Low Risk Of Hepatic Fibrosis In Young Egyptian Patients With Severe Hemophilia A After Long Standing Hepatitic C Virus Infection

Mohsen S. Elalfy [1], Shereen M. Abd El-Ghany [1], Mai M. Sherif [2]

[1] Pediatric Departement, Hematology Unit, Faculty of medicine, Ain Shams University, Cairo, Egypt.
[2] Clinical Pathology Departement, Faculty of medicine, Cairo University, Cairo, Egypt.

OBJECTIVES

Most patients with hemophilia A in Egypt were treated with cryoprecipitate between 1985-1995 with a high risk of infection with hepatitis C virus (HCV) and possible development of hepatic fibrosis. We aimed to assess the liver fibrosis status of adolescent and young adult patients with severe hemophilia A with non-treated HCV infection or failed response to anti-HCV treatment after contracting HCV infection in early life and lasting for more than a decade without doing liver biopsy.

PATIENTS and METHODS

This study was included twenty-six patients with severe hemophilia A, who were regularly attending the hemophilia clinic Children's Hospital, Ain Shams University. Inclusion criteria included: patients with severe hemophilia A, aged 12-21 years, with HCV RNA positive who contracted infection during the first 5 years of life (as recorded in files) and had not previously received therapy for hepatitis C or failed response to anti-HCV treatment were selected for further assessment of liver fibrosis using FibroTest (FT) and FibroScan (FS). Serum sample to measure FT was taken within 24 hours from performing the FS. Exclusion criteria included patients co-infected with HBV, HIV, and/or acquired HCV infection after the age of 5 years. Non-applicabilty conditions of FT and FS.

Table (1): Characteristics of the 26 severe hemophilia A patients with chronic HCV infection

Variables	
Age (years), Mean ± SD	15.9 ±2.9
Male gender, n (%)	26 (100)
AST (IU/L)	33.5 (32.5)*
ALT (IU/L)	42.0 (36)*
Total Bilirubin (mg/dl)	0.8 (0.4)*
Serum Albumin (g/l)	4.2 (0.7)*
Platelets ($10^3/\mu L$))	248 (81)*
Duration of hepatitis (years)	12.9 (3.1)*
Stage of fibrosis n (%)	n (%)
FibroTest	
F1	14 (53.8)
F2	5 (19.2)
F3	7 (26.9)
F4	0 (0)
FibroScan	
F1	14 (53.8)
F2	7 (26.9)
F3	5 (19.2)
F4	0 (0)

*Data are represented as median and interquartile range

Table (2): Comparison between fibrosis scores and age of patients at evaluation

		Fibrosis score by FT (n=26)			P	F0 vs F1	F0 vs F2	F1 vs F2
Age of the patients at evaluation (years)		F0 (n=14)	F1 (n=5)	F2 (n=7)				
	Median	14.5	14.0	20.0	0.012	0.81	0.006*	0.018*
	IQR	4.25	3.0	5.0				
		Fibrosis score by FS (n=26)			p	F0 vs F1	F0 vs F2	F1 vs F2
Age of the patients at evaluation (years)		F0 (n=14)	F1 (n=7)	F2 (n=5)				
	Median	14.7	15.0	20.0	0.018	0.43	0.01*	0.03*
	IQR	4.25	4.0	4.0				

n = number. IQR = interquartile range. vs= versus. Krauskal-Wallis test with Mann-Whitney test. * = significant p value.

