Non-alcoholic Fatty Liver Disease

Nonalcoholic fatty liver disease (NAFLD) is becoming the most common cause of chronic liver disease in the developing world, found in 17-30% of the population in Western countries and 2-4% worldwide. NAFLD is diagnosed predominantly in the fourth through sixth decades of life, although the childhood obesity epidemic has caused an increase in the rate of pediatric NAFLD. The prevalence of NAFLD varies by ethnicity, affecting ~45% of Hispanics, 33% of Whites, and 24% of Blacks. Among Whites, NAFLD is more common in men than in women but not in other racial background (Angulo, P. (2007)).

**Definition:**

NAFLD is a spectrum of disease ranging from simple steatosis to nonalcoholic steatohepatitis (NASH) and it occurs when the accumulation of fatty acid content exceeds 5% of liver weight.

Histologically, NASH is defined by the presence of macrovesicular steatosis, lobular inflammation, and hepatocellular ballooning. The pathology is often indistinguishable from alcoholic fatty liver disease; therefore, the diagnosis can only be made in the absence of significant alcohol use, defined as less than 30 g/ day for men and 20 g/day for women [Sanyal et al. 2011].

**CASE 1:**

1. **Diagnosis:** Inclusion ICD-9 code: In the ICD-9 branch of chronic liver disease (571) we will include 571.5 (Cirrhosis of liver without mention of alcohol), 571.8 (Other chronic nonalcoholic liver disease) and 571.9 (Unspecified chronic liver disease without mention of alcohol). \*571 is different from 571.0.
	1. ICD-10: K75.81, non-specific=K76.0, K76.9

**AND**

1. **Medication:** Exclude those using a medication listed below (preferably exclude when use exceeds 3 months):

**AND**

1. **Diagnostic:** Evidence of hepatic steatosis, either by imaging or by histology in **biopsy report**
	1. **Method - Natural Language:** Text positive for diagnostic phrases (Table 3)

**CASE 2:**

1. **Diagnosis:** Inclusion ICD-9 code: In the ICD-9 branch of chronic liver disease (571) we will include 571.5 (Cirrhosis of liver without mention of alcohol), 571.8 (Other chronic nonalcoholic liver disease) and 571.9 (Unspecified chronic liver disease without mention of alcohol). \*571 is different from 571.0.
	1. ICD-10: K75.81, K76.0, K76.9

**AND**

1. **Medication:** Exclude those using a medication listed below (preferably exclude when use exceeds 3 months):

**AND**

1. **Diagnostic:** Evidence of hepatic steatosis, in **clinical notes**:
	1. **Method - Natural Language:** Text positive for diagnostic phrases (Table 3)

**CASE Exclusion criteria**

1. **Diagnosis:** Exclude patients who have any diagnosis from Table 1. Applies to Case 1 and Case 2.

**Table 1. Case Exclusion Diagnosis**

|  |  |
| --- | --- |
|  | Case Exclusion Codes |
| ICD-9 | **ICD-10** | Description |
| 273.4 | **E88.01** | Alpha-1-antitrypsin deficiency |
| 759.89 | **Q44.7** | Alagille Syndrome (Congenital malformation syndromes affecting multiple systems) |
| V42.7 | **Z94.4** | Liver Transplant |
| 277.00 | **E84.9** | Cystic fibrosis |
| 571.4 | **K73\*** | Chronic hepatitis |
| 571.40 | **K73\*** | Chronic hepatitis, unspecified |
| 573.3 | **K71.6, K75.9** | Hepatitis, unspecified |
| 751.61 | **Q44.2, Q44.3** | Biliary atresia |
| 571.0\* | **K70.0** | Alcoholic fatty liver |
| V58.69 | **Z76.0, Z79.891, Z79.899** | parenteral nutrition |
| 70.xx | **B15-B19** | Viral hepatitis |
| 272.5 | **E78.6** | Abetalipoproteinemia, LCAT deficiency |
| 272.6 | **E88.1** | Lipodystrophy |
| 275.1 | **E83.00, E83.01, E83.09**  | Disorders of copper metabolism (wilson) |
| 291.xx | **F10.1\*** | Alcohol-induced mental disorders |
| 303.xx | **F10.2\*** | Alcohol dependence |
| 331.81 | **G93.7** | REYE'S SYNDROME |
| 277.8x and 277.9 | **E71.4\*, E88.9** | inborn error of metabolism |
| 571.1 | **K70.10** | Acute alcoholic hepatitis |
| 571.2 | **K70.30** | Alcoholic cirrhosis of liver, |
| 571.3 | **K70.9** | ALCOHOL LIVER DAMAGE NOS |
| 571.42 | **K75.4** | Autoimmune hepatitis |
| 642.5x | **O14.2\*** | HELLP syndrome |
| 646.7 | **O26.61\*** | Acute fatty liver of pregnancy  |
| 790.3 | **R78.0** | excessive blood level of alcohol |
| 994.2 | **T73.0** | Starvation |

