Original Article

Drugs-Herbs-Dietary Supplements-induced Liver Injury: A Hidden but Emerging Clinical Problem

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Background: Drug-induced liver injury (DILI) is becoming increasingly common. Additionally, there have also been worldwide increases in herbal-induced liver injury (HILI) and supplement-induced liver injury (SILI). Studies on DILI, HILI, and SILI have shown that liver injury is the result of an idiosyncratic reaction and was geographically distinct.

Objective: To describe the clinical characteristics and outcomes of DILI, HILI, and SILI in a Thai population.

Materials and Methods: We retrospectively included patients (both outpatients and inpatients) who were diagnosed with DILI-HILI-SILI at a tertiary care university hospital setting from January 2014 to December 2019. The Roussel Uclaf Causality Assessment Method (RUCAM) score was used to assess causality in suspected cases with a cut-off score of ≥3. R ratio was used to identify the 3 types of liver injury: hepatocellular, cholestasis, or mixed type.

Results: Seventy patients were suspected to have DILI during the study period. Twenty-three patients were excluded due to incomplete data or RUCAM score <3. The remaining 47 patients were included. Of these, 26 cases (55.3%) were due to herbs or supplements and 17 (36.2%) were admitted for a high degree of liver injury. Chinese traditional complementary (12.7%) and multi-herbal products (12.7%) were the common causes of HILI and SILI, respectively. Antimicrobial agents (19.1%) and analgesics (10.6%) were the common causes of conventional drug-induced liver damage. The liver injury patterns in DILI from conventional drugs were hepatocellular (R>5) in 47.6% and cholestatic pattern (R<2) in 33.3%, which was not significantly different (p>0.05). For the HILI and SILI groups, the liver injury patterns were hepatocellular in 46.2% and cholestatic pattern in 15.4% (p = ns). The duration of exposure to diagnosis was similar between the DILI and HILI-SILI groups (3.7 vs. 5.6 months, p = 0.42). The DILI group had longer hospital stay than the HILI and SILI groups (13.5 vs. 7 days; p = 0.63). The overall mortality rate was 2.9%, with one death in each group.

Conclusion: Herbal and dietary supplements played an important role in DILI and showed a trend of shorter hospital stays. Hepatocellular liver injury pattern was the most common clinical finding in patients with DILI, HILI, and SILI.

Keywords: Drug-induced liver injury, DILI-HILI-SILI, Hepatitis, R pattern

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Drug-induced liver injury (DILI) is defined as liver injury caused by various medications, herbs, or other supplements leading to liver dysfunction or abnormalities in liver function tests, with the exclusion of other etiologies. DILI is an increasing medical problem worldwide, and the reported estimated annual incidence was 13.9 to 24.0 per 100,000[1]. Additionally, the annual extrapolated incidence of cases hospitalized in university hospitals of Korea was 12/100,000 persons/year[1,2]. Conventional medications, particularly antimicrobials, are the leading cause of DILI in several studies[2-5]. Herbal-induced liver injury (HILI) is also on the rise worldwide, and especially in Asia[6]. Recently, herb and drug supplement (HDS) products account for 16% of DILI cases overall in the United States[5], and the incidence is increasing[6]. The mortality rate of DILI in patients with pre-existing liver disease was higher than in those without[5]. Data from China shows that HILI was responsible for 24.2% DILI, with a mortality rate of 7.8%[7]. In Southeast Asia, the traditional Chinese complementary medicine was a leading cause of liver injury and the majority of them present with hepatocellular liver injury patterns[3]. Currently, the liver injury caused by DILI, HILI, and SILI is understood to be the result of an idiosyncratic reaction and have geographical differences.

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In Thailand, the incidence rate of DILI was 0.03 to 0.12% with an in-hospital mortality rate of 3.4%[4,8]. The two most common drugs that cause DILI were acetaminophen and anti-tuberculosis drugs[4,8]. The common causative agents of DILI were antimicrobial agents, specifically anti-tuberculosis drugs (85%) and antibiotics (15%)[8]. There are only few studies regarding HILI or SILI in Thailand. Therefore, the present study was conducted to compile DILI data in King Chulalongkorn Memorial Hospital, a tertiary care hospital in Thailand, in both the outpatient and inpatient setting. We aimed to describe the clinical information regarding the type of drugs-herbs-supplements-induced liver injury (DILI-HILI-SILI), as well as their clinical outcomes in Thai population.

