International Journal of Psychosocial Rehabilitation, Vol. 24, Issue 10, 2020
ISSN: 1475-7192

Impact of (HCV) and (HBV) co-infection among HIV infected patients

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Abstract

Background: *The biggest public health problems are still HIV, HBV and HCV. These virus infections are in the top ten deaths caused by infectious diseases. The variability of HIV/hepatitis coinfection incidence in the world is complex and depends on geographical areas, risks and exposure types for infections.*

Objective: *To investigate HBV and HCV prevalence in HIV patients.*

Patients and Methods: *This study was conducted on HIV infected, and AIDS patients attending Alexandria Fever Hospital during the period from August 2018 to July 2019, assuming prevalence of HCV in HIV patients is 15% sample was calculated to be 141 patients using epi info version 7 program with test power 80%, CI 95%.*

Results: *The incidence of infection with hepatitis C virus was 45 patients (31.9%), all the 45 tested positive for PCR for HCV RNA as HIV accelerated progression of the disease making it almost impossible for HCV spontaneous clearance. It is much higher than average people and is 9 patients with hepatitis B infection (6.4 percent). In patients with immunodeficit the incidence of co-infection between Hepatitis C and HBV was 2,8 percent, with a combined infection in 4 of 141 patients of the three viruses.*

Conclusion:*The findings of current work emphasize the importance of continued HIV-positive screening for HBV and HCV markers prior to beginning HAART as this procedure could direct the right choice of medicinal combination.*

Keywords: *HCV, HBV, HIV, AIDS*

I. INTRODUCTION

(HIV) is a lentivirus (a member of the retrovirae family) that is attacking the immune system, leading to cell-mediated immunity defects which are shown to be more susceptible to opportunistic infections and certain rare cancers. HIV infection has been the most progressive level of immune deficiency syndromes (AIDS)**(1).**

HIV infects important cells in the human immune system, such as T-helpers (CD4+T cells, in particular), macrophages and dendritic cells. The HIV infections trigger low levels of CD4+ T cells through

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three main mechanisms; first; direct viral killing of infected cells; second; increased rates of cell apoptosis, third; elimination of CD8 cytotoxic lymphocytes infected by the CD4+ T cells; the loss of cell mediated immunity and the body's being pre-infected cell numbers, thirdly; The majority of HIV-1 infected persons develop AIDS [(2)].

The three most common chronic viral infections reported worldwide are HIV and hepatitis B and C (HBV and HCV). Similar methods of transmission of viruses, such as blood and blood products, needle sharing, and sexual intercourse, are normal occurrences, facilitating co-infection of these viruses. [(3)].Hepatitis B virus (HBV) transmission from mother to child is frequent, while HCV transmission is uncommon. [(4)].

The underlying effects, such as the hepatological complications associated with these viruses, have shown a decrase in lifespan in people with HIV, are highly significant for HBV and HCV co-infections of HIV positive individuals [(3)].As a chronic infection, the liver may scar and eventually, cirrhosis, which is normally noticeable after several years. In certain cases people with cirrhosis will develop hepathy or other complications, such as liver cancer or esophageal or gastric varicose veins that endanger their lives [(5)].The presence of one virus in co-infection affects the other virus' natural history. HIV accelerates the normal course of the infection of HBV and HCV and allows for a quicker growth in hepatic carcinoma and cirrhosis diseases [(6)].In HIV positive patients, progression from disease is almost three times faster than in HIV negative patients [(7)].

Thus almost 2-3 million Egyptians in Egypt are chronic HBV carriers[(8)].And HCV antibodies, of which over 4.5 million people have active HCV infection, with the highest global HCV prevalence, are estimated at over 6.8 million people aged 15-59 [(9)].The exceptionally high incidence of HCV rises with an age, the highest recorded for parenteral anti schistosomal treatment (PAT) in the age group older than 40 years, due to the history of unsterile injection devices used in mass treatment of the general populations from the twenties to the 1980s [(10)].

It is unclear how many people have HIV in the country. UNAIDS estimates more than 22,000 by end of 2018[(11)].

II. AIM OF THE WORK

General objective

To investigate HBV and HCV prevalence in HIV patients.

Specific objective

1- To detect main route of transmission of HIV.

2- To detect serologic markers of HBV in HIV patients.

3- To detect anti-HCV in HIV patients.

