Poster 730

Adherence to AASLD Guideline Recommendations for Laboratory Monitoring of Chronic Hepatitis B Patients Who are Not Receiving Antiviral Treatment

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BACKGROUND

- Over 1 million US residents have chronic hepatitis B (CHB) infection, with an estimated prevalence of 0.3%-0.5%. In spite of the availability of an effective vaccine, the number of US residents with CHB infection remains high, primarily due to the slow progression of CHB and the influx of immigrants with chronic infection.[1]
- Approximately 15% to 40% of untreated CHB patients will develop serious hepatitic sequelae during their lifetime, including cirrhosis, hepatic decompensation, hepatocellular carcinoma (HCC), and death.[2-6]
- Regular laboratory monitoring of untreated patients is recommended in order to determine when to initiate antiviral therapy.[2]
- American Association for the Study of Liver Diseases (AASLD) guidelines recommend monitoring of ALT and HBV DNA levels at least annually, although based on laboratory results frequency of monitoring may be higher.[2]

OBJECTIVES

- To assess adherence to AASLD guideline-recommended laboratory monitoring of CHB patients not receiving antiviral treatment:
  - identify predictors of monitoring
  - identify predictors of initiation of antiviral treatment (i.e. oral nucleos(t)ide analogues or interferon)

METHODS

Study design:

- This retrospective cohort study used private health insurance claims data from the Ingenix LabRx dataset over a five-year period (1/1/2003 to 12/31/2007)
- The dataset contains healthcare claims for over 15 million commercially insured lives across the United States
- Inclusion criteria included:
  - 18-65 years of age
  - At least 2 claims with an ICD-9 code for chronic hepatitis B (070.3x)
  - At least 2 positive hepatitis B surface antigen (HBsAg) test
  - At least 12 months of continuous enrollment after initial diagnosis

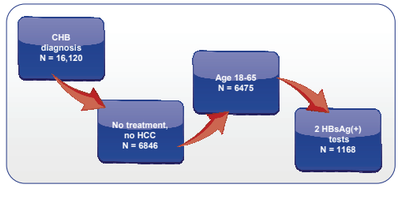
Exclusion criteria included:

- Hepatocellular carcinoma
- Any prescription for an antiviral medication during the observation period, including
  - lamivudine
  - adefovir
  - telbivudine
  - entecavir
  - tenofovir
  - emtricitabine
  - interferon-α2a/pegylated-interferon-α2a

Outcomes of interest

- The primary outcome of interest was frequency of serum laboratory testing for:
  - Alanine aminotransferase (ALT)
  - HBV DNA level to assess viral load (VL)
  - ALT *and* VL
- Secondary outcomes of interest included:
  - Predictors for monitoring
  - Predictors for initiation of antiviral treatment

Patient Flow



Methods (cont'd)

- Descriptive statistics assessed characteristics of the study sample, including:
  - Age, gender, geographical region
  - Time to antiviral treatment
  - Specialty of physician at the time of diagnosis
  - The proportion of patients with claims for
    - ALT at any time during follow-up
    - VL at any time during follow-up
    - ALT *and* VL at any time during follow-up
    - ALT *and* VL at least once every 12 months (+/- 60 days) during follow-up
- Bivariate statistics compared demographic, treatment, and monitoring characteristics of patients diagnosed by gastroenterologists (GIs), primary care providers (PCPs), and other specialities
- Multivariate logistic regression was used to determine predictors of monitoring using ALT, VL, and ALT+VL at any time during follow-up as dichotomous outcome variables. Predictor variables included age, gender, region, physician specialty, Deyo Charlson comorbidity index (a higher score indicates a greater burden of comorbid disease), and preindex diagnosis of human immunodeficiency virus (HIV) or hepatic cirrhosis
- Multivariate logistic regression was also used to determine predictors of antiviral therapy using the same predictor variables as well as ALT or VL monitoring as additional predictors

RESULTS

Table 1: Sample Characteristics

Variable	%, mean (SD)
Male	58.3%
Age (years)	40.6 (10.6)
Follow-up time (days)	728 (510.9)
Subsequent antiviral treatment	32.1%

- Approximately 32% of patients were eventually treated with an antiviral medication during the monitoring period

Table 2: Overall Monitoring Rates

Monitoring	N Total =1168	%
ALT at any time point	1095	93.8%
at least q12m	622	53.3%
HBV DNA at any time point	930	79.6%
at least q12m	455	39.0%
ALT + HBV DNA at any time point	892	76.4%
at least q12m	410	35.1%

- Only 35% of patients were monitored for ALT and HBV DNA levels on an annual basis

Table 3: Monitoring by Specialty

Monitoring	GI N = 767	PCP N = 313	Other N = 88
ALT at any time point	**95.7%***	**91.7%***	84.1%*
at least q12m	58.3%*	46.0%*	35.2%*
HBV DNA at any time point	**88.4%***	**64.5%***	56.8%*
at least q12m	46.7%*	24.0%*	25.0%*
ALT+HBV DNA any time point	**85.7%***	**59.7%***	54.6%*
at least q12m	42.9%*	20.1%*	20.5%*

* *P* value < 0.001 (based on Chi-square comparing all physician specialties).

