HHS Public Access

Author manuscript

Dig Dis Sci. Author manuscript; available in PMC 2020 June 01.

Published in final edited form as:

Dig Dis Sci. 2019 June ; 64(6): 1705–1710. doi:10.1007/s10620-018-5441-5.

Older Age and Disease Duration are Highly Associated with Hepatocellular Carcinoma in Patients with Autoimmune Hepatitis

Lara Dakhoul, MD[1], **Keaton R Jones, MD**[1], **Samer Gawrieh, MD**[1], **Marwan Ghabril, MD**[1], **Chelsey McShane, MD**[2], **Raj Vuppalanchi, MD**[1], **Eduardo Vilar-Gomez, MD, PhD**[1], **Lauren Nephew, MD, MSCE**[1], **Naga Chalasani, MD**[1], and **Craig Lammert, MD**[1]

[1]Division of Gastroenterology and Hepatology, Indiana University School of Medicine, Indianapolis, IN

[2]Department of Internal Medicine, Indiana University School of Medicine, Indianapolis, IN

Abstract

Background: Hepatocellular carcinoma (HCC) is rare in patients with autoimmune hepatitis (AIH). However, the overall burden of AIH cirrhosis in causing HCC and patients' risk factors are not well understood.

Aims: To characterize the proportion of HCC linked to AIH at a large academic health center, and to identify variables associated with HCC in patients with AIH in a case-control study design.

Methods: Over a 14.5-year period, medical records of all patients with HCC were reviewed. Cases are AIH patients identified from the cohort and controls are patients with AIH without HCC. Three controls were randomly chosen from the Genetic Repository of Autoimmune Liver Disease and Coexisting Exposures database for each eligible case.

Results: Out of 1,250 eligible patients, 20 were linked to AIH (1.6%). Their median age was 64 years, 40% men, and 100% Caucasian. 10% of AIH patients did not have evidence of cirrhosis at HCC diagnosis. The proportion of HCCs due to AIH decreased during the time intervals of the study. Compared to controls, cases were more likely men (40.0% vs. 18%, P=0.049), with longer AIH duration (median 16 years vs. 5 years, P=0.004). Prolonged AIH duration (OR 1.68, p=0.006) and older age (OR 1.15, p=0.049) were risk factors for HCC.

Conclusions: AIH is a rare cause (1.6%) for HCC in Midwestern United States with a decreasing trend over 14.5 years. 10% of AIH-HCC patients occurs without cirrhosis. Patients with prolonged duration of the disease and older age are at high risk to develop HCC.

Keywords

Liver Cancer; Autoimmune Liver Disease; Older Age; Disease Duration.

Corresponding Authors: Naga Chalasani (nchalasa@iu.edu), Craig Lammert (clammert@iu.edu), Indiana University School of Medicine, 702 Rotary Circle, Suite 225, Indianapolis, IN 46202, Telephone 317-278-0414, Fax 317-278-1949.

Conflicts of Interest: Authors declare no conflicts of interest relevant for this paper.

Introduction

Autoimmune hepatitis (AIH) is a rare autoimmune disease affecting predominantly Caucasian females. Its prevalence is estimated at 18.3 per 100,000 (95% CI: 17.3–19.4) with an incidence peak in middle-aged women.[1] The etiopathogenesis of AIH is likely to be explained by complex interactions between environmental exposures and susceptible genetic predispositions.[2] Symptoms, severity, and outcomes vary widely according to geographical locations and racial distributions. Recent reports suggest a recent increase in the disease incidence, prevalence as well as mortality and morbidity rates in both sexes.[3–5]

Hepatocellular carcinoma (HCC) is an important complication in patients with underlying liver disease and cirrhosis. It is rare in patients with cirrhosis due to AIH compared to other chronic liver disease risk factors; however, these patients are routinely screened for HCC. The true incidence of HCC linked to AIH remains unknown due to the lack of large sample studies. Large variations exist between reported numbers; it was recently estimated to be 3.06 per 1000 person-years.[4] In addition, the overall burden of AIH cirrhosis and risk factors for developing HCC in AIH in the absence of co-existing etiologies are not well understood. Therefore, the cost-effectiveness of established screening strategies in this population is controversial. Male gender, prolonged immunosuppressive treatment and features of portal hypertension were identified as predictors for HCC in patients with AIH.[6] In addition to the obvious increased risk of HCC in patients with underlying cirrhosis, studies reporting HCC occurring in patients in the absence of cirrhosis are scarce.

