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Validity of Diagnostic Codes and Laboratory Tests of Liver Dysfunction to Identify Acute Liver Failure Events

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Abstract

Purpose—Identification of acute liver failure (ALF) is important for post-marketing surveillance of medications, but the validity of using ICD-9 diagnoses and laboratory data to identify these events within electronic health records is unknown. We examined positive predictive values (PPVs) of hospital ICD-9 diagnoses and laboratory tests of liver dysfunction for identifying ALF within a large, community-based integrated care organization.

Methods—We identified Kaiser Permanente Northern California health plan members (2004–2010) with a hospital discharge diagnosis suggesting ALF (ICD-9 570, 572.2, 572.4, 572.8, 573.3, 573.8, or V42.7) plus an inpatient international normalized ratio ≥ 1.5 (off warfarin) and total bilirubin ≥ 5.0 mg/dL. Hospital records were reviewed by hepatologists to adjudicate ALF events. PPVs for confirmed outcomes were determined for individual ICD-9 diagnoses, diagnoses plus prescriptions for hepatic encephalopathy treatment, and combinations of diagnoses in the setting of coagulopathy and hyperbilirubinemia.

Results—Among 669 members with no pre-existing liver disease, chart review confirmed ALF in 62 (9%). Despite the presence of co-existing coagulopathy and hyperbilirubinemia, individual

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ICD-9 diagnoses had low PPVs (range, 5%–15%); requiring prescriptions for encephalopathy treatment did not increase PPVs of these diagnoses (range, 2%–23%). Hospital diagnoses of other liver disorder (ICD-9 573.8) plus hepatic coma (ICD-9 572.2) had high PPV (67%; 95% CI, 9%–99%) but only identified 2 (3%) ALF events.

Conclusions—Algorithms comprising relevant hospital diagnoses, laboratory evidence of liver dysfunction, and prescriptions for hepatic encephalopathy treatment had low PPVs for confirmed ALF events. Studies of ALF will need to rely on medical records to confirm this outcome.

Keywords

hepatotoxicity; liver injury; validity; ICD-9 codes; acute liver failure

INTRODUCTION

Acute liver failure is the most serious clinical outcome of drug-induced liver injury¹ and is defined by the rapid onset of coagulopathy and hepatic encephalopathy in patients without underlying liver disease.^{2,3} In the United States, nearly 60% of acute liver failure cases reported from tertiary care centers are related to medication use, with many “indeterminate” cases thought to have an underlying drug-induced etiology.^{4–7}

Despite the clinical importance of acute liver failure arising from drug-induced hepatotoxicity, it has only rarely been evaluated in pharmacoepidemiologic studies,⁸ primarily because methods to identify this outcome within electronic health data have not been developed and validated. The ability to accurately identify acute liver failure events within electronic healthcare databases would allow for evaluation of the relative incidences and risk of acute liver failure in users of medications or drug classes and could provide a more valid characterization of the hepatotoxicity profile of medical products.

A prior study by the Mini-Sentinel Severe Acute Liver Injury Workgroup found that hospital International Classification of Diseases, Ninth Revision (ICD-9) diagnoses had low positive predictive value (PPV) for medical record-confirmed acute liver failure.⁹ We hypothesized that algorithms comprised of hospital discharge diagnoses suggestive of acute liver failure recorded with laboratory evidence of severe liver injury could improve accuracy for identifying acute liver failure events in electronic health data. We focused on laboratory measures of liver synthetic dysfunction, specifically coagulopathy and hyperbilirubinemia, since these are key features of acute liver failure. We also evaluated the accuracy of algorithms that included prescriptions for medications used to treat hepatic encephalopathy, in addition to inpatient ICD-9 diagnoses and laboratory-confirmed liver dysfunction, to explore whether we could further improve identification of acute liver failure events.

