METABOLICAL CHANGES IN HBV/ HIV COINFECTIONS

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Abstract

The aim of this study was to evaluate the main metabolic changes in the case of hepatitis B virus (HBV) / human imunodeficiency virus (HIV) coinfection. A retrospective study, on 482 HIV infected patients was assesed, at Iasi Regional HIV-AIDS Center Iasi, between 2000-2014. Subjects were divided into 2 groups, according to the presence or absence of HBV coinfection. HIV prevalence was higher in the 20-29 years aged group (86.5%), parenteral routes being the predominant mode of HIV transmission (61.5% vs 58.5%). Mean ALT levels were significantly higher ($p<0.001$) in the HBV group (49.92 IU/L vs 32.93 IU/L). Average total cholesterol levels were significantly higher ($p<0.001$) in the HBV group(182.58 vs 167.59 mg%). The average levels of serum triglycerides in the HBV group were significantly lower ($p<0.001$) than those recorded in the nonHBV group (130.72 vs. 164.59 mg%). Dyslipidemia was common in the HIV/HBV coinfected group (107 vs. 82). Hepatitis B virus infection induced a 2-fold higher relative risk for the occurence of hepatic cytolysis syndrome .

Keywords: *alanine aminotransferanse (ALT), dyslipidemia, HIV/HBV coinfection, hypercholesterolemia*

Introduction

Worldwide, infection with human immunodeficiency virus is constantly expanding, with epidemiological profiles influenced by regional factors; it remains a topical issue on health due to its impact on health system, being a leading cause of death and a factor generating other infectious diseases. In Romania, according to the National Commission for Fight against AIDS, at the end of 2013 there were 12.273 people living with HIV/AIDS. The specifity of the 1987-1990 HIV outbreak among children in Romania was given by its hight incidence rate and recognized parenteral route of transmission. Given this epidemiological features we are now faced with a group patients (6000 in number) subjected to various treatments in which resistance to antiretroviral medication is a major problem. Metabolic disorders (dyslipidemia, diabetes mellitus, and lipodystrophic syndrome), as potential long-term complications in these patients, requires special management [2].

Currently, liver disease is an important cause of morbidity among HIV-infected patients worldwide, while the classic manifestations of opportunistic infections secondary to severe immunodeficiency have declined dramatically as a result of successful large-scale implementation of HAART, e.q. highly active antiretroviral therapy [8].

Due to the common transmission routes, both sexual and parenteral, HIV/HBV coinfection is common, about 10% of HIV-infected people worldwide presenting concomitant chronic HBV infection. Its prevalence is higher in the at-risk groups (especially homosexuals and intravenous drug users) and in areas where chronic HBV infection is endemic [5,6].

The aim of this study was to determine the impact of HBV coinfection on the biochemical profile of the HIV-infected patients in the Northeastern Romania and to assess the risk factors associated to metabolic disorders in this population.

Material and methods

This retrospective study included 482 patients cared and assessed at the Iasi Regional HIV/AIDS Center in the interval 2000-2014. Depending on the association of HBV coinfection the study group was divided into 2 groups: HBV group – 252 patients with HIV/HBV coinfection and nonHBV group – 230 patients without HBV coinfection, which served as control group.

HIV infection was documented in adults and children > 18 months by two positive ELISA

tests (antibodies to HIV are present) and confirmatory HIV-1 Western Blot test. The study participants were defined as positive for HBV infection if two HBsAg determinations at least 6 months apart were positive.

The biochemical parameters were determined in serum by enzymatic methods in view of defining the cytolysis syndrome, hypercholesterolemia, and hypertriglyceridemia. As recommended by the international guidelines we used the cut-off values: alanine aminotransferase (ALT) > 32 IU/l, total cholesterol> 200 mg%) and triglycerides> 150 mg%. Dyslipidemia was defined as the total cholesterol > 240 mg/dl or triglycerides > 200 mg/ dl, or both.

Information on the epidemiological, clinical and viro-immunological data were obtained from patient monitoring sheets and medical records.

The results were evaluated and interpreted based on the frequency and structure indicators, and processed using SPSS statistical functions using Student t-test, Pearson's chi-squared test, and the linear trend. P values were considered significant at < 0.05.

Results and discussions

Of the total 1358 patients cared at the Iasi Regional HIV/AIDS Center included in this study were 482 HIV-infected patients who had been serologically tested for HBV at least once, the incidence of chronic HBV hepatitis being 19.19%.