Two objectives of this study were: (a) to describe the trend of HCC associated with AIH over a 14.5-year period at a large liver center in the Midwestern United States and (b) to identify variables associated with HCC in patients with AIH in a case-control study design.

Materials and Methods

All adult patients with HCC seen at Indiana University and Methodist Hospitals in Indianapolis, Indiana from January 2000 to June 2014 were retrieved from the Indiana State Cancer Registry. Medical records of all such retrieved patients were manually reviewed to confirm the diagnosis of HCC. Patients with uncertain HCC diagnosis, fibrolamellar HCC or cholangiocarcinoma, insufficient data, or who were seen for tumor recurrence were excluded. The demographics, comorbidities, liver disease and tumor characteristics, and treatment modalities were obtained from the medical records. The presence of underlying cirrhosis was ascertained based on clinical, laboratory, and imaging criteria, as previously described by Mittal et al.[7] From this cohort, we identified HCCs associated with AIH (AIH-HCC) and compared their proportion relative to all other causes of liver disease over 3 time intervals (2000–2004; 2004–2009; and 2010 through June 2014).

Subsequently, we conducted a case-control study comprising of AIH-HCC patients (cases) and patients with AIH but no HCC (controls) randomly chosen from a database of all AIH subjects seen at our facility at least once between the year 2000 and June 2014. An autoimmune liver disease database, Genetic Repository of Autoimmune Liver Disease and Coexisting Exposures (GRACE), is a well-established repository of all AIH cases evaluated

at Indiana University including demographics, clinical data, and biologic samples.[8] At the time of the study, the GRACE database contained 350 unique patients. Three random controls were selected by SPSS statistical software for each case and were not matched to any variable. Medical records for both cases and controls groups were reviewed for AIH-specific details including AIH duration, medications used, and disease course. Demographics, clinical and disease characteristics were compared between the two groups. Age at AIH diagnosis was estimated by the difference between the date of birth and the AIH diagnosis date. The duration of AIH was calculated by the time difference between the date of AIH diagnosis and the date of last contact or death. Serum anti-nuclear antibodies (ANA) and anti-smooth muscle antibodies (ASMA) > 1:40 dilutions were considered positive. Survival data was obtained from the Cancer Registry and the medical records for AIH patients who developed HCC. For patients who are still alive or dead with unknown date of death, the date of last contact was utilized to calculate the overall survival.

Statistical Analysis

Continuous variables are presented as mean ± standard deviation (SD) or median with interquartile range (IQR), and categorical variables as numbers and percentages. Chi-square test was used for comparison between different groups for discrete variables and independent-samples, non-parametric tests (Mann-Whitney) for comparison of continuous variables. The linear-by-linear progression p-value compared the time-trend between AIH-HCC and other HCCs. Univariate and multivariate analyses were conducted with HCC as the outcome for each variable using logistic regression models. All statistical tests were performed using IBM SPSS statistical software version 24. A p-value <0.05 was considered as statistically significant.

Results

During the study period, 1,290 unique patients with reported HCC were seen at our institution. After excluding 40 patients in whom we could not ascertain the HCC diagnosis or had mixed HCC/cholangiocarcinoma, there were 1,250 patients with HCC eligible for inclusion in this study. Viral hepatitis with or without alcohol (56%), alcoholic liver disease (12.2%), and nonalcoholic fatty liver disease (NAFLD) (16.6%) were other dominant causes of underlying liver disease in this cohort. Twenty four patients had underlying AIH: 20 with AIH alone whereas 4 with co-existing viral hepatitis or significant alcohol consumption. For the remainder of this paper, we focused on 20 patients with HCC developing in patients with AIH.

The proportion of HCCs arising in patients with underlying AIH during 2000–2004, 2005–2009, and 2010 - June 2014 was 3.1%, 1.6%, and 0.9% respectively compared to 96.9%, 98.4% and 99.1% respectively for HCC cases linked to other etiologies (p=0.02 for the trend comparison). Selected characteristics of 20 AIH patients with HCC are described in Table 1. Their median age was 64 years with an IQR of 9, their mean body mass index (BMI) was 30.9 ± SD of 7.4 kg/m^2, and all of them were Caucasian. Ninety percent had underlying cirrhosis at the time of HCC diagnosis their mean Model for End-Stage Liver Disease (MELD) score at presentation was 13.2. Thirty-five percent received a liver transplant, 20%

underwent surgical resection, and 45% had catheter-based therapies. Their 1, 3, and 5-year survival rates were 60%, 40%, and 30% respectively. Out of 20 AIH-HCC patients, 9 patients (45%) were alive at the end date of the study, and 11 (55%) were deceased. Out of the 11 deceased patients: 4 (36%) died from liver related complications, 2 (18%) had non-liver related deaths, and 5 patients (46%) were unknown.

