

Hepatitis (C) Virus, Hepatitis (B) Virus and Human Immunodeficiency (HIV) Virus Coinfection and Their Impact Outcome on the Liver

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ABSTRACT

Background: Hepatitis C virus (HCV), hepatitis B virus (HBV) and human immunodeficiency virus (HIV) are the commonest chronic viral infections worldwide, they share most common routes of infections, they are hepatotropic viruses and their combined infections had bad outcome on the liver.

Objective: To evaluate the risk of coinfection of the liver by both HCV, HBV and HIV on the liver outcome.

Patients and Methods: This is a retrospective study of 241 patients attending different fever hospitals coinfecting by HCV and or HBV with HIV but not HCV or HBV without HIV infections.

Result: There was significant difference between male 59.8% and female 40.2%, age of patients, also there was significant difference as regard liver enzymes, cirrhosis, splenomegaly, international normalization ratio in triplet coinfections.

Conclusion: There is high risk on liver outcome in the presence of coinfection between HCV or HBV and HIV.

INTRODUCTION

Human immunodeficiency virus (HIV) is a lentivirus which target the immune system resulting in depression of cell mediated immunity with resulting serious opportunistic infection and rare malignancies⁽¹⁾.

Worldwide hepatitis (B) virus, hepatitis (C) virus and human immunodeficiency virus (HIV) are the commonest chronic viral infections. They have common routes of transmissions as they are blood born infectious diseases (blood and blood products), needle transmission, and sexual activity⁽²⁾. HBV is characterized by special route of transmission which is the vertical one (from mother to baby) which is rare in HCV. Coinfection between the three hepatotropic viruses are of great risk as the viruses may impact the natural history of the other one, HIV accelerates the natural course of both HBV and HCV with consequent destructive effect on the liver and progression to cirrhosis and hepatocellular carcinoma (HCC). Worldwide among HIV infected patients about 2-4 millions have chronic HBV coinfection and 4-5 million coinfecting with HCV⁽³⁾.

In Egypt about 2-3 million are chronic carriers for HBV and 6-8 million are HCV positive patients so we decided to study the effect of coinfection between HIV and HCV and HBV on the liver outcome in some Egyptian fever hospitals in a retrospective study⁽⁴⁾.

HBV and HCV coinfection with HIV in very important as triplet infection increase the risk of hepatological complications⁽⁵⁾.

As infection with the triplet viruses may hasten the scarring of the liver with consequent cirrhosis and hepatocellular carcinoma (HCC) life expectancy with these viruses are decreased⁽⁶⁾. Infection by the three viruses is different according to geographic regions and

behavior of infected persons⁽⁷⁾. It is unclear how many people have

HIV in the country so we decided to study in cross-section of retrospective study the true triplet coinfection and its effect on the liver^(6,8).

Aim of the work was to evaluate the risk of coinfection of the liver by both HCV, HBV and HIV and the liver outcome.

PATIENTS AND METHODS

This study is a cross sectional study between Mayo 2018 and June 2019. It included 241 patients with no sex predilection aged between 20-75 years old attending Alexandria, Al Abasia and Al Ahrar fever hospitals. This study depended on file records of patients attending these hospitals to follow up and treatment. Objectively this study measures the prevalence of coinfection between HIV, HCV and HBV but not HCV or HBV alone without HIV infection and its impact out come on the liver.

Ethical approval:

An approval of the study was obtained from Zagazig University academic and ethical committee. Every patient signed an informed written consent for acceptance of the operation.

Inclusion criteria:

All patients included in the study had HIV infection with work up to investigate other serological markers of HCV and HBV but not HCV or HBV alone.

Exclusion criteria:

Any patient have any liver disease weather acute or chronic and patients with HCV or HBV without HIV.

All patients included in the study were subjected to filling data records of age, sex, onset of disease,



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course duration, complications clinical assessment, family history, sexual history and drug history.

Laboratory investigations:

- Routine laboratory investigations CBC, ESR, CRP.
- Kidney function tests.
- Complete liver function tests.
- Bleeding profile; PT, PTT, and INR.
- Tumour marker Alfa foetoprotein.
- Serological makers.
- HBC infection by HBV surface antigen (HBsag) positivity but negative HBVC Ab (core antibody).
- HCV infection by HCRAB (HCV antibody) positivity and confirmed by HCV polymerase reaction (PCR).
- HIV infection by ELTSA test (Enzyme linked immunosorbent assay).

Imaging:

- Chest X-ray.
- Pelvic-abdominal U/S.

