SERUM HYALURONIC ACID LEVELS AS MARKERS OF FIBROSIS SEVERITY IN PATIENTS WITH CHRONIC LIVER DISEASES OF DIFFERENT ETIOLOGIES

Emilia Hadziyiannis, Aikaterini Margariti, Anastasia Georgiou, Spilios Manolakopoulos, Melanie Deutsch, Hariklia Kranidioti, Athina Katoglou, Georgia Kafiri#, Dina Tiniakos*, George Papatheodoridis.

2nd Department of Internal Medicine, Athens University Medical School, Hippokration Hospital of Athens; #Department of Pathology, Hippokration Hospital of Athens; *Laboratory of Histology & Embryology, Athens University Medical School, Greece.

INTRODUCTION/ AIM

• Hyaluronic acid (HA) is a component of the extracellular matrix that is taken up and degraded in liver endothelial sinusoidal cells.

• As liver disease, and therefore fibrosis, progresses, serum HA levels increase due to both decreased uptake of HA from sinusoidal cells – owing to increased hepatic sinusoidal cell capillarisation – and increased production of HA owing to the fibrogenetic processes.

• Consequently, HA are a direct marker of liver fibrosis and have been used as markers of fibrosis severity in chronic liver disease (CLD).

• Liver stiffness measurements (LSM) by means of transient elastography (TE) constitute an indirect marker of hepatic fibrosis and have been used in assessing fibrosis severity in CLD of different etiologies.

• The **aim** of this study was to evaluate serum HA levels in patients with CLD and compare them to LSMs for the assessment of liver fibrosis severity

METHODS

○ 209 untreated patients with CLD; chronic HBV infection: 52 [chronic HBV inactive carriers: 20, HBeAg-negative chronic hepatitis B (CHB): 32], chronic hepatitis C (CHC): 86, non-alcoholic fatty liver disease (NAFLD) were included in the study

○ Anthropometric (height, weight, body mass index), clinical and biochemical data (AST/ALT)

○ Serum **levels of HA** were determined using HALT test (Wako Chemicals), which is based on latex agglutination

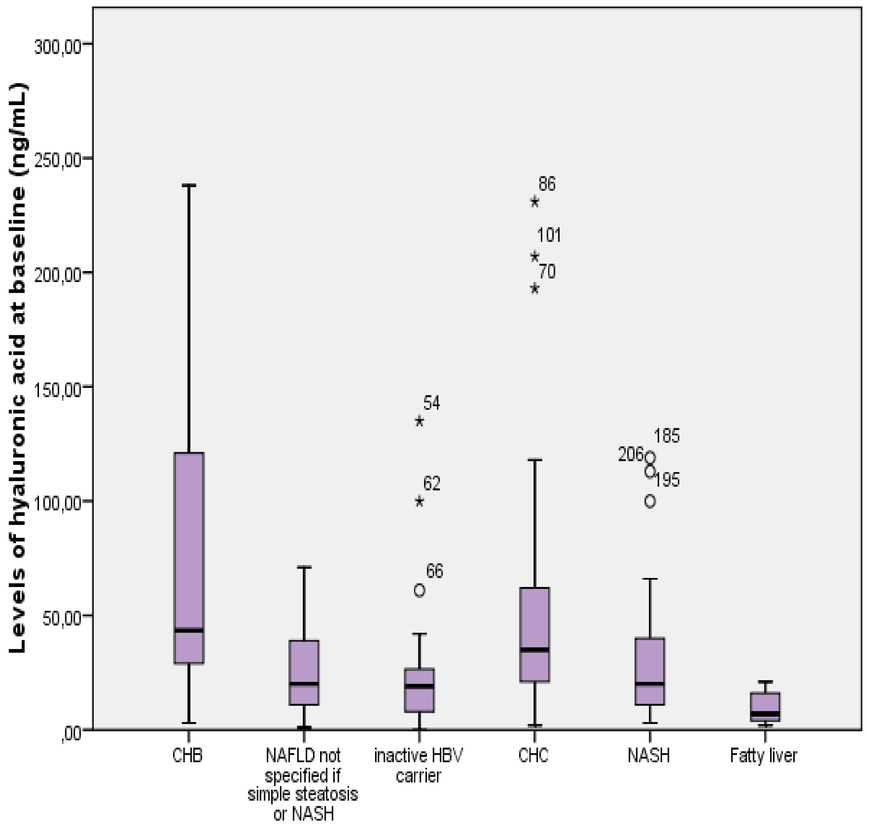
○ Reliable **liver stiffness measurments** (LSMs) (success rate > 60%, LSM/Interquartile range< 3) by TE (FibroScan®, Echosens) were available for 140 patients

○ **Baseline Liver biopsy** was available for 64 patients (chronic HBV: 23, CHC: 7, NAFLD: 34) and scored by Ishak's (HBV/CHC) or Brunt's (NAFLD) classifications.

