SAT 587

Fatty Liver and Aldosterone levels in African Americans: The Jackson Heart Study

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INTRODUCTION

- Fatty liver disease is one of the most common forms of chronic liver disease throughout the world. This condition consists of a spectrum ranging from fatty liver to steatohepatitis which can then progress to cirrhosis and hepatocellular carcinoma.
- Fatty liver is associated with obesity, type 2 diabetes mellitus and hypertension; leading to significant morbidity and mortality.
- The current standard of care for treatment of patients with fatty liver disease focuses on lifestyle interventions, particularly diet and exercise, while pharmacologic therapeutic options are limited.
- Activation of renin angiotensin aldosterone system (RAAS) has been implicated in the pathogenesis of fatty liver and is thought to play a role in liver inflammation and fibrosis. As a result, RAAS blockers are being explored as therapeutic options for fatty liver disease.
- Most data on the benefit of RAAS blockade (by the use of angiotensin receptor blockers and aldosterone antagonists) in fatty liver disease comes from animal studies and small scale clinical studies.
- Animal studies have shown that RAAS blockade can prevent hepatic stellate cell activation, thereby preventing hepatic inflammation and fibrogenesis.
- Aldosterone has been shown to be produced locally during hepatic fibrogenesis and aldosterone antagonists have shown benefit in fatty liver.(1)
- In a clinical study, spironolactone in combination with vitamin E was reported to improve insulin resistance in patients with non alcoholic fatty liver disease.(2)
- Although multiple studies have investigated RAAS suppression in fatty liver, there is limited data regarding the association between serum aldosterone and fatty liver disease.
- A pilot study by Fallo et al showed that fatty liver is a frequent finding in primary aldosteronism,(3) however data regarding association between serum aldosterone and liver fat content from large cohort studies is lacking.

OBJECTIVE

- **To investigate the association of serum aldosterone with liver fat content in the Jackson Heart Study (JHS), a community based observational study of African Americans.**

METHODS

- The original JHS cohort enrolled participants from September 2000 to March 2004 and includes 5306 participants between the ages of 21-84 when they enrolled in the study.
- Participants were recruited from Jackson, MS metropolitan area in Hinds, Madison and Rankin counties.
- Serum aldosterone was measured in the original cohort by radioimmunoassay (Siemens).
- As part of the JHS exam 2 during 2007-2009, a subset of subjects underwent multi detector CT scanning. Liver fat was estimated by measurement of liver attenuation (LA) in Hounsfield Units (HU) on CT scan which has been shown to accurately predict liver fat, with lower attenuation corresponding to higher liver fat.(4)
- Our study included 2940 participants on whom liver HU attenuation data was available.
- There was an average difference of 1735 days (~ 5 years) between measurement of serum aldosterone and liver fat assessment.

Baseline characteristics of study participants

Characteristics	Overall (n = 2,940)	Women (n = 1,910)	Men (n = 1,030)	p
Age (years)	55.36 (10.98)	55.92 (10.94)	54.34 (10.99)	<0.001
BMI (kg/m^2)	30.49 [8.04]	31.64 [9.04]	28.82 [6.09]	<0.001
Average number of alcoholic drinks per week	1.15 (1.74)	0.70 (1.24)	1.72 (2.08)	<0.001
Visceral Adipose Tissue (cm^3)†	830.56 (383.65)	802.26 (362.54)	883.00 (415.08)	<0.001
Subcutaneous Adipose Tissue (cm^3)†	2329.50 (1014.53)	2657.51 (962.94)	1722.19 (806.63)	<0.001
Fasting triglycerides	90.00 [60.00]	88.00 [57.00]	94.00 [63.00]	0.002
Diabetes (Y/N)	561 (19%)	374 (20%)	187 (18%)	0.330
HOMA IR (Molar Units)	2.96 [2.08]	3.06 [2.20]	2.73 [1.91]	<0.001
Hypertension (Y/N)	1745 (59%)	1160 (61%)	585 (57%)	0.037
Plasma Adiponectin (ng/mL)	4156.84 [3903.97]	4915.33 [4195.88]	3090.44 [2769.75]	<0.001
Leptin (ng/mL)	23.00 [28.40]	33.15 [23.85]	8.15 [8.50]	<0.001
Average Liver Attenuation (Hounsfield Units)†	59.10 (9.22)	59.67 (9.02)	58.04 (9.50)	<0.001
High Sensitivity C-Reactive Protein (Serum mg/dL)	0.70 [0.17]	0.69 [0.18]	0.70 [0.14]	0.016
Serum Aldosterone (ng/dL)	4.30 [4.50]	4.10 [4.50]	4.80 [4.40]	<0.001