Statistical analysis

Collected data were coded and entered using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. Qualitative data were presented as number and percentage and were compared by Chi square test (X^2).

Quantitative data were presented as mean \pm SD, median, and range and were compared by one-way ANOVA test. P value was set at <0.05 for significant results and <0.001 for high significant result.

RESULT

Table (1): Age and gender of the studied group

		Age	
Mean \pm SD		38.19 \pm 8.5	
Median		38.0	
		N	%
Sex	Male	97	40.2
	Female	144	59.8
	Total	241	100.0

Table (2): Some characters of the studied group

		N	%
Addiction	No	199	82.6
	Yes	42	17.4
Smoking	No	170	70.5
	Yes	71	29.5
Splénomegaly	No	192	79.7
	Yes	49	20.3
Cirrhosis	No	217	90.0
	Yes	24	10.0
	Total	241	100.0

Table 3 is showing levels of of AST, ALT, Urea, Cr, PT and INR in the studied groups.

Table (3): Lab measurements of the studied group

	AST	ALT	Urea	Cr	PT	INR
Mean \pm SD	39.56 \pm 13.5	44.18 \pm 14.6	29.24 \pm 9.54	1.04 \pm 0.21	12.43 \pm 2.0 1	1.11 \pm 0.18
Median	30.0	32.0	27.0	1.0	12.4	1.1

Table (4): Frequency of opportunistic infection in the studied group

		N	%
Pneumonia	-VE	161	66.8
	+VE	80	33.2
UTI	-VE	232	96.3
	+VE	9	3.7
Meningitis	-VE	147	61.0
	+VE	94	39.0
	Total	241	100.0

Table (5): Prevalence of the viruses' coinfection in the studied group

		N	%
Groups	HIV only	169	70.1
	HIV+HBV	20	8.3
	HIV+HCV	39	16.2
	HIV+HBV+HCV	13	5.4
	Total	241	100.0

Table (6): Comparison among the studied patients according to viruses' coinfection.

Data are presented as mean±SD or as number and percentage

			HIV only N=169	HIV+HBV N=20	HIV+HCV N=39	HIV+HBV+H CV N=13	F	P
Age (years)			34.21±6.24#	44.75±2.55	46.56±3.88	54.56±5.28*	101.624	0.001**
AST (U/L)			29.61±5.53	95.6±16.33*	34.25±8.5	89.23±13.82*	527.509	0.001**
ALT (U/L)			31.86±5.76	102.0±20.4*	36.35±7.08	93.15±13.5*	504.709	0.001**
Urea (mg/dL)			28.36±6.01	26.1±1.02	26.56±5.49	28.61±9.5	2.731	0.187
Cr (mg/dL)			1.018±0.15	1.0±0.211	1.01±0.14	1.08±0.41	1.102	0.324
PT			11.84±1.53*	13.18±1.83	13.09±1.22	13.95±2.93	14.189	0.001**
INR			1.08±0.103*	1.14±0.05	1.11±0.16	1.12±0.24	31.028	0.001**
Sex	Male	N	55	9	24	9	16.2	0.001**
		%	32.5%	45.0%	61.5%	69.2%		
	Female	N	114	11	15	4	38.99	0.001**
		%	67.5%	55.0%	38.5%	30.8%		
Addiction	No	N	149	20	26	4	43.83	0.001**
		%	88.2%	100.0%	66.7%	30.8%		
	Yes	N	20	0	13	9	122.5	0.001**
		%	11.8%	0.0%	33.3%	69.2%		
Smoking	No	N	140	11	15	4	107.17	0.001**
		%	82.8%	55.0%	38.5%	30.8%		
	Yes	N	29	9	24	9	10.78	0.013*
		%	17.2%	45.0%	61.5%	69.2%		
Spleno- megaly	No	N	160	0	28	4	3.98	0.26
		%	94.7%	0.0%	71.8%	30.8%		
	Yes	N	9	20	11	9	6.03	0.11
		%	5.3%	100.0%	28.2%	69.2%		
Cirrhosis	No	N	169	20	24	4		
		%	100.0%	100.0%	61.5%	30.8%		
	Yes	N	0	0	15	9		
		%	0.0%	0.0%	38.5%	69.2%		
Pneumonia	No	N	121	11	25	4		
		%	71.6%	55.0%	64.1%	30.8%		
	Yes	N	48	9	14	9		
		%	28.4%	45.0%	35.9%	69.2%		
UTI	No	N	160	20	39	13		
		%	94.7%	100.0%	100.0%	100.0%		
	Yes	N	9	0	0	0		
		%	5.3%	0.0%	0.0%	0.0%		
Meningitis	No	N	106	11	26	4		
		%	62.7%	55.0%	66.7%	30.8%		
	Yes	N	63	9	13	9		
		%	37.3%	45.0%	33.3%	69.2%		
Total		N	169	20	39	13		
		%	100.0%	100.0%	100.0%	100.0%		