III. SUBJECTS AND METHODS

Subjects:

This study was conducted on HIV infected, and AIDS patients attending Alexandria Fever Hospital during the period from August 2018 to July 2019, assuming prevalence of HCV in HIV patients is 15% sample was calculated to be 141 patients using epi info version 7 program with test power 80%, CI 95%.

Inclusion criteria:

1. Confirmed HIV patient.

2. Male or female patient.

3. Age > 18 years.

4. Extremely active retroviral therapy patients (HAART).

5. Any stage of HIV.

6. HCV or HBV or both Co-infection with HIV.

Exclusion criteria:

Any patient who is HCV positive or HBV positive or both, but HIV negative.

Ethical consideration and written informed consent:

The study was accepted by the Academic and Ethics Committee of the University of Zagazig. An informed written consent was signed by each patient to approve the operation.

Methods

Data collection methods:

The demographic review of clinical symptoms, prospects, clinically classified phases and HBV and HCV screening is used for all HIV patients.

The following data were obtained from the patients' records: name, age, sex and modes of transmission, and confidentiality of records was considered.

All filing data from the institution were revised chronologically stressing on:

1) Age of patient.

2) Sex.

3) Onset of the disease.

4) Duration of the disease.

5) Complications.

6) Clinical assessment.

7) History:

- Family History.
- Sexual History.
- Drug Addiction.

8) Investigations:

A. Laboratory tests:

- Routine normal lab: CBC, ESR, CRP.
- Renal functions: Urea, creatinine.
- Liver functions: AST, ALT, bilirubin total and direct, serum albumin.
- Bleeding profile: INR, PT, PTT.
- Tumor markers: AFP (Alpha feto protein)

B. Radiological investigations:

- Ultrasonography of Abdomen and pelvis using Mindray 1100 plus device.

C. Serological Hepatitis markers:

- A positive HBS surface antigen (HBsAG), which was acquired from Dialab, Austria, using the ELISA technique, was specified for the co-infection with HBV/HIV.
- And anti-HBcIgM to detect Occult HBV infection. by ELISA technique using REF Z01365 Kit that was purchased from Dialab, Austria.
- HCV/HIV coinfection was defined by a positive HCV antibody by ELISA technique using REF Z01370 kit that was purchased from Dialab, Austria.
- · And the HCV RNA Quantitative PCR test. The standardized quantitative Real-Time PCR in compliance with the Manufacturer's Protocol was carried out in the Artus1HCV-RG RT-PCR Package (cat No. 4518265, QIAGEN1, Qiagen) and the thermal cycler ABI 7500 Fast Real-Times PCR was amplified (Applied Biosystems, Foster City, CA, USA).

Statistical analysis:

The data was fed and analyzed via IBM SPSS version 20.0 software package. Using number and percentage, quality data have been identified. Quantitative data were defined by means of mean, standard deviation and median range (minimal and maximum). The Chi-square test was used to test the comparison of various classes with categorical variables. With more than 20 per cent of cells under 5, chi-square correction was carried out using the Fisher's Exact Test or the Monte-Carlo correction.

The following tests were done:

- Chi-square (x^2) test of significance was used in order to compare proportions between two qualitative parameters.

- The p-value was considered significant as the following:

- P-value <0.05 was considered significant.

- P-value <0.001 was considered as highly significant.

- P-value >0.05 was considered insignificant.

IV. RESULTS

Table (1): Distribution of the studied cases according to demographic data

	No.	%
Sex		
Male	111	78.7
Female	30	21.3
Age (years)		
<30	41	29.1
30 – 40	70	49.6
>40	30	21.3
Min. – Max.	21.0 – 69.0	
Mean ± SD.	35.27 ± 9.33	
Median	33.0	

Table (1): This table shows that this study included 111 males, and 30 females, also that most HIV patients were in the age group 30-40.

Table (2): Distribution of the studied cases according to U/S abdomen

U/S abdomen	No.	%
Normal	56	39.7
Abnormal	**85**	**60.3**

Splenomegaly	29	20.6
Cirrhotic	40	28.4
Ascites	8	5.7
Lymph node	1	0.7
Nephropathy	1	0.7
Splenomegaly + nephropathy	1	0.7
HCC + cirrhotic	1	0.7
Splenomegaly + ascites	1	0.7
Cirrhotic and splenomegaly	2	1.4
Cirrhotic + nephropathy	1	0.7

Table (2) shows that among studies cases screened with Ultrasound abdomen (39.7%) were normal while (60.3%) were abnormal. Where 20.6% had splenomegaly and 28.4 showed cirrhotic changes only 5.7% had Ascites and only one case had Nephropathy, or HCC, or showed lymph node at percentage of 0.7% of studied cases per each.