METHODS

Design and data source

We conducted a cross-sectional study between January 1, 2004 and December 31, 2010 using data from Kaiser Permanente Northern California (KPNC), an integrated health care organization that provides inpatient and outpatient services to Northern California

residents.¹⁰ Data collected by KPNC include: demographic information; outpatient and hospital diagnoses (recorded using ICD-9 codes); procedures; inpatient and outpatient laboratory results; emergency and referral services at non-Kaiser Permanente facilities; and dispensed medications, including dosage, administration, and days' supply. Prescription drug benefits are utilized by more than 90% of members, and prior analyses have established the accuracy of pharmacy data.¹¹ The study was approved by the KPNC and University of Pennsylvania Institutional Review Boards.

Health plan members selected for validation

We identified KPNC members who had: 1) a hospital discharge ICD-9 diagnosis (in any position) suggestive of acute liver failure (Table 1) recorded between January 1, 2004 and December 31, 2010; 2) 18 years of age with at least 6 months of continuous membership prior to the inpatient acute liver failure diagnosis date; 3) an inpatient international normalized ratio (INR) ≤ 1.5 and total bilirubin ≤ 5.0 mg/dL; and 4) no warfarin prescribed within 182 days before or after the inpatient acute liver failure diagnosis date (since this would prevent identification of coagulopathy due to acute liver failure). The ICD-9 codes selected (Table 1) focused on diagnoses suggestive of acute liver failure.^{12,13} We evaluated discharge ICD-9 diagnoses that were recorded in a principal or secondary position because we sought to identify acute liver failure events that not only developed in the outpatient setting, but also those events that developed exclusively in the hospital setting. INR and total bilirubin were included as laboratory criteria because they reflect liver synthetic function. The cut-offs selected were based on the very low likelihood of acute liver failure in the setting of laboratory results below these values.^{1,14}

Since the presence of pre-existing chronic liver disease precludes a diagnosis of acute liver failure,² we excluded patients who had, at any time prior to their acute liver failure diagnosis: 1) an ICD-9 diagnosis of alcoholic liver disease, alpha-1-antitrypsin deficiency, autoimmune hepatitis, cirrhosis, hemochromatosis, hepatic decompensation, cancer in the liver/biliary tree, viral hepatitis, or Wilson's disease [see Appendix 1 for diagnoses], or 2) laboratory evidence of hepatitis B (hepatitis B surface antigen, e antigen, core immunoglobulin M [IgM] antibody, or DNA), hepatitis C (hepatitis C antibody or RNA), or hepatitis D (delta antibody) virus infection. Further, since our focus was to identify primarily drug-induced acute liver failure events, we also excluded patients who had acute hepatitis A (hepatitis A IgM antibody-positive) or hepatitis E (hepatitis E IgM antibody-positive) diagnosed within 30 days prior to or after the inpatient acute liver failure diagnosis date. Since prior studies have demonstrated that abnormalities in serum liver aminotransferases, total bilirubin, or INR can be present for up to 26 weeks prior to the development of drug-induced acute liver failure,^{1,15} we did not exclude patients who had abnormalities in liver-related laboratory tests prior to their inpatient acute liver failure diagnosis date to minimize the likelihood of missing acute liver failure cases. All eligible KPNC members were selected for inclusion.

Acute liver failure definition

We defined acute liver failure based on criteria specified by the American Association for the Study of Liver Diseases.^{2,3} A *definite* diagnosis of acute liver failure was confirmed if a

patient had: 1) no pre-existing liver disease; 2) coagulopathy (INR ≥ 1.5) in the absence of anticoagulation therapy; and either 3a) hepatic encephalopathy, or 3b) liver transplant with the stated indication of “acute liver failure.” A patient was classified as having hepatic encephalopathy if the diagnosis was recorded within a gastroenterologist’s consultation or progress note, or, if the diagnosis was not recorded in the medical record, altered mentation was accompanied by asterixis and/or hyperammonemia in the absence of other etiologies of encephalopathy. The acute liver failure date was defined as the earlier of either the date that hepatic encephalopathy initially presented or the date of liver transplant. A *possible* diagnosis of acute liver failure was confirmed if a patient met criteria 1 and 2 (above) and had either: 1) altered mentation in the absence of a recorded diagnosis of hepatic encephalopathy but had hepatic encephalopathy treatment (i.e., lactulose or rifaximin) with no other central nervous system abnormality by brain imaging, or 2) underwent liver transplantation surgery for an unspecified etiology. For these patients, the acute liver failure date was the first of either the date of initial encephalopathy treatment or the date of liver transplant.