We subsequently compared 20 AIH-HCC patients (Cases) and 60 patients with AIH but no HCC (Controls) (Table 2). The median age was 56.6 years (IQR 21.4) vs. 49 years (IQR 21) in cases and controls respectively; however, the difference was not significant (p=0.23). Cases were more frequently male (40% vs. 18%; p=0.049) and exclusively white (100%). The median duration of AIH was significantly longer among AIH-HCC patients (16.3 years) compared to controls (5.0 years, p=0.004). A total of 5 patients with AIH-HCC (41.7%) had underlying liver cirrhosis at AIH diagnosis compared with 14 (26.9%) of the AIH non-HCC group (p=0.31); however, this information was unavailable for 16 patients overall (cases and controls). The majority of patients from both groups had positive ANA (68.8% of cases and 74.5% of controls). On the other hand, only 21.4% of cases had positive ASMA compared to 70.6% of controls (p=0.001). To compare the course of AIH between the 2 groups, we collected the number of clinical relapses throughout disease course. This data was unavailable in 65% of the AIH-HCC group and 25% of the control group. In the remaining patients, 43% and 53% of the cases and controls respectively had at least one relapse since diagnosis (p=0.60).

Medications received by patients were assessed until HCC diagnosis for cases and throughout the disease course for controls. Most of the patients from both groups were started on steroids (prednisone/budesonide) (62.5% of cases and 78.3% of controls) or azathioprine (62.5% of cases and 65% of controls) to treat disease-associated hepatic inflammation. Treatment with 6-mercaptopurine or ursodeoxycholic acid (UDCA) was less prevalent (20% of cases vs. 15% of controls for 6-mercaptopurine and 15% of cases vs. 12% of controls for UDCA). Fourteen percent of cases vs. 1.7% of controls were not on any medications (p=0.03). AIH-HCC patients and AIH patients without HCC received liver transplantation equally (p=0.19).

As a next step, we performed univariate and multivariate analyses using logistic regression models to better understand what variables may be independently associated with HCC in AIH patients. We computed this analysis for variables that were different among cases and controls with p-values <0.10. These variables include male sex (female sex used as reference), AIH duration, positive ASMA and no medications received. Although age was not significantly different between the compared groups in our study, we included it in this analysis as increased age was reported to be associated with HCC in the literature.[9] This multivariate logistic regression analysis showed older age (OR: 1.15, 95% CI 1.001–1.314, p=0.049), and increased AIH duration (OR: 1.68, 95% CI: 1.16–2.45, p=0.006) to be significant risk factors for developing HCC whereas positive ASMA was again negatively associated with HCC (OR: 0.02, 95% CI 0–0.73, p=0.03).

Discussion

This study evaluated the disease burden, trend and risk factors of AIH-HCC in a large cohort of 1,250 patients with well-characterized HCC from a large tertiary referral center in the Midwestern U.S. between 2000 and June 2014. Out of 1,250 patients, we were able to identify 20 patients (1.6% of the cohort) with HCC due to underlying AIH. This finding is similar to other studies reporting the percentage of HCC associated with AIH to be ≤3%, [7,10–12] and is significantly lower compared to other etiologies of chronic liver disease. [4,13] A recently published meta-analysis that included 25 studies estimated an overall HCC incidence rate of 3.06 per 1000 patient-years (95% CI, 2.22–4.23) among patients with AIH. [4] Many studies have suggested an increase in the incidence rate of HCC cases linked to AIH.[3–5] Although we cannot draw conclusions regarding the incidence rate of HCC in AIH patients from this study, we observed a significant downtrend in the proportion of these cases over the 14.5 years of the study compared to the rest of the HCC cases (p=0.02). This observation of less HCC over time might be explained by the ability to achieve higher frequencies of biochemical response, maintenance of remission, fibrosis stability/regression or fewer relapse rates in a majority of AIH patients with current multiple immunosuppressive modalities. [14]