Table (3): Distribution of the studied cases according to mode of transmission

Mode of transmission	No.	%
I V drug users	31	22.0
Sexual	110	78.0

Table (3) shows that sex was reported as the mode of transmission in 110 of the patients while only 31 was due to drug abuse.

Table (4): Relation between mode of transmission and Gender

Gender	Mode of transmission				χ^2	^{FE}p
	I V drug users (n=31)		Sexual (n=110)			
	No.	%	No.	%		
Male	30	96.8	81	73.6	7.7299	.005413*
Female	1	3.2	29	26.4		

- FE**: Fisher Exact**

*: Statistically significant.

In table 4, modes of HIV transmission were compared in relation to gender. Sex was the only mode of transmission reported in 29 (26.4 %) female patients whereas it was reported among 81 (73.6 %) male patients. Drug abuse was reported as mode of transmission in only 1 (3.2 %) female patients whereas it was reported among 30 (96.8%) male patients.

A statistical significance was found between gender and mode of HIV transmission (P value = 0.005413).

Table (5): Relation between mode of transmission and hepatitis B and C markers

	Mode of transmission				p
	I V drug users (n=31)		Sexual (n=110)		
	No.	%	No.	%	
HBsAg					
Negative	30	96.8	102	92.7	$^{FE}p>0.05$
Positive	1	3.2	8	7.3	
HCV Ab					
Negative	23	74.2	73	66.4	>0.05

Positive	8	25.8	37	33.6	

FE**: Fisher Exact**

Table 5 shows the relation between mode of transmission of HIV with hepatitis B and C markers.

Table (6): Relation between Gender and hepatitis B and C markers

	Gender				**p**
	Male (n=111)		**Female (n=30)**		
	No.	**%**	**No.**	**%**	
HBsAg					
Negative	103	92.8	29	96.7	$^{FE}p=$ >0.05
Positive	8	7.2	1	3.3	
HCV Ab					
Negative	74	66.7	22	73.3	>0.05
Positive	37	33.3	8	26.7	

FE**: Fisher Exact test**

Table 6 shows the relation between gender with hepatitis B and C markers.

Table (7): Relation between age and hepatitis B and C markers

	Age (years)						**p**
	<30 (n=41)		**30 – 40 (n=70)**		**>40 (n=30)**		
	No.	**%**	**No.**	**%**	**No.**	**%**	
HBsAg							

Negative	41	100.0	63	90.0	28	93.3	MC
Positive	0	0.0	7	10.0	2	6.7	>0.05
HCV Ab							
Negative	29	70.7	45	64.3	22	73.3	>0.05
Positive	12	29.3	25	35.7	8	26.7	

MC: **Monte Carlo test**

Table 7 shows the relation between age and hepatitis B and C markers.

V. DISCUSSION

This study was conducted on 141 HIV infected patients attending Alexandria Fever Hospital for diagnosis and follow up. Patients enrolled in the study were positive for anti-HIV antibody by EIA. They were screened for the following markers by ELISA technique: anti-HCV, HBsAg.

Among the HIV patients, 29.1% were less than 30 years old, 49.6% were from 30 up to 40 years old, and 21.3% were from older than 40 years old, the mean age was 33 years. In France, it was reported that 61% were more than 40 years and 39% less than 40 years **(12).** While in Morocco the mean age of HIV patients was 40 years **(13).** A mean age of 33.9 years reported in Kenya in 2013 **(14)** was close to that reported in present study. This may be due to increased sexuality in this age group which is the main reason of transmission of HIV.