Confirmation of outcomes

Two trained abstractors reviewed the hospital records of eligible KPNC members. Since KPNC provides emergency and referral services at non-Kaiser Permanente facilities,¹⁰ we were able to determine whether a patient was transferred to a different center for liver transplantation or was subsequently either re-admitted to a KPNC hospital or admitted to a non-Kaiser Permanente facility for worsening hepatic function after the initial KPNC hospitalization with potential acute liver failure. In such instances, additional medical records from these visits were obtained. Records were abstracted onto structured forms that collected information from physician admission and progress notes, gastroenterologist/hepatologist consultations, hospital discharge summaries, brain imaging reports, and liver biopsy reports (Appendix 2). A 10% random chart re-abstraction was performed to validate the accuracy of data collection.

Data forms were independently reviewed by two hepatologists (K.A.F.; D.G.), who served as endpoints adjudicators. They classified acute liver failure events as: 1) definite, 2) possible, or 3) no event. For patients classified as not having acute liver failure, the most likely etiologies for the liver injury were determined by the adjudicators. Disagreement on any classification resulted in review by a third hepatologist (K.R.R.) to arbitrate the event.

Collection of demographic and clinical data

Age at hospital admission, sex, race, and ethnicity were collected from all eligible KPNC members. Prescriptions for lactulose or rifaximin (treatments for hepatic encephalopathy) recorded during the hospitalization were also extracted.

Statistical analyses

PPVs (with 95% confidence intervals [CIs]) for confirmed acute liver failure were determined for individual inpatient discharge ICD-9 diagnoses and commonly recorded combinations of these diagnoses, recorded in the presence of an inpatient INR ≥ 1.5 (off warfarin) and total bilirubin ≥ 5.0 mg/dL. Next, we determined if the addition of an inpatient

prescription for lactulose or rifaximin (medications used for treating hepatic encephalopathy) increased PPVs. We then evaluated if exclusion of patients with a prior diagnosis of alcohol dependence/abuse (Appendix 3) improved PPVs. We also examined whether algorithms comprised of ICD-9 diagnoses only in a principal/primary position increased PPVs. We sought to identify an algorithm with a PPV exceeding 80%. Our focus was on PPV because a sufficiently high PPV provides confidence that identified outcomes are true events.

We estimated that for any algorithm, 75 patients would allow determination of the PPV with a maximum 95% CI of ± 0.10 , assuming a PPV of 80%. Data were analyzed using SAS 9.4 (SAS Institute Inc., Cary, NC) and Stata 13.0 (Stata Corporation, College Station, TX).

RESULTS

Among 5,484,224 KPNC members enrolled between January 1, 2004 and December 31, 2010, 669 patients (0.01%) had a hospitalization with potential acute liver failure, were at least 18 years of age with at least 6 months of continuous membership prior to the inpatient acute liver failure diagnosis, lacked pre-existing chronic liver disease based on recorded diagnoses or viral hepatitis serologic/virologic laboratory tests, and were not dispensed warfarin (Figure 1). Among these 669 patients, a median of 20.3 (interquartile range [IQR], 10.2 – 26.6) years was available from the time of KPNC enrollment to the inpatient acute liver failure diagnosis to determine the presence of pre-existing chronic liver disease. The median age of the 669 members was 61 years (IQR, 49 – 72), 315 (47.1%) were female, 484 (72.3%) were of white race, and 114 (17.0%) were Hispanic. During the hospitalization, 261 (39.0%) members were prescribed either lactulose or rifaximin.