Materials and Methods

We retrospectively enrolled outpatients who were diagnosed with DILI-HILI-SILI at the Liver clinic and hospitalized patients at the King Chulalongkorn Memorial Hospital (KCMH) from during January 2014 to December 2019. Inclusion criteria were patients with a history of drugs, herb, or supplement usage and who had abnormal liver function tests. The exclusion criterion was abnormal liver function test that could be explained by any other causes. Demographic data, type of drugs, herbs, and supplements as well as laboratory and clinical findings and outcomes were recorded. We use the Roussel Uclaf Causality Assessment Method (RUCAM) scale[9-11] to assess causality in suspected cases with a cut-off score >3 in the present study. R ratio was used to identify the three patterns of liver injury[12]: hepatocellular pattern if R ratio >5, cholestatic pattern if R ratio <2, and mixed pattern if R ratio between 2 and 5.

A coagulogram; complete blood counts; renal function tests; and liver function tests including levels of total bilirubin (TB), direct bilirubin (DB), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), albumin, and total protein were obtained at diagnosis. Viral hepatitis profile (anti-HAV IgM, HBsAg, anti-HCV antibody, anti-HEV IgM, and IgG) was collected to exclude other causes of hepatitis. Liver imaging such as ultrasonography was performed in some patients to exclude biliary tract obstruction. The study protocol was approved by the Institutional Review Board committee of Faculty of Medicine, Chulalongkorn University (IRB No. 617/61).

Statistical analysis

Baseline characteristics and clinical outcomes of the patients were analyzed. We identified risk factors that may be associated with severity of DILI. We compared the differences of baseline characteristics, clinical presentation, hospitalization, length of hospital stays, and laboratory results among the DILI, HILI, and SILI groups. All statistical data were analyzed using SPSS statistical analysis package (version 23.0, IBM Corp., Armonk, NY, USA). Categorical variables were analyzed by Chi-square or Fisher's exact tests. Continuous variables were analyzed using t-test or Mann-Whitney test. The p-value <0.05 was considered to indicate statistical significance.

Results

Baseline characteristics

Initially, 70 patients were included. Twenty-three patients were then excluded owing to incomplete data or RUCAM score <3; 47 patients (67.1%) were included for the final analysis. Twenty-seven patients (57.4%) were male and 20 (42.6%) were female. The mean age at diagnosis was 51.6 years. Baseline body mass index (BMI) was 23.9$\pm$3.3 kg/m^2. Twenty patients (57%) were overweight (mean BMI 26.1 kg/m^2). According to the RUCAM criteria, 38 patients (80.9%) had a possible relationship, 9 patients (20.1%) had a probable relationship, and no patient had a highly probable relationship by RUCAM score.

Thirty-one patients (66%) had underlying medical conditions other than liver disease, and 55% of them had more than one underlying disease. The most common underlying disease was hypertension, followed by dyslipidemia, tuberculosis, diabetes mellitus, cancer, HIV infection, chronic kidney disease, and gout. Thirteen of the 31 patients who had underlying disease had medication-induced DILI such as by anti-tuberculosis medication in the patient with tuberculosis, trimethoprim/sulfamethoxazole in the patient with *Pneumocystis jiroveci* pneumonia in HIV, and chemotherapy drugs in the patient with cancer.

Twenty patients (42.6%) had underlying liver disease. Non-alcoholic fatty liver disease was the most common cause in our study (n = 10) followed by hepatitis B virus infection, cirrhosis, autoimmune hepatitis, liver mass, chronic hepatitis C infection, and post liver transplantation. There were no statistical differences with respect to RUCAM score, time from drug exposure to diagnosis, symptomatic or asymptomatic at diagnosis, hospitalization, and length of hospital stay between patients with and without underlying liver disease (p = 0.39, p = 0.89, p = 0.81, p = 0.89, and p = 0.28, respectively).