HCC usually occurs in patients with cirrhosis, but can also develop in non-cirrhotic livers. [15] The latter is primarily seen in patients with Hepatitis B[16] and more frequently reported recently from NAFLD;[7,17,18] However, HCC occurring in non-cirrhotic patients is very rare. HCC patients with AIH arise almost exclusively in cirrhotic livers,[12,13,19,20] with a risk of 1.9% per year.[21] Tansel and colleagues reported a pooled HCC incidence rate among patients without cirrhosis of 1.14 per 1000 person-years with 95% CI: 0.60–2.17. [4] Furthermore, they also found that 23% of AIH patients with HCC who did not have liver cirrhosis at the time of initial AIH diagnosis eventually developed cirrhosis during follow-up.[4] In our cohort, 2 patients (10% of AIH-HCC) had no evidence of cirrhosis, both biopsy-proven and interestingly males. Although the nature of our center as a tertiary referral center might be overestimating the proportion of AIH-HCC cases emerging in the absence of cirrhosis, this finding is concerning and should be looked at further at a larger scale.

Our data suggest that the duration of the disease and older age are risk factors for liver cancer: OR=1.68 for AIH duration (p=0.006) and OR=1.15 for older age (p=0.049). Literature assessing the association of the AIH duration and the risk of HCC is scarce. In Wang et al study, AIH patients with HCC had a prolonged duration of the illness compared to non-HCC patients.[20] Teufal et al also reported a long period of AIH patients who developed HCC,[13] but to our knowledge, our study is the first to describe this finding regardless of the presence of underlying liver cirrhosis. It remains possible that prolonged chronic low-grade hepatocellular inflammation could be a factor associated with HCC development. The effect of age on the outcomes of autoimmune hepatitis is controversial. Elderly patients present with an acute onset of the disease and have a significantly higher frequency of cirrhosis at the time of diagnosis.[22,23] With the known risk of HCC in patients with cirrhosis, these results are in agreement with ours. Similarly, Macaron et al [9] reported a hazard ratio of 1.1 (p<0.001) for older age which also supports our findings.

Our study has few limitations. Disease-linked variables such as AIH severity, symptoms at presentation, number of relapses, AIH disease course, and causes of deaths were difficult to adequately assess because of incomplete electronic medical records. Despite a large number of patients with HCC, our cohort still may lack the needed statistical power to show differences in outcomes between AIH-HCC and AIH non-HCC subjects because of the low frequency of AIH-associated HCC. There is also a small possibility that 3 out of our AIH-HCC patients may have had concomitant nonalcoholic fatty liver disease viewing the presence of 3 risk clinical factors. We still remain enthusiastic about our findings, as our resultant sample size of 20 patients (cases) is larger than most similar studies.[6,21,24,25]

In conclusion, AIH is a rare cause (1.6%) for HCC in Midwestern United States. The proportion of HCC linked to AIH is downtrending from 3.1% between the year 2000 and 2004 to 0.9% between 2010 and June 2014 compared to HCC linked to other etiologies. 10% of HCC patients with AIH occur without underlying liver cirrhosis. AIH Patients with prolonged AIH duration and older age are at high risk to develop HCC. Further prospective studies are needed to confirm our findings and to explore whether screening for HCC in patients with AIH can be limited to a certain subset of subjects with selected risk factors.

Acknowledgments

Source of Funding: There was no external funding for this study.

Abbreviations:

AIH	Autoimmune Hepatitis
HCC	Hepatocellular Carcinoma
GRACE	Genetic Repository of Autoimmune Liver Disease and Coexisting Exposures
ANA	Anti-Nuclear Antibodies
ASMA	Anti-Smooth Muscle Antibodies
SD	Standard Deviation
IQR	Interquartile Range
NAFLD	Non-Alcoholic Fatty Liver Disease
BMI	Body Mass Index
MELD	Model for End-Stage Liver Disease
UDCA	Ursodeoxycholic Acid
APRI	AST to Platelet Ratio Index
AFP	Alpha-Fetoprotein
BCLC	Barcelona Clinic Liver Cancer.