Among these 669 members, 62 (9.3%) were confirmed by the adjudicators to have had acute liver failure (45 definite, 17 possible). The overall percent agreement in events between the two adjudicators was 92.7% (620/669; 95% CI, 90.4% – 94.5%). A third hepatologist was required to arbitrate disagreements in 7.3% of cases.

Table 2 reports the PPVs of individual inpatient discharge ICD-9 diagnoses and combinations of diagnoses for confirmed acute liver failure events in the presence of coagulopathy (INR ≥ 1.5) and hyperbilirubinemia (total bilirubin ≥ 5.0 mg/dL). The PPVs of individual diagnoses were low, ranging from 5% – 15% (Table 2). A hospital diagnosis of either toxic hepatitis (573.3) or hepatic necrosis (570) captured the highest proportion of events (56/62 [90.3%]) among the coding algorithms evaluated, but had a low PPV (13%; 95% CI, 10% – 17%). Algorithms comprised of a hospital ICD-9 diagnosis suggestive of acute liver failure plus a prescription for either lactulose or rifaximin did not substantially increase PPVs (Table 2). Further exclusion of patients with a prior diagnosis of alcohol dependence/abuse also did not appreciably change PPVs (data not shown). The PPVs remained low when algorithms included ICD-9 diagnoses recorded only in a principal/primary position (Appendix 4).

Algorithms comprised of various combinations of discharge ICD-9 diagnoses (in any position) yielded higher PPVs, but identified few acute liver failure cases. A hospital

diagnosis for other liver disorders (573.8) plus hepatic coma (572.2) had the highest PPV (67%; 95% CI, 9% – 99%), but identified only two acute liver failure events (Table 2).

Table 3 provides a list of the diseases observed among the 607 members who were adjudicated as not having acute liver failure, by ICD-9 diagnosis. Among the 607 classified as not having acute liver failure, the majority (370 [61%]) had pre-existing liver or biliary disease that was not electronically detected by prior clinical, serologic, or virologic diagnosis and/or evidence of acute liver injury (primarily from acute hepatic ischemia due to septic or cardiogenic shock) without hepatic encephalopathy (292 [48%]).

DISCUSSION

This study examined the ability of hospital discharge ICD-9 diagnoses, laboratory tests of liver synthetic dysfunction, and prescriptions for treatment of hepatic encephalopathy to identify acute liver failure events within KPNC. In the setting of coagulopathy (INR 1.5) and hyperbilirubinemia (total bilirubin 5.0 gm/dL), individual hospital ICD-9 diagnoses suggestive of acute liver failure yielded low PPVs for hepatologist-confirmed outcomes, and requiring prescriptions for treatments of hepatic encephalopathy did not appreciably increase the PPVs of these diagnoses. PPVs for algorithms comprised of combinations of select ICD-9 diagnoses were increased, but none exceeded 80%.

Two prior small studies evaluated the ability of diagnosis codes to identify acute liver failure events within electronic healthcare data. In a study of 57 health plan members in the Mini-Sentinel Distributed Database with a principal hospital diagnosis suggestive of acute liver failure (listed in Table 1) and no pre-existing liver/biliary disease diagnoses, only one (1.8%; 95% CI, 0.04% – 9.4%) had hepatologist-confirmed acute liver failure.⁹ The PPVs for individual ICD-9 diagnoses for confirmed acute liver failure were all very low (range, 1.8% – 9.1%). Myers and colleagues¹³ performed a separate analysis evaluating the PPVs of ICD-9 and ICD-10 diagnoses for acute liver failure in patients with acetaminophen overdose within the Calgary Health Region in Canada. Among 36 members with a diagnosis code of interest, 20 (PPV, 56%; 95% CI, 38% – 72%) had confirmed acute liver failure.