As regards gender, 78.7% males and 21.3% females were included in the study. This finding was similar to that obtained previously in France in a study reporting 68% males and 32 % females among studied HIV subjects**(12).** Otherwise in Ethiopia in 2013, 30.5% were males and 69.5% were females **(15).**

As per mode of HIV transmission, the sexual route in this study was reported in 78% and drug abuse in 22%. Similarly, in France and Morocco sexual transmission of HIV was the major route of transmission**(12, 13).**

In the current study anti-HCV antibody was present in 45 (31.9%) of HIV infected patients. It was significantly higher among males than females (33.3 vs 26.7 %). This observation was comparable to previous studies in Kenya (11.6% vs 9.4%) (14), Morocco (9.8% vs 1.1%), and in Ethiopia, where females coincided more with (5.6%) than males. This observation is contrary to other results in Ethiopia (2.8 percent)**(15).**

Egypt is a middle endemic country of HBV (2 percent -7 percent). An HBsAg carriage survey registered a 2 percent prevalence**(16).** In the present study only 9 (6.4%) HIV patients were HBsAg carriers, in 2013,**Rebbasni et al.**, reported 5.2% HBsAg prevalence among HIV patients in Morocco which has also intermediate endemicity for HBV **(13)**. In 2012 in Nigeria 28.4% of studied HIV patients were HBsAgcarriers**(17)**. This may be because Nigeria is a high HBV endemic country, and the prevalence is different. Just four of the 9 patients tested positively in HBsAg (2.8%) were positive in HCV antibodies as well. These results were similar

to those previously obtained in Kenya (1 percent)[14],The low rates of such trio infections are maintained in Nigeria (1.5%)(17%) and Ethiopia (1.1%) (15).

In this study the rate of HIV/HCV co-infection was higher for men than women (33.3 vs 26.7 percent). Multiple sex partners may have made this discovery and still have sex with no safety, whether their relationships are polygamous or because prisoners are being exploited by intravenous drugs.

In the current report, 45 (31.9%) of positive HIV patients were co-infected in HIV/HCV while 4 (2.8%) had triple HIV/HBV/HCV infection. In 2008, almost half (48.57%) of HIV-positive patients in Georgia found co-infected with HCV, while 43.42% co-infected HBV and 5.14% had triple HIV/HBV/HCV infection[18].The values in this study are comparatively superior to the values observed. In 2005, HIV co-infection was 12.8% in Australia, while HBV co-infection was 4.8% in Australia [19]. In India, in three separate studies [2.1% / 6.4%], [2.2% / 9%] and [1.69% / 2.61%] have been co-infected by HCV and HBV in patients co-infected with HIV, respectively[20, 21].25% of HIV patients in another study in New York City co-infected HCV and 4.47% co-infected HBV and about 1.6% were infected by HBV three times over[22].

The lack of HBcIgM in the participant sample suggested that their HBV infections were long-standing infections. Anti-HBcIgM indicated occult HBV infection was not found in either of them. Similar study performed in Ghana 2011, came out with the same conclusion as HIV accelerates progression of the disease into chronicity (chronic HBV infection) [23].

VI. CONCLUSIONS

Hepatitis B and C are an infectious disease primarily affecting the liver, in addition, HIV, HBV, HCV share familiar routes of transmission by sexual intercourse or drug abuse by Parenteral injection, so co-infection is not uncommon.

We have seen more HCV-HIV coinfection than HBV-HIV co-infection in our study, HBV or HCV co-infection or the reduced survival and increased hepatotoxicity in both patients infected with HIV. It may also speed up the liver damage resulting in a prolonged rise in ALT and AST, and reduce the pre cirrhosis duration, as well as increase the risk of developing HCC, and HCC should be screened at HCC every 6 to 12 months in patients with chronic hepatitis B and C. The alpha-fetoprotein serum and the liver ultrasound should be finished. This is independent of apparent cirrhosis as 10 to 30% of patients with HCC have no previous cirrhosis.

So, all HIV patients should receive HAART regimen and also should be vaccinated against hepatitis B; those with coinfection (HBV and HCV) should be treated for both viruses.

VII. RECOMMENDATIONS

1) Routine screening of HIV infected patients for HBV and HCV markers prior to start of HAART therapy is mandatory.

2) Administration of HBV and HAV vaccine should be carried out for all non-vaccinated HIV patients.

3) Further studies are required to monitor the outcome wof HIV cases screening of Hepatitis viruses and receiving their corresponding treatment.

4) HIV infected patients should be health educated as regards safe sex practice.

5) For patients presenting with anti-HBc as the sole HBV marker, PCR testing should be carried out to explore the presence of occult HBV.

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