Table (3): Comparison between fibrosis scores and duration of hepatitis C

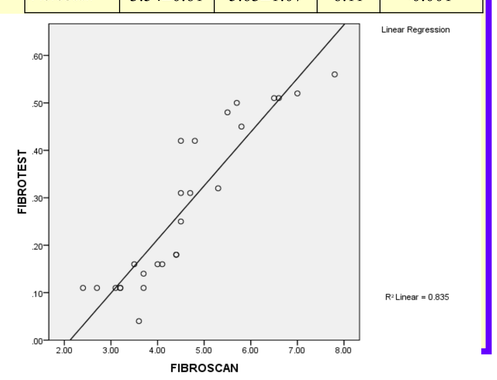
		Fibrosis score by FT (n=26)			P	F0 vs F1	F0 vs F2	F1 vs F2
Duration of hepatitis (years)		F0 (n=14)	F1 (n=5)	F2 (n=7)				
	Median	10.5	12.0	17.0	<0.001*	0.017*	<0.001*	0.01*
	IQR	2.0	1.5	5.0				
		Fibrosis score by FS (n=26)			P	F0 vs F1	F0 vs F2	F1 vs F2
Duration of hepatitis (years)		F0 (n=14)	F1 (n=7)	F2 (n=5)				
	Median	10.5	12.0	18.0	<0.001*	0.004*	<0.001*	0.017*
	IQR	2.0	3.0	4.5				

n = number. IQR = interquartile range. vs= versus. Krauskal-Wallis test with Mann-Whitney test. * = significant p value.

Table(4): Comparison between patients with normal and elevated ALT as regards mean values of FT and FS t= independent t test, *= significant

Variables	ALT ≤40 IU/L (n =13) Mean±SD	ALT >40 IU/L (n=13) Mean±SD	t	P value
FibroTest	0.13±0.04	0.43±0.1	10.06	<0.001*
FibroScan	3.54±0.61	5.63±1.07	6.11	<0.001*

Fig(1): Correlation between mean values of FT and FS (r=0.8, p<0.001).



RESULTS

Screening of 250 Egyptian haemophilia A patients attending the Ain Shams Hemophilia Centre revealed that 60% (150/250) of them had positive anti-HCV antibodies and 2% (5/250) had positive HBs Ag, while none of the screened patients had HIV infection. Twenty-six patients who fulfilled the inclusion criteria were enrolled in this study for further assessment of liver fibrosis using FibroTest and FibroScan. All patients were males with a mean age of 15.9± 2.9 years (12-21 years). They were exposed for 10-20 years to cryoprecipitate and plasma derived factor VIII concentrates with mean duration of hepatitis 12.9 ± 3.1 years.

The distribution of fibrosis among the studied patients was: F0 (no fibrosis) in 14 patients (53.8%) by FT and FS, F1 (minimal fibrosis) in 5 (19.2%) by FT and 7 (26.9%) by FS, F2 (mild fibrosis) in 7 (26.9%) by FT and 5 (19.2%) by FS. However, none of the studied patients had advanced liver fibrosis (F3, F4). There was a statistically significant association between patient age at evaluation and fibrosis scores by FT (P= 0.012) and FS (P=0.018). Patients with F2 have significantly higher age compared to patients with F1 (p=0.018, 0.03), and F0 (p=0.006, 0.01) by FT and FS respectively. However, no significant difference was found in the mean age between patients with F1 and F0 as estimated by FT (P=0.81) and FS (P=0.43) (table 2). A highly significant positive correlation was found between patient age at evaluation and mean values of FT (r=0.58, P= 0.002) and FS (r=0.66, P<0.001).

Similarly, there was a statistically significant association between duration of hepatitis and fibrosis scores by FT (P<0.01) and FS (P<0.01). Statistically significant longer duration of hepatitis was found in patients with F1 compared to patients with F0 (P=0.017, 0.004) and in patients with F2 compared to F1 (P=0.01, 0.01) and F0 (p=0.001, 0.001) as estimated with FT and FS respectively (table 3). A highly significant positive correlation was found between duration of hepatitis and mean values of FT (r=0.84, P<0.01) and FS (r=0.85, P<0.01). In this study, the mean values of FT and FS were significantly higher in patients with high ALT > 40 IU/L (P<0.001) (table 4), with a highly significant correlation between ALT and both FT (r=0.82, p<0.001) and FS (r=0.8, P<0.001) mean values. A highly significant association was found between FT and FS with regard to the estimated degree of fibrosis (P<0.001) (table 5). Also a highly significant correlation was also found between mean values of FT and FS (r=0.91, P<0.001) (fig 1).

CONCLUSION

None of the studied HCV-RNA positive severe hemophilia A patients for more than a decade progressed to moderate or severe liver fibrosis. Meanwhile less than half of them started early fibrosis.

References

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Infectious Complications

Mohsen Elalfy

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