Age was significantly younger among 1st group and significantly older among 4th group. AST, ALT were significantly higher among 2nd and 4th groups. As regard PT and INR they were significantly lower among 1st group. Addiction was significantly associated with last group. Splenomegaly was significantly associated with 2nd and 4th group. Cirrhosis was with 3rd and 4th and as regard pneumonia it was significantly associated with 2nd and 4th group.

DISCUSSION

HIV, HBV and HCV are still major public health problems. Infections with these viruses rank among ten leading causes of death attributable to infectious diseases^(8, 9). The variability in the prevalence of HIV/hepatitis coinfection worldwide is multi factorial, and depends on geographic distributions, infections risk factors and route of exposure⁽⁹⁾.

HC/HIV coinfection has been associated with rapid decline in CD4 count, rapid progression of HIV infection and increased morbidity and mortality. HCV and HBV coinfection with HIV accelerates disease progression⁽¹⁰⁾. Individuals coinfecting with HIV/HBV are more likely to develop chronic hepatitis B with increased risk for acquiring liver related mortality. In Egypt, number of people living with HIV in 2017 was approximately 22000 individuals^(11, 12).

The mean age of patients in our study was 38.19 ± 8.5 which is in close association with a study done by **Rebbasni et al.**⁽¹³⁾ (under 40 years) and it is also in agreement with the study done at **Bojuwoye et al.**⁽⁸⁾ (33 ± 9). As regard sex distribution; in our study females were 59.8% and males were 40.2%, which is in agreement with a study done by **Azevedo et al.**⁽¹⁴⁾ and disagreement with a study done by **Konopnicki et al.**⁽¹⁵⁾ with male predominance.

As regard other parameters 17.4% were addicted, 29.5% was smokers, 20.3% had splenomegaly and 10% has liver cirrhosis. Moreover sexual transmission was 78%, and drug abuse was 22% which was in agreement with studies done by **Rebbasani et al.**⁽¹³⁾ and **Graham et al.**⁽¹⁶⁾ as sexual transmission was the main route of infection. In addition to the above; HIV represented 70.1% alone, HIV + HBV 8.3%, HIV + HCV 16.2 and HIV, HBV, HCV (triplet infection) 5.4. Other studies showed anti-HCV positive prevalence in HIV infected patients ranged between 3.3% in South Africa, 42.3% in North America, 9.1% in Libya, 32.4% as found by **Tremeau et al.**⁽¹⁾, **Cooper et al.**⁽²⁾ and **Koziel et al.**⁽¹⁷⁾. As regard HB sero prevalence in HIV; in our study it was 8.3%. Also our study found increased ALT and AST. Addiction was significant with HIV + HCV + HBV (triplet infection), splenomegaly was significantly enlarged in HIBV + HIV and triplet infection groups, cirrhosis was highly significant in HCV + HIV and triplet infection groups, and also pneumonia was significantly high with HBV + HIV and triplet infection groups. HIV infection was significantly high in younger age group while in triplet infection group it was significantly high in old age.

Our study found that HIV was highly significant in younger age group (sexually active groups, more prone to drug abuse and overactive in the community, but triplet infection in older age group (decreased immunity). Also our study had revealed that bleeding parameters (PT, INR) were significantly high in double

or triple infections. As regard HIV infection alone (liver parenchyma dysfunction) HIV and HBV and triplet infection had significant AST elevations than other groups. Our study had revealed also that patients addicting drugs were significantly more with triplet coinfection.

Our study also showed significant level in prevalence of meningitis in combined and triplet confection.

CONCLUSION

From the results of our study we concluded that:

- HIV infection occurs more in younger age groups (sexually active group + drug addicts).
- Liver complications as cirrhosis, splenomegaly are more common in combined infection.
- Opportunistic infection is also common in combined infection.

RECOMMENDATION

Strict follow up, diagnosis of HIV individuals with associated hepatotropic viral infection as HBV and HCV is mandatory to avoid complications and mass screening of peoples at high risk.

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