References

1. van Gerven NM, Verwer BJ, Witte BI, et al. Epidemiology and clinical characteristics of autoimmune hepatitis in the Netherlands. Scandinavian journal of gastroenterology. 2014;49:1245–1254. [PubMed: 25123213]
2. Heneghan MA, Yeoman AD, Verma S, Smith AD, Longhi MS. Autoimmune hepatitis. Lancet. 2013;382:1433–1444. [PubMed: 23768844]
3. Gronbaek L, Vilstrup H, Jepsen P. Autoimmune hepatitis in Denmark: incidence, prevalence, prognosis, and causes of death. A nationwide registry-based cohort study. Journal of hepatology. 2014;60:612–617. [PubMed: 24326217]
4. Tansel A, Katz LH, El-Serag HB, et al. Incidence and Determinants of Hepatocellular Carcinoma in Autoimmune Hepatitis: A Systematic Review and Meta-Analysis. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2017.
5. Schramm C, Lohse AW. Autoimmune hepatitis on the rise. Journal of hepatology. 2014;60:478–479. [PubMed: 24295874]
6. Montano-Loza AJ, Carpenter HA, Czaja AJ. Predictive factors for hepatocellular carcinoma in type 1 autoimmune hepatitis. The American journal of gastroenterology. 2008;103:1944–1951. [PubMed: 18564111]
7. Mittal S, El-Serag HB, Sada YH, et al. Hepatocellular Carcinoma in the Absence of Cirrhosis in United States Veterans is Associated With Nonalcoholic Fatty Liver Disease. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2016;14:124–131.e121. [PubMed: 26196445]
8. Lammert C, Comerford M, Love J, Bailey JR. Investigation Gone Viral: Application of the Social Mediasphere in Research. Gastroenterology. 2015;149:839–843. [PubMed: 26306768]
9. Macaron C, Hanouneh I, Lopez R, Zein NN. S1883 Incidence and Risk Factors of Hepatocellular Carcinoma in Patients With Primary Biliary Cirrhosis and Autoimmune Hepatitis [Abstract]. Gastroenterology.138:S–809.
10. Watanabe T, Soga K, Hirono H, et al. Features of hepatocellular carcinoma in cases with autoimmune hepatitis and primary biliary cirrhosis. World journal of gastroenterology. 2009;15:231–239. [PubMed: 19132775]
11. Tateishi R, Okanoue T, Fujiwara N, et al. Clinical characteristics, treatment, and prognosis of non-B, non-C hepatocellular carcinoma: a large retrospective multicenter cohort study. Journal of gastroenterology. 2015;50:350–360. [PubMed: 24929638]
12. Park SZ, Nagorney DM, Czaja AJ. Hepatocellular carcinoma in autoimmune hepatitis. Digestive diseases and sciences. 2000;45:1944–1948. [PubMed: 11117564]
13. Teufel A, Weinmann A, Centner C, et al. Hepatocellular carcinoma in patients with autoimmune hepatitis. World journal of gastroenterology. 2009;15:578–582. [PubMed: 19195059]
14. Lamers MM, van Oijen MG, Pronk M, Drenth JP. Treatment options for autoimmune hepatitis: a systematic review of randomized controlled trials. Journal of hepatology. 2010;53:191–198. [PubMed: 20400196]
15. van Meer S, van Erpecum KJ, Sprengers D, et al. Hepatocellular carcinoma in cirrhotic versus noncirrhotic livers: results from a large cohort in the Netherlands. European journal of gastroenterology & hepatology. 2016;28:352–359. [PubMed: 26629867]
16. Arora A, Sharma P, Tyagi P, et al. Hepatitis B Virus Infection can Cause Hepatocellular Carcinoma in Less Advanced Liver Cirrhosis: A Comparative Study of 142 Patients from North India. Journal of clinical and experimental hepatology. 2013;3:288–295. [PubMed: 25755516]
17. Alexander J, Torbenson M, Wu TT, Yeh MM. Non-alcoholic fatty liver disease contributes to hepatocarcinogenesis in non-cirrhotic liver: a clinical and pathological study. Journal of gastroenterology and hepatology. 2013;28:848–854. [PubMed: 23302015]
18. Perumpail RB, Wong RJ, Ahmed A, Harrison SA. Hepatocellular Carcinoma in the Setting of Noncirrhotic Nonalcoholic Fatty Liver Disease and the Metabolic Syndrome: US Experience. Digestive diseases and sciences. 2015;60:3142–3148. [PubMed: 26250831]