**Table 2-Case Exclusion Medication**

|  |
| --- |
| anti-retroviral medicines |
| atazanavir |
| darunavir (TMC114) |
| fosamprenavir |
| indinavir |
| lopinavir/ritonavir |
| nelfinavir |
| ritonavir |
| saquinavir |
| tipranavir |
| Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs) |
| abacavir |
| didanosine (ddI) |
| emtricitabine (FTC) |
| lamivudine (3TC) |
| stavudine (d4T) |
| tenofovir DF |
| zalcitabine (ddC) |
| zidovudine (AZT) |
| Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) |
| delavirdine |
| efavirenz |
| Etravirine |
| nevirapine |
| enfuvirtide (T-20; fusion inhibitor) |
| maraviroc (CCR5 antagonist) |
| raltegravir (integrase inhibitor) |
| Other Medications |
| Amiodarone |
| Tamoxifen |
| Methotrexate |
| Tacrolimus (FK506, Prograf) |
| Cytoxan (cyclophosphamide) |
| Corticosteroids (systemic) |
| Valproate |

**Table 3. NASH Text**

|  |
| --- |
| steatosis |
| steatohepatitis |
| non-alcoholic fatty liver disease |
| non-alcoholic steatohepatitis |
| fatty liver-non-alcoholic |
| NAFL |
| NAFLD |
| NASH |
| NAS |
| fatty liver |
| activity score |

**CONTROL**

1. Any patient who does not have a diagnosis of ICD-9 codes of 570-579.99,

(ICD-10= K70-K77)

**Covariates:** A number of conditions might be associated with NAFLD but we will not exclude these conditions, instead we will incorporate them as covariates in conditional analyses or for adjustment including, age, gender, demographic, obesity and Type 2 Diabetes, dyslipedemia, Table 4.

**Covariate Measures**

We will collect the following lab and clinical measures. An increasing number of studies have found NAFLD in patients with normal liver function tests [Angulo, 2007].

1. LFT (AST, ALT, Bilirubin, LDH and ALP) (see Table 5)
2. Height
3. Weight
4. BMI
5. ICD-9 codes and date of encounters

**Table 4: Risk Factors Associated with NAFLD**

|  |  |  |
| --- | --- | --- |
|  |  | Conditions with established association  |
| 52.7, 45.62 | 0DT9\*, 0DTA\*, 0DTB\* | Pancreato-duodenal resection (ICD-PROC) |
| 244\* | E03\* | Hypothyroidism |
| 250.00 | E11\* | Type 2 diabetes mellitus  |
| 253.2 | E23.0 | Hypopituitarism |
| 256.4 | E28.2 | Polycystic ovary syndrome |
| 257.2 | E29.1 | Hypogonadism |
| 272 | E78.5 | Dyslipidemia  |
| 278.0 | E66\* | Obesity  |
| 304.00 | F11.2\* | Drug Dependence |
| 327.23 | G47.33 | Obstructive Sleep apnea |

**Table 5: Lab Result LOINC codes.**

|  |  |
| --- | --- |
| Result Name | LOINC Code |
| BILIRUBIN, TOTAL | 1975-2 |
| AST/SGOT | 1920-8 |
| ALT | 1742-6 |
| LDH | 2532-0 |

**Alcoholic Fatty Liver Disease (ALD):**

In order to compare the genetic or clinical results between non-alcoholic and alcoholic fatty liver disease, we will also collect individuals with alcoholic fatty liver condition using available ICD-9 code:

**Inclusion for alcoholic fatty liver:**

# ALD CASE: (CASE 3 for Data Dictionary)

1. **Diagnosis:** Inclusion ICD-9 code: In the ICD-9 branch of chronic liver disease (571) we will include 571.0 (Alcoholic fatty liver), 571.1 (Acute alcoholic hepatitis) and 571.2 (Alcoholic cirrhosis of liver). 571.3 (Alcohol Liver Damage NOS).
	1. (ICD-10: non-specific=K70.\*)

**ALD CASE Exclusion:**

**Table 6: ALD Case Exclusion**

|  |  |  |
| --- | --- | --- |
| Case Exclusion |  | Description |
| 070.x | B15-B19 | Viral hepatitis  |
| 271.0 | E74.x | Glycogenosis, glycogen storage disease |
| 272.5 | E78.6 | Abetalipoproteinemia, LCAT deficiency |
| 272.6 | E88.1 | Lipodystrophy |
| 275.1 | E83.0x | Disorders of copper metabolism |
| 331.81 | G93.7 | Reye's syndrome |
| 571.42 | K75.4 | Autoimmune hepatitis |
| 642.5x | O14.2x | HELLP syndrome |
| 994.2 | T73.0XXA | Starvation |
| V58.69 |  | Parenteral nutrition |
| 070.x | B15-B19 | Viral hepatitis  |

**ALD Case exclusion of medications: (same as NAFLD)**

**Alcohol dependence without any liver disorder: (CASE 4 for Data Dictionary)**

Identify those with alcoholic dependence (ICD9=303.\*, ICD10=F10.\* condition but have not been diagnosed with liver disease: 570-579.99, (ICD-10= K70-K77)

For all subjects, we will need lab measures described above (height, weight, BMI, LFT).

**References:**

Angulo, P. (2007) GI epidemiology: nonalcoholic fatty liver disease. Aliment Pharmacol Therapeut 25: 883–889.

Sanyal, A.J., Brunt, E.M., Kleiner, D.E., Kowdley, K.V., Chalasani, N., Lavine, J.E., et al. (2011) Endpoints and clinical trial design for nonalcoholic steatohepatitis. Hepatology 54: 344–353.