Our development of electronic algorithms to identify acute liver failure based on relevant hospital diagnoses, laboratory evidence of severe liver injury, and treatment for hepatic encephalopathy sought to improve upon prior analyses that exclusively focused on diagnosis codes. The algorithms we developed yielded PPVs that were higher than previously reported,^{9,13} but remained too low to be acceptable for use within observational studies. There are several reasons that sufficiently high PPVs might not have been observed. First, acute liver failure is a diagnosis that occurs very rarely.¹⁶ Consequently, the low prevalence of acute liver failure likely resulted in the low PPVs of the electronic algorithms we developed. Second, there is no ICD-9 diagnosis code that specifically indicates acute liver failure. Although the ICD-9 diagnoses we selected focused on liver injury (Table 1),^{12,13} they did not exclusively indicate acute liver failure. Hepatic failure is included as a specific diagnosis in the ICD-10 coding system (K72), but these diagnoses have not yet been in wide use within the United States, and the validity of this diagnosis code for acute liver failure is unknown. Further, hepatic failure is not a specific clinical diagnosis, so it might not result in

increased PPVs. Third, many patients had pre-existing liver or biliary disease that was not electronically detected by our selected clinical, serologic, or virologic diagnoses. Common causes of false-positive classifications in our study were hepatic ischemia, alcoholic liver disease, and cancer in the liver. We attempted to exclude patients with alcoholic liver disease, but this was incomplete without review of medical records. Hepatic ischemia was often a consequence of septic or cardiogenic shock on admission; consequently, it was not possible to exclude these patients based on pre-hospitalization diagnoses. Modest improvement in the PPV of the algorithm might be possible by exclusion of patients with a cancer that could potentially metastasize to the liver prior to the hospitalization, but this would not be sufficient to obviate the need for chart review. Finally, the complexities of the acute liver failure definition,^{2,3} particularly with regard to the challenge of confirming hepatic encephalopathy in clinical practice,¹⁷ could have led to inaccurate coding of these diagnoses.

This study has several potential limitations. First, it is possible that acute liver failure events could have been misclassified during adjudication. However, we minimized the likelihood of this by classifying events using a standard definition and employing two adjudicators to confirm events, with a third to arbitrate cases in instances of disagreement. Second, we did not determine the negative predictive value of our algorithms, since we did not evaluate acute liver failure among a sample of KPNC members without the diagnoses or laboratory abnormalities of interest. Third, the small number of confirmed acute liver failure cases limited the precision of our PPV estimates. Finally, our sample was comprised of commercially-insured persons, potentially limiting the generalizability of our results to other populations.

In conclusion, despite the presence of laboratory evidence of liver dysfunction, individual hospital ICD-9 diagnoses suggestive of acute liver failure yielded low PPVs for confirmed events. Requiring prescriptions for treatments of hepatic encephalopathy did not substantively increase the PPVs of these ICD-9 diagnoses. Furthermore, algorithms comprised of combinations of ICD-9 diagnoses suggestive of acute liver failure also did not result in sufficiently high PPVs. Until an electronic algorithm for acute liver failure is developed that has sufficiently high PPV, studies evaluating acute liver failure will need to rely on medical records to confirm this outcome.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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List of abbreviations

ALT	alanine aminotransferase
AST	aspartate aminotransferase
CI	confidence interval
ICD-9	International Classification of Diseases, Ninth Revision
IgM	immunoglobulin
M INR	international normalized ratio
IQR	interquartile range
PPV	positive predictive value
ULN	upper limit of normal

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KEY POINTS

- The validity of hospital International Classification of Diseases, Ninth Revision (ICD-9) diagnoses and inpatient laboratory tests indicative of liver synthetic dysfunction to identify hospital acute liver failure events is not well known.
- In the setting of an inpatient international normalized ratio ≥ 1.5 (off warfarin) and total bilirubin ≥ 5.0 mg/dL, hospital ICD-9 diagnoses suggestive of acute liver failure yielded low positive predictive values for health plan members in Kaiser Permanente Northern California. Requiring prescriptions for treatments of hepatic encephalopathy did not increase the positive predictive values of these ICD-9 diagnoses.
- Combinations of select ICD-9 diagnoses suggestive of acute liver failure plus international normalized ratio ≥ 1.5 (off warfarin) and total bilirubin ≥ 5.0 mg/dL did not achieve positive predictive values exceeding 80%.