Twenty-one patients (44.7%) were affected by conventional drugs, with antimicrobial agents (n = 9) being the most common cause, followed by analgesic drugs (n = 5) (Figure 1). The list of drugs included antimicrobial drugs (amoxicillin, norfloxacin, levofloxacin, trimethoprim/sulfamethoxazole, rifampicin, pyrazinamide and voriconazole); analgesic drugs (paracetamol, gabapentin, meloxicam, and piroxicam); endocrine drugs (flutamide, finasteride, and progesterone); antineoplastic drugs (tamoxifen and letrozole); lipid-lowering drug (atorvastatin); and anti-rheumatologic medication (allopurinol).

The remaining twenty-six patients (55.3%) were affected by herbs or supplements as show in Figure 2. The common herb was traditional Chinese complementary medicines (n = 6), followed by multi-herbal products (n = 6), supplementary drugs (n = 5), and *Tinospora spp.* (n = 4).

Thirty patients (64.8%) who were asymptomatic and had abnormal liver function tests were identified from

annual health check-up or during follow-up for other illnesses. The remaining 17 patients (36.2%) had symptoms at diagnosis. The most common presenting symptom was jaundice, followed by nausea, vomiting, fatigue, and abdominal pain.

Seventeen patients (36.2%) were hospitalized and 13 patients (76.5%) had symptoms. The remaining four patients (23.5%) were asymptomatic, but admitted for clinical observation and further investigations.

The laboratory results are shown in Table 1. This data varies remarkably due to the severity of the patients, especially in the in-patient and out-patient groups. We found that the in-patients group showed significantly higher AST (p = 0.029), ALT (p = 0.038), ALP (p = 0.001), and prothrombin time (p = 0.045) and lower albumin levels (p = 0.013) than the out-patients group. There was no statistical significance in TB, DB, hemoglobin, and white blood cell and platelet counts between the out-patient and in-patient groups. We additionally compared patients with and without underlying liver disease and found that there was no statistically significant difference regarding to laboratory results.

All patients underwent testing for hepatitis A, B, C and E infection. In our patient cohort, one patient each had chronic hepatitis B viral (HBV) infection and past HBV infection, and two patients had chronic hepatitis C infection. No patient had had hepatitis A or E infection.

Twenty-five patients (53.2%) underwent liver imaging to exclude biliary tract obstruction. Ultrasonography of the liver was the most common imaging modality (n = 22), followed MRI (n = 2) and computed tomography (n = 1).

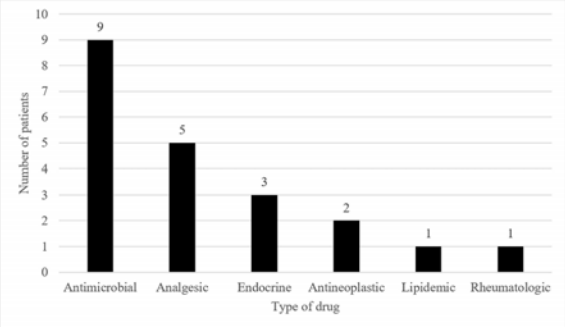

Figure 1. The common causes of DILI from the conventional drug group.

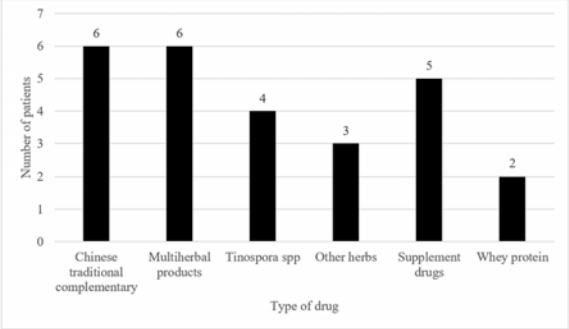

Figure 2. The common causes of HILI and SILI. Traditional Chinese complementary medicine refers to ginseng (n = 2), cordyceps (n = 1), and unclear ingredients (n = 3). Other herbs refer to Senna, Cannabis, and Ginkgo.