- The frequency of monitoring across all lab tests was significantly higher among GI specialists compared to PCPs or other specialties. In addition, treatment rates were also higher among GIs compared to PCPs (41% vs 15% respectively).

RESULTS (cont'd)

Table 4: Predictors of Any ALT Monitoring

Variable	Odds ratio	*P* value
Age	1.012	0.3419
Male	1.607	0.0582
Region (reference = Northeast)		
South	0.898	0.7592
West	1.167	0.7997
Midwest	0.925	0.8626
Specialty on index date (reference = GI)		
PCP	0.824	0.5608
Other	0.905	0.7536
Charlson co-morbidity index	1.896	0.0005*

* *P* value based on multivariate logistic regression.

- The only significant predictor of ALT monitoring was the Deyo-Charlson comorbidity index

Table 5: Predictors of Any HBV DNA Lab Monitoring

Variable	Odds ratio	*P* value
Age	0.994	0.4003
Male	1.493	0.0085
Region (reference = Northeast)		
South	0.683	0.0894
West	0.649	0.2167
Midwest	0.294	<0.0001
Specialty on index date (reference = GI)		
PCP	0.469	0.0004
Other	0.514	0.0013
Charlson co-morbidity index	1.045	0.2703

P value based on multivariate logistic regression.

- Monitoring of viral load was significantly predicted by gender, region and specialty

Table 6: Predictors of Monitoring for both ALT and HBV DNA

Variable	Odds ratio	*P* value
Age	0.998	0.8258
Male	1.461	0.0084
Region (reference = Northeast)		
South	0.672	0.0594
West	0.678	0.2448
Midwest	0.320	<0.0001
Specialty on index date (reference = GI)		
PCP	0.538	0.0018
Other	0.572	0.0034
Charlson co-morbidity index	1.100	0.0216

P value based on multivariate logistic regression.

- The significant predictors of monitoring for both ALT and HBV DNA were the same predictors of each individual assay, with increasing Deyo-Charlson Comorbidity index score and male gender both positively associated with dual monitoring and Midwest location and non-GI care negatively associated

RESULTS (cont'd)

Table 7: Predictors of Antiviral Treatment

Variable	Odds ratio	*P* value
Age	1.002	0.7845
Male	1.500	0.0030
Region (reference = Northeast)		
South	1.011	0.9511
West	1.187	0.5683
Midwest	0.773	0.2999
Specialty on index date (reference = GI)		
PCP	0.547	0.0005
Other	0.683	0.0181
Charlson co-morbidity index	1.215	<0.0001
ALT monitored at any time	0.261	<0.0001
HBV DNA monitored at any time	2.077	<0.0001

* *P* value based on multivariate logistic regression.

- Initiation of antiviral treatment was more likely among male patients, patients with higher Deyo-Charlson Comorbidity index scores and those who had received HBV DNA monitoring
- Initiation of antiviral treatment was less likely among those treated by PCPs or by specialists other than GIs, and those who received ALT monitoring only

SUMMARY

- The results of this study suggest low rates of guideline-recommended laboratory monitoring of untreated patients with CHB, with high variability in monitoring across specialties, region, and by specific laboratory test
- Only about one-third of patients received both ALT and HBV DNA tests on an annual basis. While ALT assessment is the more frequently applied of the two tests, only slightly more than half of all patients receive annual ALT testing
  - ALT also appears to be used in a non-specific manner, since the only predictor of monitoring was co-morbidity burden
- HBV DNA monitoring rates are lower than ALT monitoring; less than half of all patients diagnosed by GIs received annual monitoring
  - HBV DNA monitoring appears more specific in that it is not predicted by comorbidities. However, diagnosis by a non-GI or treatment in the Midwest are negative predictors of HBV DNA monitoring
- Rates of monitoring for ALT and HBV DNA are similar, suggesting that HBV DNA monitoring is a rate-limiting feature (i.e. most patients who receive HBV DNA monitoring also receive ALT monitoring)

CONCLUSION

- Guideline-recommended laboratory monitoring of untreated CHB patients remains low in a commercially insured population, particularly measures of HBV DNA viral load
- These findings suggest that initiation of appropriate antiviral therapy may be delayed, leaving patients at risk for disease progression
- Improving monitoring rates may increase the rates of medically appropriate treatment of CHB, preventing delay of treatment and complications of the disease
- More education is needed about importance of appropriate CHB monitoring as recommended by the guideline

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DISCLOSURES

- Timothy Juday, Hong Tang, Melissa L Harris, George Hanna are employees for Bristol-Myers Squibb company
- Edward Kim, Annette Z Powers are employees for Eisai, Inc, previously worked for Bristol-Myers Squibb company

AASLD, The Liver Meeting in Boston, MA, October 30 – November 3, 2009