19. Danielsson Borssén Å, Lindgren S, Bergquist A, Almer S, Sangfelt P, Werner M. 927 RISK FOR HEPATOCELLULAR CARCINOMA IN AUTOIMMUNE HEPATITIS – IS THERE AN INDICATION FOR SURVEILLANCE? [Abstract]. J Hepatol. 2013;58:S382–S383.
20. Wang KK, Czaja AJ. Hepatocellular carcinoma in corticosteroid-treated severe autoimmune chronic active hepatitis. Hepatology. 1988;8:1679–1683. [PubMed: 2461338]
21. Wong RJ, Gish R, Frederick T, Bzowej N, Frenette C. Development of hepatocellular carcinoma in autoimmune hepatitis patients: a case series. Digestive diseases and sciences. 2011;56:578–585. [PubMed: 21046244]
22. Floreani A, Niro G, Rosa Rizzotto E, et al. Type I autoimmune hepatitis: clinical course and outcome in an Italian multicentre study. Alimentary pharmacology & therapeutics. 2006;24:1051–1057. [PubMed: 16984499]
23. Czaja AJ, Carpenter HA. Distinctive clinical phenotype and treatment outcome of type 1 autoimmune hepatitis in the elderly. Hepatology. 2006;43:532–538. [PubMed: 16496338]
24. Yeoman AD, Al-Chalabi T, Karani JB, et al. Evaluation of risk factors in the development of hepatocellular carcinoma in autoimmune hepatitis: Implications for follow-up and screening. Hepatology. 2008;48:863–870. [PubMed: 18752332]
25. Migita K, Watanabe Y, Jiuchi Y, et al. Hepatocellular carcinoma and survival in patients with autoimmune hepatitis (Japanese National Hospital Organization-autoimmune hepatitis prospective study). Liver international : official journal of the International Association for the Study of the Liver. 2012;32:837–844. [PubMed: 22221966]

Table 1.

Selected Characteristics of patients with AIH and HCC.

Variables	AIH-HCC (n=20)
Baseline Characteristics	
Age at HCC diagnosis (years), median (IQR)	64 (9)
BMI (Kg/m^2), mean (SD)	30.9 (7.4)
Females (%)	60
Caucasians (%)	100
Medical comorbidities	
Diabetes Mellitus (%)	30
Coronary artery disease (%)	20
Liver Disease Severity	
ALT (U/L), mean (SD)	61 (75)
Total bilirubin (mg/dL), mean (SD)	2.9 (2.5)
Albumin (g/dL), mean (SD)	3.0 (0.7)
Platelet count (K/mm^3), mean (SD)	110 (83)
MELD, mean (SD)	13.2 (5.5)
Cirrhosis at HCC diagnosis (%)	90
APRI index (%)	
<1	16
1-2	63
>2	21
Tumor Characteristics	
Tumor size (cm), median (IQR)	2.6 (2.4)
Tumor within Milan criteria (%)	55
AFP (ng/mL) (%)	
<20	65
20–200	12
>200	23
BCLC stages (%)	
A	44
B	12.5
C	31
D	12.5
Treatment Modalities Received* (%)	
Surgical resection	20
Orthotopic liver transplantation	35
Catheter delivered therapies	45
Survival Rates (%)	

Variables	AIH-HCC (n=20)
1-year	60
3-year	40
5-year	30

*At any time throughout the disease course

APRI: AST to platelet ratio index; AFP: alpha-fetoprotein; BCLC: Barcelona Clinic Liver Cancer.

Table 2.

Summary of the comparison analysis results of all variables between AIH patients with and without HCC.

Variables	AIH-HCC (n=20)	AIH Without HCC (n=60)	p-value
Baseline Characteristics			
Age at AIH diagnosis (years), median (IQR)	56.6 (21.4)	49.0 (21.0)	0.23
Male sex (%)	40	18.3	0.049
Race (%)			0.20
White	100	80	
Black	0	15	
Asian	0	3.3	
Hispanic	0	1.7	
AIH duration (years), median (IQR)	16.3 (17.1)	5.0 (7.3)	0.004
Liver Disease Severity			
Liver cirrhosis at AIH diagnosis (%)	41.7	26.9	0.31
Autoimmune Profile			
Positive ANA (%)	68.8	74.5	0.65
Positive ASMA (%)	21.4	70.6	0.001
Treatment Modalities Received*			
Medications (%)	62.5	78.3	0.16
Prednisone/Budesonide	62.5	65	0.85
Azathioprine	20	15	0.64
6-Mercaptopurine	15	11.7	0.70
Ursodiol	35	20.3	0.19
None	35	20.3	0.19
Liver Transplantation (%)			

*At any time throughout the disease course