Changes in Liver Fibrosis Stage among Treatment-ineligible People Living with Chronic Hepatitis B in Senegal

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Adrià Ramírez Mena[1,2,3], Bruce Shinga Wembulua[2], Aboubacar Badiane[2], Kiné Ndiaye[4], Judicaël Tine[2], Alassane Ndiaye[4], Maguette Fall[2], Hubert Akotia[5], Melissa Sandrine Pandi[5], Daye Ka[2], Louise Fortes[6], Ousseynou Ndiaye[5], Ndeye Fatou Ngom[4], Moussa Seydi[2], Gilles Wandeler[1,2,7] for SEN-B.

Background

- Hepatitis B virus (HBV) infection is the most important cause of liver cirrhosis and cancer in West Africa.
- Although close to 80% of persons with HBV (pwHBV) are ineligible for antiviral therapy at presentation, it is unclear how stable liver fibrosis stages measured by transient elastography remain over time, and how frequent monitoring should be performed.
- We aimed to assess changes in liver fibrosis stage in people with chronic HBV infection from a prospective cohort in Senegal (SEN-B)

Methods

Study setting and population

- SEN-B includes individuals aged >18 years with a positive HBsAg followed at the Infectious and Tropical Disease Service and the Ambulatory Treatment Center at Fann University Hospital, Dakar, Senegal,
- In this analysis, we included all participants enrolled from 2019 to 2023 who did not received antiviral treatment before or up to 12 (∓6) months of follow-up and without HIV co-infection.
- Sociodemographic, clinical and laboratory data as well as liver stiffness measurements (LSM) were collected at inclusion and 6-monthly thereafter.

Laboratory measurements

- **Liver stiffness** was evaluated using transient elastography (TE) and was categorized as normal (<7.0 kPa; equivalent to Metavir stage F0-1), significant fibrosis (7.1-11.0 kPa; Metavir F2-3), or cirrhosis (>11.0 kPa; Metavir F4).
- **HBeAg** and **HBV DNA** were measured on site using e411 cobas® and cobas®/TaqMan® (Roche Diagnostic Systems, Basel, Switzerland)

Statistics

- Participant characteristics were compared between men and women using the χ^2 test for categorical variables and the Wilcoxon rank-sum test for continuous ones.
- We determined the proportion of participants within each fibrosis stage group who exhibited a transition in their **fibrosis stage (F0-1↦F2-4, F0-1↦F4, or F2-3↦F4)** between months 0 and 12 (∓6).
- We used multivariable logistic regression to explore potential risk factors of fibrosis progression, including sex, age, body mass index (BMI), ALT and HBV DNA levels, HBeAg and alcohol consumption.

Results

Study population

- Of 752 SEN-B treatment-naïve participants, 63/752 (8.4%) did not have a 12-month follow-up visit and 133/752 (17.7%) initiated antiviral treatment before the second LSM and were subsequently excluded from the study.

Affiliations
(1) Department of Infectious Diseases, Bern University Hospital, University of Bern, Bern, Switzerland. (2) Service de Maladies Infectieuses et Tropicales, Fann University Hospital, Dakar, Senegal. (3) Graduate School of Health Sciences, University of Bern, Bern, Switzerland. (4) Department of Biomedicine, University Hospital Basel, University of Basel, Basel, Switzerland (5) Centre de Recherche et Formation Clinique, University Hospital Dakar, Dakar, Senegal. (6) Institute for Infectious Diseases, University of Bern, Bern, Switzerland. (7) Clinical Trials Unit, Institute of Social and Preventive Medicine, University of Bern, Switzerland. (8) Centre de Traitement Ambulatoire, University Hospital Fann, Dakar, Senegal. (9) Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland.

Main findings

- In Senegal, 5% of persons with HBV who are ineligible for antiviral therapy experienced a progression in their liver fibrosis stage during the first year of follow-up.
- Men presented a significantly higher risk of liver fibrosis stage progression than women.

Table 1: Characteristics of study participants by sex

Characteristics	Men N = 284	Women N = 272	p-value
Age, years	31 (25-37)	31 (25-39)	0.79
>30	146 (51.4%)	148 (50.7%)	0.87
BMI, kg/m²	21.4 (19.3-23.8)	23.7 (20.6-28.0)	<.001
>25.0	42 (14.8%)	121 (44.5%)	<.001
HCC family history	10 (3.5%)	15 (5.5%)	0.26
Hazardous drinking	7 (2.5%)	2 (0.7%)	0.11
ALT, IU	18 (14-24)	16 (12-22)	0.002
>40	14 (4.9%)	15 (5.5%)	0.76
HBeAg positivity	3 (1.1%)	2 (0.7%)	0.69
LSM, kPa	5.2 (4.4-6.0)	4.6 (3.9-5.5)	<.001
Categories			0.01
<7.0 (F0-F1)	265 (93.3%)	266 (97.8%)	
7.1 - 11.0 (F2-F3)	19 (6.7%)	6 (2.2%)	
HBV DNA, IU/mL	511 (114-2070)	344 (43-1230)	0.04
Categories			0.20
<20	37 (13.0%)	49 (18.0%)	
20-2,000	174 (61.3%)	165 (60.7%)	
2,001-20,000	59 (20.8%)	42 (15.4%)	
>20,000	14 (4.9%)	16 (5.9%)	