Most patients in both groups belonged to the age group 20-29 (86.5% vs. 72.4%). The mean age of patients in the HBV group was significantly lower (25.56 vs. 27.14 years) (p=0.025). In more than half of the study patients (58.5%) HIV infection was transmitted by parenteral route (nosocomial) consistent with the specifity of HIV outbreak in our country. The estimated average time from HIV diagnosis to the time of entry into the study was 9.27 years in the coinfected group, significantly longer compared with that of 7,99 years recorded in nonHBV group (p=0.001).

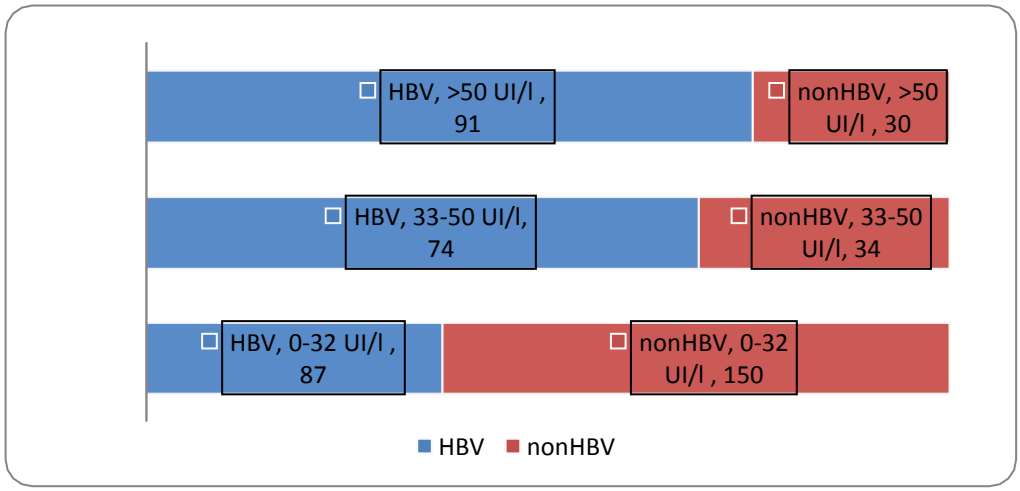

Fig. 1. Groups distribution according ALT levels

Most study patients were in advanced stages of HIV infection, 46.82% being classified as CDC stage C, 34.9% stage B, and only 18.25% as stage A.

Individual ALT levels in HIV/HBV-coinfected patients ranged from 10 to 323 IU/I with a very wide variance, the average level in this group being significantly higher than that recorded in the non HBV group (49.90 vs. 32.93 IU/I, p=0.001). It should be noted that in the presence of elevated ALT levels the relative risk induced by HBV coinfection is more than 2 times higher (RR = 2.19, 1.78/2.74). Over 65% of the patients in the HBV group had ALT levels above the reference value (32 IU/I) with 36.1% of them exceeding the average group value of 49.90 IU/I. In nonHBV

group ALT was within normal ranges in 70.1% of patients, levels above 50 IU/I being identified in only 14% of the subjects. Statistically, the odds ratio according to ALT level showed significant percentage differences (p = 0.001) between the study groups, 70-75% of subjects with ALT above the upper reference range belonging to the HBV group (Table 1).

Table 1.

ALT values(UI/I) & main statistical indicators of the study groups

Group	No.	Mean	Confidence interval		Min	Max	P
			-95%	95%			
HBV	252	49.90	44.29	53.72	10	323	0.001
nonHBV	214	32.93	28.79	37.07	8	250	
Total	466	41.6	38.37	44.87	8	323	

Individual total cholesterol levels in the HBV group ranged from 68 to 338 mg% with moderate variance, the average group level being significantly higher (182.58 vs. 167.59 mg%) than that recorded in the nonHBV group (p = 0.001) (Table 2).

Table 2.

Total cholesterol values (mg%) & main statistical indicators of the study groups

Group	No.	Mean	Confidence interval		Min	Max	P
			-95%	95%			
HBV	248	182.58	176.08	189.08	68	338	0.001
nonHBV	213	167.59	161.10	174.07	22	348	
Total	461	175.65	171.02	180.29	22	348	

The relative risk induced by the HBV coinfection was 1.73 times in the patients with total cholesterol above the reference range. In our study group, 21.8% of the subjects in the HBV group and 12.6% in the nonHBV group presented individual total cholesterol levels above the reference range (200 mg%) (Fig. No. 2).