RESULTS

Table 1. Main characteristics of the study participants

	Chronic HBV infection		Non alcoholic fatty liver disease, N= 71	Chronic HCV infection, N= 86	P
	Inactive carriers, N= 20	Chronic Hepatitis B, HBeAg (-), N= 32			
Gender, male n (%)	7 (35)	20 (63)	45 (63)	48 (55)	0.116
Age, years	42±16	53±13	47±12	42±15	**<0.001**
BMI, kg/m^2	23±4	26±4	30±4	25±4	**< 0.001**
ALT, IU/L	19 (10- 35)	94 (30- 678)	69 (17- 216)	63 (14- 580)	**< 0.001**
Fibrosis, at least moderate (≥ 2), n/N (%)	3/ 18 (17)	4/ 5 (80)	16/ 34 (47)	5/7 (71)	**0.016**
LSM, kPa	6.5 (3.6- 11.3)	6.4 (3.0- 27.0)	6.3 (3.0- 35.3)	6.6 (3.2- 40.3)	0.973
HA levels, ng/mL	43.5 (3- 832)	19 (0- 135)	17 (1- 119)	35 (2- 1000)	**< 0.001**



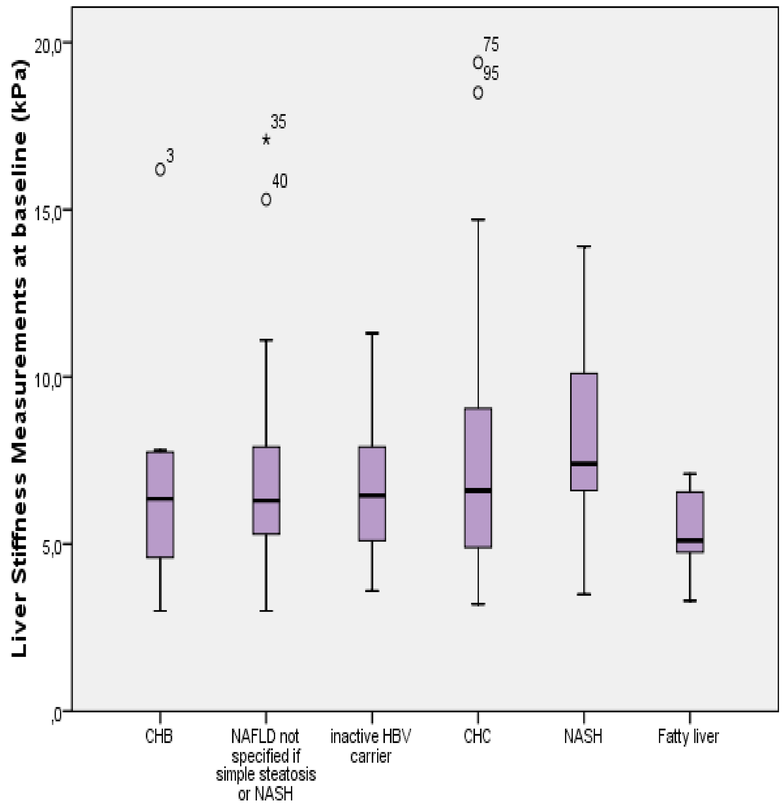


Table 2. Comparison of serum levels of hyaluronic acid among patients with CLD

		P
CHB	vs NAFLD (including all cases)	**< 0.001**
	vs inactive carrier	**0.002**
	vs CHC	0.118
	vs NASH	0.015
NAFLD (including all cases)	vs inactive carrier	0.992
	vs CHC	**< 0.001**
Inactive HBV carrier	vs CHC	**0.003**
	vs non alcoholic fatty liver	**0.033**
CHC	vs NASH	**0.041**
NASH	vs non alcoholic fatty liver	**0.005**

Table 3. Correlation between serum levels of HA and LSMs among patients with CLD

	rho	P
Chronic Hepatitis B HBeAg (-)	0.378	0.225
Inactive HBV carriers	0.191	0.420
Chronic Hepatitis C	**0.301**	**0.020**
NAFLD (including all cases)	0.190	0.534
Non alcoholic fatty liver	**0.575**	**0.064**
NASH	0.183	0.209

Table 4. Comparison of LSMs among patients with CLD

		P
CHB	vs NAFLD (including all cases)	0.771
	vs inactive carrier	0.893
	vs CHC	0.690
	vs NASH	0.247
NAFLD (including all cases)	vs inactive carrier	0.953
	vs CHC	0.841
Inactive HBV carrier	vs CHC	0.714
	vs non alcoholic fatty liver	0.145
CHC	vs NASH	0.319
NASH	vs non alcoholic fatty liver	**0.026**

CONCLUSIONS

- Patients with NAFLD and even NASH have lower serum HA levels than CHB or CHC patients despite similar LSMs by TE.
- Serum levels of HA correlate positively with LSMs among patients with CHC and tend to correlate positively among patients with fatty liver, but not NASH or CHB