Figure 1.

Selection of patients for medical record review.

*Inpatient discharge diagnoses included ICD-9 codes 570 (acute/subacute hepatic necrosis), 572.2 (hepatic coma), 572.4 (hepatorenal syndrome), 573.3 (toxic [noninfectious] hepatitis), 573.8 (other liver disorder, chemical/drug-induced), 572.8 (liver disease sequelae), V42.7 (liver transplant).

†Patients may have had more than one exclusionary diagnosis recorded.

Table 1

International Classification of Diseases, Ninth Revision (ICD-9) diagnosis codes evaluated for their ability to identify potential cases of acute liver failure.

ICD-9 DIAGNOSIS	ICD-9 DIAGNOSIS CODE DESCRIPTION
570	Acute/subacute hepatic necrosis
572.2	Hepatic coma
572.4	Hepatorenal syndrome
572.8	Liver disease sequelae
573.3	Toxic (non-infectious) hepatitis
573.8	Other liver disorder, chemical/drug-induced
V42.7	Liver transplant

Table 2

Positive predictive values (with 95% confidence intervals) of hospital discharge International Classification of Diseases, Ninth Revision (ICD-9) diagnosis codes and code combinations recorded in any position (principal/primary or secondary), in the presence of coagulopathy (international normalized ratio ≥ 1.5) and hyperbilirubinemia (total bilirubin ≥ 5.0 mg/dL), for medical record-confirmed acute liver failure among 669 Kaiser Permanente Northern California health plan members without pre-existing liver/biliary disease.

Hospital-Recorded ICD-9 Diagnostic Code or Code Combination (Diagnoses Recorded in Any Position)		No. with Code(s) *	No. with Acute Liver Failure	Positive Predictive Value (95% Confidence Interval)
Individual diagnoses				
573.3	Toxic (non-infectious) hepatitis	97	15	15% (9% – 24%)
573.8	Other liver disorder, chemical/drug-induced	67	5	7% (2% – 17%)
570	Acute/subacute hepatic necrosis	350	49	14% (11% – 18%)
572.2	Hepatic coma	163	22	13% (9% – 20%)
572.4	Hepatorenal syndrome	78	5	6% (2% – 14%)
572.8	Liver disease sequelae	116	6	5% (2% – 11%)
V42.7	Liver transplant	0	0	-
Individual diagnoses plus a prescription for lactulose or rifaximin				
573.3	Toxic (non-infectious) hepatitis	39	9	23% (11% – 39%)
573.8	Other liver disorder, chemical/drug-induced	21	4	19% (5% – 42%)
570	Acute/subacute hepatic necrosis	117	26	22% (15% – 31%)
572.2	Hepatic coma	103	12	12% (6% – 19%)
572.4	Hepatorenal syndrome	35	1	3% (0% – 15%)
572.8	Liver disease sequelae	47	1	2% (0% – 11%)
V42.7	Liver transplant	0	0	-
Combinations of diagnoses				
573.3 + 573.8	Toxic hepatitis + other liver disorder	4	2	50% (7% – 93%)
573.3 + 570	Toxic hepatitis + hepatic necrosis	24	8	33% (16% – 55%)
573.3 or 570	Toxic hepatitis <i>or</i> hepatic necrosis	423	56	13% (10% – 17%)
573.3 + 572.2	Toxic hepatitis + hepatic coma	9	3	33% (7% – 70%)
573.3 + 572.4	Toxic hepatitis + hepatorenal syndrome	6	2	33% (4% – 78%)
573.3 + 572.8	Toxic hepatitis + liver disease sequelae	11	1	9% (0% – 41%)
573.3 + V42.7	Toxic hepatitis + liver transplant	0	0	-
573.8 + 570	Other liver disorder + hepatic necrosis	12	4	33% (10% – 65%)
573.8 + 572.2	Other liver disorder + hepatic coma	3	2	67% (9% – 99%)
573.8 + 572.4	Other liver disorder + hepatorenal syndrome	1	0	0% (0% – 0%)
573.8 + 572.8	Other liver disorder + liver disease sequelae	1	0	0% (0% – 0%)
573.8 + V42.7	Other liver disorder + liver transplant	0	0	-
570 + 572.2	Hepatic necrosis + hepatic coma	42	14	33% (20% – 50%)
570 + 572.4	Hepatic necrosis + hepatorenal syndrome	25	4	16% (5% – 36%)
570 + 572.8	Hepatic necrosis + liver disease sequelae	20	4	20% (6% – 44%)
570 + V42.7	Hepatic necrosis + liver transplant	0	0	-