Table 1. Laboratory results of patients with HDS-induced liver injury

Laboratory parameters	Overall	Hospitalization	Non-hospitalization	*p*-value
Total bilirubin (mg/dL)	8.0 (7.8)	9.3 (8.1)	5.8 (7.2)	0.26
Direct bilirubin (mg/dL)	5.8 (6.3)	6.7 (6.6)	4.3 (5.7)	0.35
Aspartate aminotransferase (U/L)	725.2 (1,906.2)	1,806.3 (2,909.7)	112.6 (138.0)	0.03
Alanine aminotransferase (U/L)	681.1 (1,711.1)	1,604.4 (2,637.2)	157.9 (154.6)	0.04
Alkaline phosphatase (U/L)	161.2 (124.6)	240.9 (125.3)	116.0 (100.7)	0.001
Albumin (g/dL)	3.7 (0.6)	3.4 (0.5)	4.0 (0.6)	0.01
Hemoglobin (g/dL)	12.8 (2.3)	12.2 (2.6)	13.4 (2.0)	0.17
White blood cell count (10^3/uL)	8.3 (4.6)	8.9 (4.9)	7.6 (4.3)	0.46
Platelet (10^3/uL)	223.4 (80.5)	202.1 (99.9)	243.3 (53.2)	0.19
Prothrombin time (second)	17.3 (7.4)	19.3 (7.9)	11.7 (0.7)	0.05
INR	2.1 (1.8)	2.4 (2.0)	1.1 (0.9)	0.08
Blood urea nitrogen (mg/dL)	24.2 (30.8)	31.9 (43.3)	16.6 (6.8)	0.39
Creatinine (mg/dL)	1.8 (3.8)	3.3 (6.3)	1.0 (0.4)	0.34

Data are expressed as mean (standard deviation)

There was no imaging evidence of biliary tract obstruction in any patient.

Six patients (12.8%) underwent liver biopsy. Of these, three had steatohepatitis, two had cholestatic hepatitis, and one had non-specific portal inflammation from histopathological results.

Following the diagnosis, most patients stopped the drug, herb, or supplements that caused liver injury. Five patients were unable to stop the drug because of the need to use medication for their underlying disease. The overall mortality rate was 2.9%, with one death in each group.

Comparison of DILI from conventional drugs with HILI-SILI

There was no difference in baseline characteristics between patients with DILI from using conventional drugs and those in the HILI-SILI group. The proportion of male and female patients was similar between both groups. Mean age at diagnosis was 50.5 years in the DILI group and 52.6 years in the HILI-SILI group (p = 0.659). Mean body weight was 62.5 kg in the DILI group and 63.8 kg in the HILI-SILI group (p = 0.659). Mean BMI was 23.8 kg/m^2 in conventional drugs group compared with 24.1 kg/m^2 on HILI-SILI group (p = 0.768). According to obesity classification from Asia-Pacific guidelines, our patients in this study were overweight. About one-third (33.3%) patients in the DILI group had underlying liver disease when compared to 50% patients in the HILI-SILI group. However, there was no statistically significant difference (p = 0.25). In both groups, the most common pattern of liver injury was the hepatocellular type, followed by cholestatic and mixed patterns in the DILI group and mixed and cholestatic patterns in the HILI-SILI group (Table 2).

The mean RUCAM score of all patients was 4.5 (DILI group: 5, HILI-SILI group: 4.1, p = 0.01) (Table 3). The median duration since taking HDS to diagnosis was 1 month for the DILI group and 2 months for the HILI-SILI groups (p = 0.45). Thirteen patients (61.9%) in the DILI group did not have any symptom at the time at diagnosis, while there were 13 patients (17%) in HILI-SILI group without significant difference (p = 0.19). The diagnosis was made by laboratory check-up for other results, e.g., annual check-up. In symptomatic patients, jaundice was the most common presenting symptom among symptomatic patients of both groups.