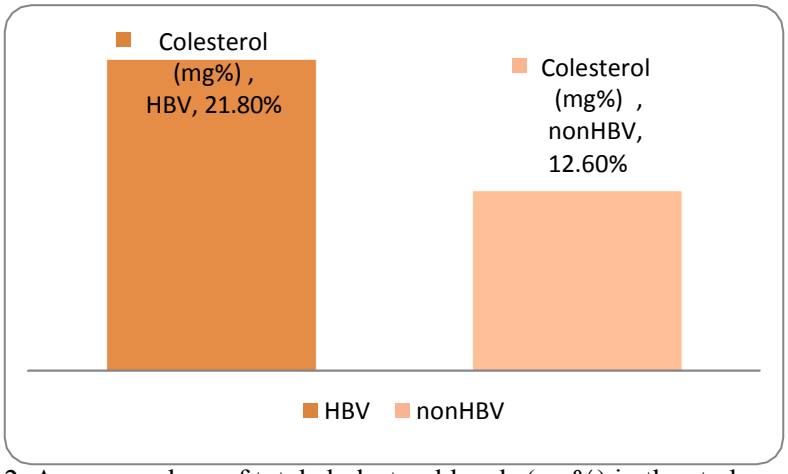

Fig. 2. Average values of total cholesterol levels (mg%) in the study groups

In the HBV group patients the individual serum triglyceride levels ranged from 11 to 256 mg% with moderate variance, the average group level being significantly lower than that recorded in the nonHBV group (130.72 vs 164.59 mg%) (p=0.001). Individual serum triglyceride levels below the reference range (160 mg%) were recorded in 67.5% of the subjects in HBV group and in only 16.8% in nonHBV group. Subunit relative risk (RR=0.59, 0.45/0.76) in HBV group patients revealed a protective role if serum triglyceride levels were within normal range (Table 3).

Table 3.

Groups structure according to serum triglyceride levels (mg%)

Triglyceride level	HBV group		NonHBV group	
	No.	%	No.	%
≤ 150 mg%	170	67.5%	36	16.8%
> 150 mg%	82	32.5%	45	21.0%

Patients with concomitant HIV/HBV coinfection presented a higher risk for having dyslipidemia or receiving lipid lowering therapy than HIV monoinfected patients (107 vs.82) (p=0.416).

Table 4.

Serum triglycerides values (mg%) & main statistical indicators in the investigated groups

Group	No.	Mean	Confidence interval		Min	Max	Variance (%)	p
			-95%	95%				
HBV	250	130.72	123.85	137.58	11	256	42.17	0.001
nonHBV	81	164.59	152.88	176.30	59	270	32.17	
Total	331	139.01	132.90	145.11	11	270	40.60	

The advent of highly active antiretroviral therapy (HAART) has been associated with a significant reduction of morbidity and mortality among HIV-infected patients [3]. As a result of this success the survival in this population has increased and chronic complications, including metabolic disorders and chronic liver diseases which may frequently coexist in these patients are of growing importance [1, 11].

In this study the prevalence of HBV infection in the HIV-infected population in the Northeastern Romania was of 19.9%, substantially higher than the prevalence in the general population of our country (5-6%) and higher than the statistical data on HIV/HBV coinfection in Europe [5]. This finding may be accounted for by the regional epidemiological peculiarities related to the route of transmission (the parenteral transmission of HIV favored the concomitant infection with HBV).

The significant proportion of patients in advanced stages of disease compared with other studies can be explained on one hand by the epidemiological characteristics of HIV infection in our country, the majority of patients belonging to the long-term survivor cohort, on the other hand by the possible influence of HBV on the acceleration of HIV disease progression.

The lack of a significant immune response against HBV was reflected in the average transaminase levels which were higher in the HIV/HBV-coinfected patients, in line with data from other studies, but which must be interpreted in the context of their association with multiple other factors, like hepatic steatosis, hepatotoxicity of antiretroviral agents, lipodystrophy [9, 10].

In agreement with previously [4] published data, we found that the rates of dyslipidemia and hypercholesterolemia in HIV/HBV-coinfected patients were higher than in the demographically matched control group. This finding, together with comparisons of lipid profiles among HBV-infected, significantly strengthens the hypothesis of a predictive role of HBV infection on the development of lipid abnormalities in HIV-infected patients.

Even though serum triglyceride levels were lower in the HBV-coinfected group, HBV can not be considered as an apparently protective factor for hypertriglyceridemia in these patients. It is worth mentioning that these lipid changes are common among HIV-positive people, possibly due to the influence of HIV itself, but also secondary to the effect of antiretroviral drugs.

Conclusions

This study provides data on the peculiarities of the biochemical profile of HIV/HBV coinfection, data that reflect the specific features of the coinfection with human immunodeficiency virus and hepatitis B virus in the North-Eastern Romania. Our results support the fact HBV infection remains a major problem in the management of HIV –infected patients.

Although hepatic cytolysis syndrome and serum lipid levels are only indirect markers of liver involvement, the factors associated with increases in these levels should be considered when selecting etiologic treatment regimens active against both viruses.

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