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HIV and Liver Fibrosis among Prison Inmates, the IeDEA West Africa collaboration

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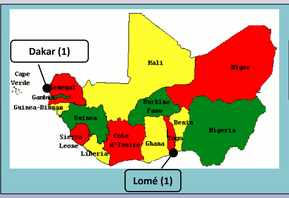
BACKGROUND

- Worldwide, deaths attributable to liver cirrhosis increased from 676,000 in 1980 to over 1 million in 2010. However, data on the causes of death in sub-Saharan Africa are poor, which limits the assessment of the true burden of liver-related complications in the region.
- Recently, several non-invasive methods of measuring liver fibrosis have been developed to overcome the challenges related to liver biopsy. Of these, transient elastography, based on the measurement of liver stiffness (LSM), has proven to be accurate in a wide range of liver diseases.
- Prisons are known to be a high-risk environment for addictive behaviors as well as blood-borne and sexually transmitted infections leading to liver damage. However, little is known about the prevalence of liver fibrosis in the context of high Hepatitis B virus (HBV) endemicity.
- In a context of expanding access to efficient antiviral therapies active against both HIV and HBV in sub-Saharan Africa, there is a real need to document liver damage in vulnerable populations such as inmates.
- Our aim was to investigate liver fibrosis and associated factors among inmates incarcerated in West Africa

METHOD



Study population

State prison, Dakar, Senegal	State prison, Lome, Togo
"Maison d'arrêt de REBEUSS"	"Prison civile de Lomé"
April-May 2014	September-October 2013

Random selection of approximately 350 adult (≥18 years) men currently incarcerated recruited in each state prison

1) Administered standardized questionnaire
- Age
- Alcohol use during the past 12 months (AUDIT questionnaire)
  - No or moderate use (score <8)
  - Hazardous use (score ≥8)
- Use of Herbal medicine
  - No or occasional user
  - Frequent user

2) Screening of liver fibrosis
Transient Elastography device (Fibroscan E401®, Echosens, Paris)



3) Screening of viral infections using rapid diagnostic tests
- HIV infection (Determine®)+confirmation according to national algorithms
- Hepatitis C Virus (HCV) infection (Oraquick®)
- HBV infection (HBs Ag) (Determine®)

If positive for HBV infection, blood sample collected for viral load quantification by PCR

Liver Stiffness= median value of ten successive validated LSM
Quality criteria to be achieved:
- success rate ≥66%
- interquartile range (IQR) less than 30% of the median value (IQR/LSM≤30%).

Statistical analysis
- A conservative cutoff value of LSM ≥9.3 KPa was used to define the presence of a significant liver fibrosis
- A multivariable logistic regression model was used to predict factors associated with significant liver fibrosis (corresponding to METAVIR score>=2). A stepwise descending procedure was applied to derive the model that best predicted the presence of significant liver fibrosis. Prevalence and Odds Ratio (OR) estimates were reported with their 95% Confidence Interval (95% CI)

RESULTS

- **A total of 680 inmates were included in Lome (n=347) and Dakar (n=333)**
- **Median age= 30 years [IQR 24-35]**
- **Median time of incarceration= 8 months [IQR 2 – 27]**
- **Significant fibrosis= 3.4% [95% CI 2.0 – 4.7]**
- **HIV infection= 2.7% [95% CI 1.4 – 3.8]**
- **HCV infection= 0.5% [95% CI 0.1 – 0.9]**
- **HBV infection= 12.5% [95 CI 10.0 – 15.0]**
- **Plasma HBV DNA level>20 000 UI/ml in HBV-infected participants with documented HBV viral load (n= 69)**
  - **Overall: 26/69 (37.7%)**
  - **In HBV-infected inmates with significant liver fibrosis: 3/7(42.9%)**
  - **In HBV-infected inmates with no significant liver fibrosis 23/62 (37.1%) (p=0.76)**

Addictive behaviors of inmates incarcerated the state prisons of Lome and Dakar, West Africa 2013-2014 (n=680)