Eight patients (38.1%) in the DILI group were admitted to KCMH, while there were nine patients (34.6%) in HILI-SILI group without significant difference (p = 0.85). Among patients who were admitted, the DILI group had longer length of stay than the HILI-SILI groups (13.5 days vs. 7 days), but this difference was not statistically significant (p = 0.629). Further, ALP levels were higher in the DILI group than in the HILI-SILI groups (p = 0.027). No other laboratory parameters showed significant differences. Tables 3 and 4 show the baseline characteristics and laboratory findings in patients with HDS-induced liver injury.

Discussion

There is increasing evidence of herbal medicine and dietary supplements usage worldwide[13-16]. However, the

Table 2. Pattern of liver injury in patients with HDS-induced liver injury

Pattern of liver injury	Conventional drugs, n (%)	Herbs and supplements, n (%)	*p*-value
Hepatocellular	10 (47.6)	12 (46.2)	0.25
Mixed	4 (19)	10 (38.4)	0.49
Cholestatic	7 (33.4)	4 (15.4)	0.23

Table 3. Comparison of baseline characteristics between the DILI and HILI-SILI groups

Variables	DILI (n = 21)	HILI-SILI (n = 26)	*p*-value
Mean age at diagnosis (years)	50.5 (20.9)	52.6 (11.7)	0.66
Weight (kg)	62.5 (10.6)	63.8 (9.3)	0.66
Body mass index (kg/m^2)	23.8 (4.1)	24.1 (2.5)	0.77
Underlying liver disease, n (%)	7 (33.3)	13 (50)	0.25
RUCAM score	5	4.08	0.01
Hospitalization, n (%)	8 (38.1)	9 (34.6)	0.81
Length of stay (days), median	13.5	7	0.63
Asymptomatic, n (%)	13 (61.9)	17 (65.4)	0.19

Data are expressed as mean (standard deviation) unless specified

clinical data regarding the prevalence, clinical characteristics, and outcomes of HDS-induced liver injury are limited in Asian countries owing to the lack of reliable studies in patients in whom other causes of liver disease have been excluded; moreover, the actual number of HDS users is also unclear[17]. The current study showed that 55% patients presented with HDS-induced liver injury and 36% of them required hospitalization. Those who needed hospitalization had more severe disease as seen by higher AST, ALT, ALP, and INR levels than those that did not need hospital admission. Among patients with DILI in previous studies, the prevalence of HDS-related liver damage was 4 to 16% in European countries[18,19], 17% in Japan[20], and 27% in Mainland China[21]. Hepatocellular injury was the most common pattern of liver damage in both the DILI (47.6%) and HILI-SILI (46.2%) groups in our study, consistent with previous literatures[21]. There were no significant differences with respect to baseline characteristics, laboratory parameters, and clinical outcomes between the DILI and HILI-SILI groups, except for the significantly higher RUCAM score and ALP levels in the HILI-SILI group than the DILI group. However, patients in the DILI group tended to have longer hospital stays than those in the HILI-SILI group. In contrast to the result from a Chinese study which showed the cases caused by Chinese herbal medicine had more proportion of female and positive rechallenge, presented with higher rate of hepatocellular injury pattern and higher mortality rate than Western medicine[22].

Traditional Thai Medicine (TTM) refers to a system of methods and practices, including herbal medicine, Thai massage, and spiritual healing that has long been a part of Thailand's healing cultures. In 1993, the Thai government organized the National Institute of Thai Traditional Medicine, under the supervision of the Ministry of Public Health to systematize and support TTM knowledge and product development[23]. Herbal medicine has become popular and used widely as an alternative therapy for several conditions among Thai people[24-26]. The true incidence of HDS use as well as Thai herbal medicine-induced liver injury was unknown, because a low number of herbal remedies were recorded in the Thai national database[4]. Our study showed that 12.7% of DILI was caused by Thai herbal medicine. Among these, the major causative agents of HILI-SILI were Chinese traditional complementary medicine (12.7%), multiherbal products (12.7%), and *Tinospora crispa* (TC) (8.5%).