‡Values in table are Mean (SD), N (%), or Median [IQR], †CT was performed during exam 2 visit
HOMA IR- Homeostatic Model Assessment of Insulin Resistance

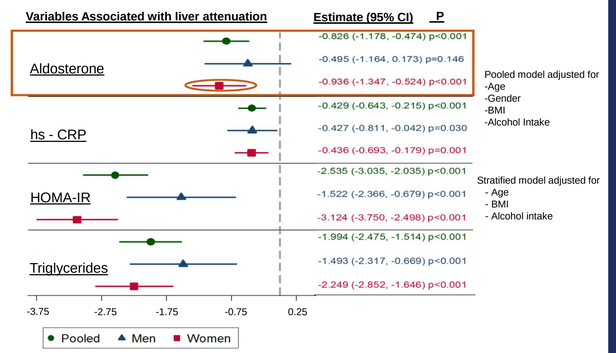
RESULTS

Factors associated with Liver attenuation on CT (Univariate Analysis)

Variables	Overall (n = 2,940)	Women (n = 1,910)	Men (n = 1,030)
Male (Y/N)	-1.62*** [-2.32,-0.93]	-	-
BMI (kg/m^2)	-0.23*** [-0.28,-0.18]	-0.24*** [-0.30,-0.18]	-0.35*** [-0.46,-0.24]
Age (years)	0.05** [0.02,0.08]	0.03 [-0.00,0.07]	0.06* [0.01,0.11]
High Sensitivity C-Reactive Protein (mg/dL)^{LOG}	-0.59*** [-0.78,-0.40]	-0.75*** [-0.98,-0.52]	-0.80*** [-1.16,-0.44]
Fasting Triglyceride Level (mg/dL)^{LOG}	-2.30*** [-2.77,-1.83]	-2.28*** [-2.86,-1.70]	-2.17*** [-2.96,-1.39]
Homeostatic Model Assessment of Insulin Resistance (molar units)^{LOG} ◊	-2.71*** [-3.16,-2.25]	-3.39*** [-3.96,-2.82]	-2.08*** [-2.83,-1.32]
Serum Aldosterone (ng/dL)^{LOG}	-0.99*** [-1.35,-0.64]	-1.03*** [-1.44,-0.62]	-0.71* [-1.37,-0.04]
Average number of alcoholic drinks per week	-0.10** [-0.16,-0.03]	0.04 [-0.10,0.17]	-0.10* [-0.18,-0.02]

p<0.05, ** p<0.01, *** p<0.001, ◊Not calculated for diabetics, including those on DM meds
†Outcome = Average Liver Attenuation (HU), ‡Cells represent: model estimates [95% CI]1

Factors associated with Liver attenuation on CT (Multivariate Analysis)



DISCUSSION

- Our study is the first population based cohort study demonstrating an association between serum aldosterone levels and liver fat content.
- This study suggests a positive association of serum aldosterone levels and liver fat content in African American women. This association was not seen in men.
- Complex interactions between RAAS and estrogen may explain the observed sexual dimorphism in our study.

LIMITATIONS

- Liver CT HU attenuation can be affected by other underlying diseases of the liver in addition to fat infiltration as iron deposition and liver edema.
- Alcohol intake in this study was determined by self report which could be a biased estimate and it is possible that alcohol intake could have played a role on liver attenuation in this study beyond what was actually estimated.
- Our study population consisted of African American individuals only, who have a lower prevalence of fatty liver when compared to other ethnicities.

CONCLUSIONS

- Our study demonstrates a positive association of serum aldosterone levels with liver fat content in African American women.
- These findings are important as they may guide the use of aldosterone antagonists in specific population subgroups which may obtain the greatest therapeutic benefit from use of these agents.
- Further studies are needed to investigate the association of aldosterone levels and fatty liver in other ethnic groups.

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