	Dakar (n=333)	Lome (n=347)	p	Total (N=680)
Alcohol use (%)			$<10^{-4}$	
No	91.6	63.7		77.4
Moderate	3.0	24.8		14.1
Hazardous	5.4	11.5		8.5
Tobacco Use (%)			$<10^{-4}$	
No	24.7	54.5		39.9
Past use	11.1	16.1		13.7
Present use	64.2	29.4		46.4
Cannabis use (%)			$<10^{-4}$	
No	54.1	77.8		66.2
Past use	38.4	14.7		26.3
Present use	7.5	7.5		7.5
Cocaine/Crack use (%)			0.42	
No	98.8	99.2		99.0
Present/Past use	1.2	0.8		1.0
Heroin use (intravenous) (%)			0.96	
No	99.4	99.4		99.4
Present/Past use	0.6	0.6		0.6

Factors associated with a significant liver fibrosis defined as a median liver stiffness measurement ≥9.3 KPa in inmates of state prisons in Dakar and Lomé, West Africa 2013-2014 (n=680)

	Univariate analysis			Multivariable analysis	
	n/N	OR (95% CI)	p	OR (95% CI)	p
Age			0.95		
≤35 years	18/527	1			
>35 years	5/153	0.9 (0.3 – 2.6)			
State prison			<10-2		**0.02**
Dakar, Senegal	4/333	1		1	
Lome, Togo	19/347	4.8 (1.6 – 14.1)		4.3 (1.3 – 13.8)	
Alcohol use			0.91		
No use	18/526	1			
Moderate/Hazardous use	5/96	1.3 (0.6 – 2.9)			
HIV infection			<10-2		**0.01**
Negative	20/662	1			
Positive	3/18	6.4 (1.7 – 23.9)		6.1 (1.4- 26.5)	
Hepatitis B infection			0.01		**$<10^{-2}$**
Negative	16/595	1			
Positive	7/85	3.2 (1.3 – 8.1)		4.1 (1.5 – 11.1)	
Hepatitis C infection			0.03		**$<10^{-2}$**
Negative	22/657	1		1	
Positive	1/3	14.9 (1.3 – 170.4)		43.0 (3.0 – 611.6)	
Use of traditional medicine			<10-2		**0.02**
No or occasional use	16/617	1		1	
Frequent use	7/63	4.7 (1.8 – 11.9)		3.1 (1.1 – 8.5)	

DISCUSSION

HIV infection
- The prevalence of HIV infection was high in inmates incarcerated in the state prisons of Lome and Dakar, two to four times higher than the respective prevalence in the general adult population of Togo and Senegal
- HIV infection was significantly associated with liver fibrosis after adjustment on HBV and HCV infections. Aside the direct hepatotoxic role of HIV itself, various unmeasured tropical hepatotoxic infectious agents may have interacted with HIV infection in the development of liver fibrosis.
- Further studies will need to explore the exact mechanisms leading to liver fibrosis in HIV-infected persons without viral hepatitis B or C in sub-Saharan Africa.

Viral hepatitis B and C infections
- A high prevalence of HBV infection was reported, in accordance with the prevalence of HBs Ag carriers in the general population in West Africa.
- Over a third of HBV-infected inmates harbored a high HBV DNA replication (>20 000 UI/ml), regardless of the presence of significant liver fibrosis. In this context, the availability of accessible means for the assessment of liver fibrosis is of paramount importance to identify and prioritize HBV-infected patients in need of antiviral therapies.
- A low prevalence of HCV infection was observed in our study population, even lower than the available regional estimates [2.8% (95%CI 2.4-3.3)] from West Africa.
- However, accurate estimates of HCV infection are currently limited by the availability of reliable serological tests and would benefit from larger standardized prevalence studies.

Other factors
- The use of traditional medicine based on herbs consumption was associated with liver fibrosis. There is now a need to explore the types of herbs in relation to liver fibrosis in order to provide herb safety recommendations in the context of traditional medicine use in West Africa.
- Alcohol use was not associated with liver fibrosis in this present report. However, the assessment of alcohol exposure through the AUDIT score did not capture the lifetime exposure to alcohol use which might be more relevant as liver fibrosis is a relatively long process.
- Additional etiologic studies including tropical infections with liver involvement and exposure to environmental factors such as Aflatoxin will ultimately be needed.

CONCLUSION
- Although mainly driven by viral hepatitis, HIV infection was identified as an independent determinant of liver fibrosis. In a time of increasing availability of efficient therapy for HIV and now hepatitis infections, appropriate monitoring strategies for liver disease need to be explored in vulnerable populations such as inmates.
- The association between liver fibrosis and other factors such as the use of traditional medicine highlights the need to provide better documentation of etiologic factors leading to liver damages in sub-Saharan Africa.

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