Characteristics & Outcomes of Liver Injury due to Herbal & Dietary Supplements in the U.S. Drug Induced Liver Injury Network

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BACKGROUND

The U.S. Drug Induced Liver Injury Network (DILIN) is a registry of patients with liver injury due to drugs or herbal and dietary supplements (HDS).

AIM

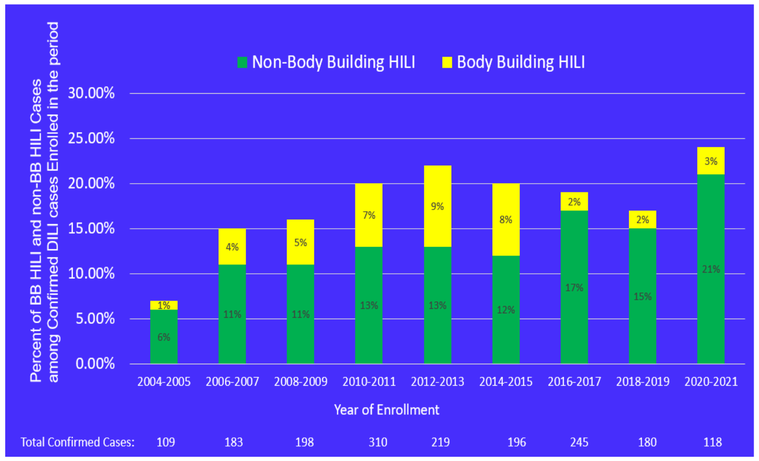
The aim of this study is to report clinical features and outcomes of HDS induced liver injury (HILI) since the DILIN's inception in 2004.

METHODS

- The DILIN enrolls patients with liver injury due to drugs and HDS.
- Entry criteria include an ALT or AST > 5 times, or alkaline phosphatase > 2 times normal on two consecutive occasions; or total bilirubin > 2 mg/dL.
- Clinical characteristics are ascertained, and patients are followed to resolution of injury.
- HILI cases are grouped as being due to bodybuilding (BB) or non-bodybuilding (non-BB) agents, based on the product's marketed purpose.
- Cases are adjudicated by structured causality assessment with expert opinion to determine the likelihood of DILI, and attribution to a drug or HDS.
- Only high confidence cases (adjudicated as definite, highly likely, or probable) cases were included in this analysis.
- Among a total of 1780 high confidence cases enrolled between 2004 and 2023, 325 (18%) were due to HDS (ie: HILI cases)

RESULTS

- Since 2004, the majority of HILI was due to non-BB agents (239 of 325; 73%).
- Since 2010, the number and proportion of BB-HILI cases fell (p<0.001 for trend) while those of non-BB HILI rose (p=0.03 for trend) (Figure)



- BB HILI cases were younger than non-BB and drug cases and occurred almost exclusively in males.
- Most HILI patients were white; non-BB HILI had a higher rate of Latinos compared to BB-HILI and DILI groups. (Table)
- BB and non-BB HILI had longer latencies than drugs; BB HILI was more likely to present with jaundice.
- Peak ALT levels were highest in non-BB HILI; peak bilirubin levels were highest in BB HILI.
- None of the BB HILI cases had severe outcomes, death or transplant; however, 27 non-BB HILI cases and 196 drug cases had severe outcomes.
- Persistent liver tests elevations (chronic DILI) were most common among drug cases.

RESULTS continued

	BB Cases N=86	Non BB Cases N = 239	Drug Cases N=1455	p value
Median Age, yrs (Min., Max.)	32 (20, 72)	46 (17, 82)	54 (2, 89)	< 0.001
Gender (% Female)	4	60	61	< 0.001
Race (%) White	83	73	79	< 0.001
Black	9	10	14	
Asian	1	7	4	
Latino	12	21	8	
Median Latency (days) (Min.,Max.)	70 (10,473)	68 (1,3607)	41 (1, 7046)	< 0.001
Median Peak ALT (U/L) Min., Max.	218 (50,8160)	1103 (20,9108)	602 (9,15065)	< 0.001
Median Peak Total Bili (mg/dL)	25.0 (0.8,63)	12.4 (0.4,46.8)	7.6 (0.3,59)	< 0.001
Outcomes (%)				
Transplant	0	7	3	0.001
Death	0	2	3	0.001
Chronic DILI	9	12	18	0.033

CONCLUSIONS

- HILI is increasing, especially due to non-BB HDS which tend to cause more severe disease and outcomes.
- Non-BB HILI is common among Latinos in the DILIN.
- Changes in HILI may reflect U.S. population characteristics and changing patterns in HDS.

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