Tinospora crispa (L.) Hook f. & Thompson or Wormwood or Bora phet is an herbaceous vine in the Menispermaceae family found in many countries in Southeast Asia. The plant is traditionally used to treat fever, diabetes, rheumatism, and boost appetite[27]. Many herbal medicinal products in the Thai National List of Essential Medicines have the TC stem extract as an ingredient. Clinical data of the TC's effect on liver damage is rather limited. However, in animal studies, a high-dosage or long-term use of TC might be related to elevation of serum aminotransferase, ALP, and bilirubin levels[28,29]. Previous literature reported two cases of TC-induced acute fulminant hepatitis. Of these, one patient had underlying chronic hepatitis C infection and hepatocellular carcinoma and was alcoholic[30]. Our study showed that TC ingestion could induce serum aminotransferase levels providing the clinical evidence for TC-induced liver injury. Two patients in our study developed symptoms after 1 to 2 weeks' ingestion of TC, while the remaining patients had a

Table 4. Comparison of laboratory findings between the between the DILI and HILI-SILI groups

Variables	DILI (n = 21)	HILI-SILI (n = 26)	*p*-value
Total bilirubin (mg/dL)	7.9 (8.9)	8.2 (5.2)	0.91
Direct bilirubin (mg/dL)	5.8 (7.1)	5.7 (4.9)	0.99
Aspartate aminotransferase (U/L)	679.5 (2125.1)	762.1 (1752)	0.85
Alanine aminotransferase (U/L)	725.0 (2098.7)	654.7 (1364)	0.88
Alkaline phosphatase (U/L)	210.0 (163.2)	121.8 (60.4)	0.03
Albumin (g/dL)	3.6 (0.7)	3.7 (0.6)	0.69
Hemoglobin (g/dL)	11.8 (2.2)	13.3 (2.3)	0.08
White blood cell count (10^3/uI)	6.9 (2.8)	9.3 (5.3)	0.17
Platelet (10^3/uI)	213.0 (99.4)	230.8 (66.4)	0.57
Prothrombin time (second)	12.8 (1.6)	18.9 (8.3)	0.26
INR	2.8 (3.2)	1.8 (0.8)	0.57
Blood urea nitrogen (mg/dL)	18.0 (8.2)	28.9 (40.7)	0.54
Creatinine (mg/dL)	1.2 (0.4)	2.1 (4.6)	0.64
Mortality, n (%)	1 (4.8)	1 (3.9)	0.63

Data are expressed as mean (standard deviation)

history of long-term TC usage up to 1 year. One patient who took TC had underlying HBV cirrhosis, but there was no clinical or laboratory-based difference compared to those who did not have chronic liver disease.

Our study has some limitations. Many patients used more than one type of medication or herbal products, making it more difficult to clarify which drug was the main cause of liver injury. In addition, the initial results for laboratory tests such as serum AST and ALT varied widely owing to the severity of clinical presentation.

However, the strength of our study was the enrollment of outpatient and inpatient data, resulting in a severity variety in the same study period. In addition, we analyzed the data of HILI and SILI, which is commonly used in the Thai population, by using the RUCAM score (≥3) to assess causality.

Conclusion

We reported the clinical findings and outcomes of patients with DILI-HILI-SILI during a six-year study period in KCMH. Patients with DILI due to conventional drugs tended to have high RUCAM score and serum ALP than those caused by the herbs and supplements.

What is already known on this topic?

Liver injury that is caused by drugs, herbal medicines, or dietary supplements is an infrequent but increasing medical problem. Clinical presentations and liver function test abnormalities of this condition are non-specific.

What this study adds?

Clinical presentations, laboratory parameters, and outcomes of patients with herbal- and dietary supplements-induced liver injury are similar to those of drug-induced liver injury which make the differential diagnosis more difficult.

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Potential conflicts of interest

The authors declare no conflict of interest.

