR = 1.27) or other cancers (RR = 1.70) was noticed.

In both groups, high plasma viremia > 100,000 copies/ml was associated with the occurrence of most opportunistic infections (except shingles and sepsis), statistically significant differences being recorded for oropharyngeal candidiasis (p =0,001), progressive multifocal leukoencephalopathy (PML) (p = 0,001), and CMV infection (p = 0,030).

Volume : 4 | Issue : 5 | May 2014 | ISSN - 2249-555X

DISCUSSIONS

In this study, which included a representative number of HIV-infected patients from Eastern Europe, the prevalence of HBV infection was substantially higher than in the general Romanian population (of about 5.6%) and above the statistical data on HIV/HBV coinfection in Europe (2,8). This increase can be accounted for by the epidemiological peculiarities of the mode of HIV transmission in the region (more than half of the subjects included in the study belonging to the 1989-1990 cohort in which HIV was transmitted parenterally which favored the concomitant infection with HBV).

Mean CD4 cell count were lower and the mean HIV RNA level higher in the HBsAg positive group possibly because of the longer duration of HIV infection to the emergence of opportunistic infection in this group.

The higher incidence of bacterial, fungal and viral (CMV and varicella zoster virus) infections may be related to the specific interactions between HBV and the poor immune response of HIV-infected patients(2).

The main strengths of the study are the large sample, the number of studied cofactors, and the rigorous coding of events. Although the HIV/HBV coinfected group was representative, the ability to perform HBV-DNA detection was limited and so was the determination of all serological markers for HBV infection. HBV infection may have been underestimated due to the presence of occult HBV in patients without detectable HBsAg (9).

CONCLUSIONS

The patients with concomitant HIV/HBV infection in our cohort had a 3.87 times higher risk of developing opportunistic infections and AIDS-defining illnesses. Coinfected patients had lower mean CD4 count and statistically significant higher HIV viremia than those without HBV coinfection.

The study reveals the particularities in a geographic area with a high rate of HBV infection in HIV-infected patients, and their impact on the decision when to start the treatment and what type of antiretroviral drug to use.

REFERENCE

1. Konopnicki D, Mocroft A, deWit S, et al.2005. Hepatitis B and HIV: prevalence, AIDS progression, response to highly active antiretroviral therapy and increased mortality in the EuroSIDA cohort. AIDS 19:593–601 | 2. Sène D., Pol S. et al.2007. Epidemiology, diagnosis and treatment of chronic hepatitis B in HIV-infected patients (EPIB 2005 STUDY). AIDS 19;21(10):1323-31 | 3. Lai C, Shouval D, Lok A.2006. Entecavir versus lamivudine for patients with HBeAg-negative chronic hepatitis B. N Engl J Med 354:1011–1020. | 4. Jain MK, Parekh NK, Hester J, Lee WM.2006. Aminotransferase elevation in HIV/hepatitis B virus co-infected patients treated with two active hepatitis B virus drugs.AIDS Patient Care STDS 20: 817–822. | 5. Lincoln D, Petoumenos K, Dore GJ.2003. HIV/HBV and HIV/HCV coinfection, and outcomes following highly active antiretroviral therapy. HIV Med 4:241–249 | 6. Matthews G, Bartholomeusz A, Locarnini Set al.2006. Characteristics of drug resistant HBV in an international collaborative study of HIV-HBV-infected individuals on extended lamivudine therapy.AIDS 20: 863–870.133 | 7. Puoti M, Airoldi M, Bruno R, Zanini B, Spinetti A, Pezzoli C et al.2002. Hepatitis B virus co-infection in HIV-infected subjects. AIDS Rev 4:27–35 | 8. Sterling RK, Chiu S, Snider K, Nixon D.2008. The prevalence and risk factors for abnormal liver enzymes in HIV-positive patients without hepatitis B or C co infections. Dig Dis Sci 53:1375–138 | 9. Gandhi RT, Wurcel A, McGovern B, Lee H, Shopis J et al. 2003 Low prevalence of ongoing hepatitis B viremia in HIV-positive individuals with isolated antibody to hepatitis B core antigen. J Acquir Immune Defic Syndr 34:439–441 |