Footnote. Data are presented as median (IQR) for continuous measures, and n (%) for categorical measures. Abbreviations: LSM: Liver stiffness measurements; HCC: Hepatocellular carcinoma

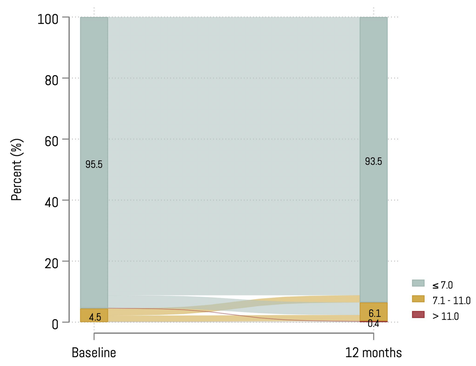


Figure 1: Sankey diagram of liver fibrosis stage changes

Characteristics of study participants

- 284/556 (51.1%) were men, the median age was 31 years (Interquartile range [IQR] 25-39), 163/556 (29.3%) participants had a BMI >25 kg/m² and 1.5% (9/556) reported hazardous alcohol drinking.
- 5/556 (0.9%) participants were HBeAg-positive, 5.2% (29/556) had ALT >40 IU and 23.6% (131/556) had HBV DNA >2,000 IU/mL.
- Women were three times more likely to be overweight (BMI>25 kg/m²) than men (44.5% vs. 14.8%; p<.001) **(Table 1)**
- The median LSM was significantly higher among men compared to women (5.2 kPa vs. 4.6; p<.001). The proportion of participants with liver fibrosis F2-F3 was higher among men compared to women (6.7% vs 2.2%; p=0.01)

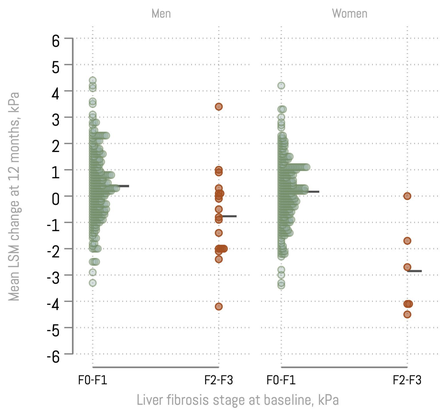


Figure 2: Mean LSM change at 12 months, by sex

Liver fibrosis stage progression

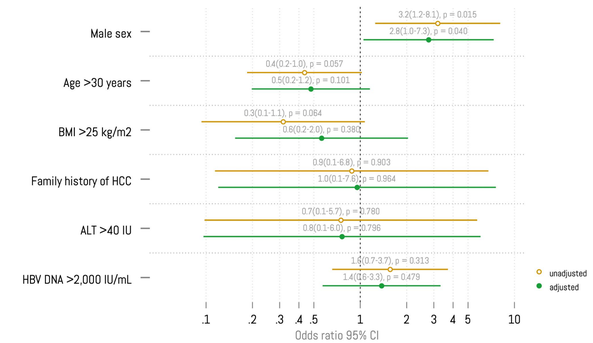
- Significant fibrosis (LSM>7.0; F2-F4) was present in 25/556 (4.5%) participants at baseline and in 36/556 (6.5%) at 12 months **(Figure 1).**
- Overall, 4.5% (25/556) of participants experienced liver fibrosis progression during follow-up, of whom 24 (96.0%) had F0-1 fibrosis stage at inclusion.
- 2 (0.2%) participants were found to have liver cirrhosis (LSM>11.0) at the 12-month follow-up, one with baseline fibrosis stage F0-F1 and the other with F2-F3.

Change of Liver stiffness measurements at 12 months

- The total mean LSM change at 12 months was +0.2 kPa (Standard deviation [SD] ∓1.3) **(Figure 2).**
- We found a significantly higher mean change of liver stiffness in men compared to women (+0.3 ∓1.3 vs. +0.1∓1.3; p=0.03)

Predictors of liver fibrosis progression

- In multivariable analyses, male sex (adjusted odds ratio 2.77, 95% confidence interval 1.05-7.33) was the only factor associated with fibrosis progression (**Figure 3**).



Footnote: The variables [HBeAg-positivity] and [Hazardous drinking] were removed from the model due to collinearity.

Figure 3: Predictors of liver fibrosis progression at 12 months of follow-up

Conclusions

- SEN-B is one of the largest prospective cohorts of people with HBV with longitudinal data on liver fibrosis in Africa.
- Five percent of individuals ineligible for antiviral therapy experienced a progression of liver fibrosis stage during the first year of follow-up and this outcome was more likely in men than women.
- Long-term data is urgently needed to understand the determinants of liver fibrosis changes in Africa in order to inform monitoring strategies.

Contact: adria.ramirez@posteo.net