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โรคตับจากยา สมุนไพร อาหารเสริม: ปัญหาอุบัติใหม่และซ่อนเร้นทางคลินิก

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ภูมิหลัง: ปัจจุบันโรคตับจากยา สมุนไพร และอาหารเสริมเป็นปัญหาที่พบบ่อยมากขึ้นทั่วโลก การศึกษาพบโรคตับที่เกิดจากสาเหตุเหล่านี้ เป็นปฏิกิริยาที่ไม่ขึ้นกับขนาดของยาและมีความแตกต่างกันในแต่ละภูมิศาสตร์

วัตถุประสงค์: เพื่อจะศึกษาลักษณะทางคลินิกและผลที่เกิดขึ้นในประชากรไทยที่มีโรคตับจากยา สมุนไพรและอาหารเสริม

วัสดุและวิธีการ: ผู้ป่วยที่ได้รับการวินิจฉัยว่ามีโรคตับจากยา สมุนไพรและอาหารเสริมและเข้ารับการรักษาในช่วงเดือนมกราคม พ.ศ. 2557 ถึง เดือนธันวาคม พ.ศ. 2562 ประเมินสาเหตุ ในผู้ป่วยที่สงสัยโดยใช้วิธีของรูซเซล อัคลาฟโดยต้องมีคะแนนมากกว่าหรือเท่ากับ 3 จากนั้นใช้ค่าอัตราส่วนอาร์ในการระบุรูปแบบของการบาดเจ็บที่ตับ

ผลการศึกษา: ผู้ป่วย 70 รายที่สงสัยว่าจะเกิดโรคตับจากยาในช่วงเวลาทำการศึกษา อย่างไรก็ตาม 23 รายได้ถูกตัดออกไปเนื่องจากข้อมูลไม่ครบถ้วนหรือค่าคะแนนไม่ถึง 3 จึงมีผู้ป่วยทั้งสิ้น 47 รายที่ได้ถูกคัดเลือกเข้ามาในการศึกษา ซึ่งในจำนวนนี้มีผู้ป่วย 26 ราย (ร้อยละ 55.3) ที่มีสาเหตุจากสมุนไพรหรืออาหารเสริมและผู้ป่วย 17 ราย (ร้อยละ 36.2) ที่ได้รับการรักษาแบบผู้ป่วยในเนื่องจากโรคตับที่รุนแรง สมุนไพรจีน (ร้อยละ 12.7) และการใช้สมุนไพรหลายชนิด (ร้อยละ 12.7) เป็นสาเหตุที่พบบ่อยในโรคตับจากสมุนไพรหรืออาหารเสริม ขณะที่ยาปฏิชีวนะ (ร้อยละ 19.1) และยาแก้ปวดเป็นสาเหตุที่พบบ่อยในโรคตับจากยาแผนปัจจุบัน รูปแบบของการบาดเจ็บที่ตับในกลุ่มที่ใช้ยาแผนปัจจุบันคือตับอักเสบ (ร้อยละ 46.7) และการคั่งของน้ำดี (ร้อยละ 33) ซึ่งพบไม่แตกต่างกัน ขณะที่โรคตับจากสมุนไพร อาหารเสริม รูปแบบของการบาดเจ็บที่ตับในกลุ่มที่ใช้ยาแผนปัจจุบันคือตับอักเสบ (ร้อยละ 46.2) และการคั่งของน้ำดี (ร้อยละ 15.4) ซึ่งไม่พบความแตกต่างอีกเช่นเดียวกัน ระยะเวลาตั้งแต่เริ่มรับประทานจนถึงวินิจฉัยนั้นไม่แตกต่างกันระหว่างผู้ป่วยที่มีโรคตับจากยาและจากสมุนไพร/อาหารเสริม (3.7 เดือนเทียบกับ 5.6 เดือน ตามลำดับ) ผู้ป่วยที่มีโรคตับจากยาแผนปัจจุบันมีระยะเวลาการนอนโรงพยาบาลที่นานกว่าจากสมุนไพร/อาหารเสริมแต่ไม่พบความแตกต่างทางสถิติ (24 วันเทียบกับ 12 วัน) อัตราการตายโดยรวมประมาณร้อยละ 2.9

สรุป: สมุนไพรและอาหารเสริมมีบทบาทสำคัญที่ทำให้เกิดโรคตับ ผู้ป่วยกลุ่มนี้มีแนวโน้มจะนอนโรงพยาบาลสั้นกว่า ตับอักเสบเป็นรูปแบบที่พบบ่อยที่สุดในโรคตับจากยาสมุนไพรและอาหารเสริม