Hospital-Recorded ICD-9 Diagnostic Code or Code Combination (Diagnoses Recorded in Any Position)		No. with Code(s) *	No. with Acute Liver Failure	Positive Predictive Value (95% Confidence Interval)
572.2 + 572.4	Hepatic coma + hepatorenal syndrome	38	2	5% (1% – 18%)
572.2 + 572.8	Hepatic coma + liver disease sequelae	30	5	17% (6% – 35%)
572.2 + V42.7	Hepatic coma + liver transplant	0	0	-
572.4 + 572.8	Hepatorenal + liver disease sequelae	16	1	6% (0% – 30%)
572.4 + V42.7	Hepatorenal syndrome + liver transplant	0	0	-
572.8 + V42.7	Liver disease sequelae + liver transplant	0	0	-
Any 2 diagnoses		134	22	16% (11% – 24%)
Any 3 diagnoses		28	6	21% (8% – 41%)

* Includes primary/principal as well as secondary/contributory diagnoses. Thus, more than one diagnosis code may have been recorded for a single member.

Table 3

Conditions observed among 607 Kaiser Permanente Northern California health plan members without electronically-identified pre-existing liver disease who were adjudicated as not having had acute liver failure, by International Classification of Disease, Ninth Revision (ICD-9) diagnosis. Some members had more than one ICD-9 code suggestive of acute liver failure recorded during the hospitalization. Up to two etiologies for the presenting liver injury were determined for each member based on medical record review by the hepatologist adjudicators.

Condition	ICD-9 570: Acute/Subacute Hepatic Necrosis (n=301)	ICD-9 572.2: Hepatic Coma (n=141)	ICD-9 572.4: Hepatorenal Syndrome (n=73)	ICD-9 572.8: Liver Disease Sequelae (n=110)	ICD-9 573.3: Toxic Hepatitis (n=82)	ICD-9 573.8: Other Liver Disorder, Chemical/Drug-Induced (n=62)	Total (n=607)
Pre-existing liver/biliary disease	125	126	70	92	45	38	370*
Alcoholic liver disease	58	95	51	43	17	8	183
Cholestasis	32	9	9	23	18	17	93
Hepatic cirrhosis of any etiology	21	50	21	25	3	6	91
Cancer in the liver	22	13	14	29	9	18	86
Autoimmune hepatitis	4	1	1	2	4	0	9
Chronic hepatitis C	2	2	2	0	0	0	2
Non-alcoholic fatty liver disease	1	0	0	0	1	0	2
Chronic hepatitis B	1	0	0	0	0	0	1
Acute liver injury, no encephalopathy	216	21	10	27	44	26	292*
Hepatic ischemia	185	16	10	23	21	22	236
Acute drug-induced liver injury	35	5	0	3	24	3	58
Hepatic hematoma due to trauma	0	0	0	0	1	1	2
Hepatic abscess	0	0	0	0	0	1	1
Hepatic resection	0	0	0	0	0	1	1
Rejection of liver transplant	0	0	0	1	0	0	1
Indeterminate etiology	9	3	0	3	2	1	16

* Since up to two etiologies were assigned per patient, 71 patients had both pre-existing liver disease and acute liver injury without encephalopathy.