Various Risk Factors Associated with Severity of Liver Disease in ALD Patients

Tripti¹, Karuna Singh²
¹ Research Scholar, Amity Institute of Food Technology, Amity University, Noida, UP. ² Assistant Professor-III, Department of Amity Institute of Food Technology, Amity University, Noida, UP.

Abstract

Introduction: Excessive intake of alcohol becomes a major healthcare issue worldwide with consequences affecting socially, economically, and clinically and recorded 3.3 million deaths in 2012 (WHO 2014)²⁹. Heavy drinking over a long period of time damages almost every organ of the body especially liver.

Objective: To assess the various risk factors associated with severity of liver disease in ALD patients

Material and Method: There were 953 total subjects taken for study. They all were drinking alcohol, out of which 60 were diagnosed as ALD patients and they were further studied for various risk factors responsible for progression of ALD.

Results: Total 953 males drinking alcohol from minimum five years were studied. Out of the 953 drinkers, 60 were ALD patients (various degree of progression). None of the were taking any medicines since last 2 months. Anti-HCV and HBsAg were negative in all patients. Various risk factors were studied like average daily alcohol intake, duration of drinking, type of alcohol beverage and drinking habits etc. Daily alcohol consumption higher than 20gm and minimum for 5 years found to be significant with progression of ALD. It was also resulted that maximum subjects (38.61%) were drinking hard liquors followed by Beer (30.74%), Multiple alcohol beverage (20.25%) and wine (10.38%). 87.82% of the total subjects were drinking alcohol at meal time or with meals and the daily alcohol intake was significantly lower than that of the alcohol consumed at any time (means with and without meals) (p<0.05).

Conclusion: The analyzed data highlights that ALD is a major and chronic health condition resulting from various risk factors which can be preventable.

Keywords: Alcoholics, Alcohol liver diseases (ALD), Risk factors, Alanine amino transferase(ALT), carbohydrate-deficient transferrin (CDT)

Introduction and Background:

Excessive intake of alcohol becomes a major healthcare issue worldwide with consequences affecting socially, economically, and clinically and recorded 3.3 million deaths in 2012 (WHO 2014)²⁹. Heavy drinking over a long period of time damages almost every organ of the body. The primary site of ethanol metabolism is the liver, so excessive drinking leads to highest degree of tissue injury to the most sustainable organ of the body i.e. liver (Lieber 2000)¹³.

Presently, there is no specific biological marker which can be used to correlate the association between alcohol and the underlying cause of liver damage. But there are numerous laboratory parameters used clinically and shows the relation of chronic alcohol consumption and alcoholic liver damage. Certainly, the sensitivity of carbohydrate-deficient transferrin (CDT) and yGT to evaluate the drinking of greater than 50 g per day is 69%
and 73%, respectively. (Angulo 2002).

Regular or heavy drinking at the early period of life enhances the risk of severe ALD development as compared to occasional or binge drinking habit. It has also found that some genetic factors are also responsible for the development of alcohol related disorders. But only few data support this comment. The available literature suggests that it is because of the changes that occurs in the genes which encodes or contain genetic codes for cytokines, inflammation causing mediators, antioxidant enzymes and the enzymes responsible for alcohol metabolism play a crucial role in the pathogenesis (Stewart 2002), some of the latest study showed that the changes that occur in the polymorphism of TNF-238A and PNPLA3 protein (patatin-like phospholipase which contains protein 3 (Thurman 2000) may affect the prognosis of alcoholic cirrhosis who takes alcohol but this data is not sufficient and may require more documented literature or genetic mutations.

The prime factors which determines the progress of liver related disorders are the type of beverages consumed and the quantity and habit of drinking (e.g. outside mealtime). consumption of >40-80 gms of pure ethanol daily in case of males and around 30-40 gms daily by females for a long period is a common predictor for the diagnosis of more severe cases of alcohol related disorders like alcoholic steatohepatitis, fibrosis (Becker et al., 1996).

It is documented that females are more prone to alcohol related liver disease. Higher blood alcohol concentrations in females than males ingesting the same amount of alcohol, resultant from a lower percentage of body water (Mumenthaler et al., 1999). Other reports also showed that female hold a lesser capacity than a male to oxidize ethanol in the gut (Frezza et al., 1990).

Age may be another risk factor responsible for the progression of ALD, but there is insufficient data on it. However, it is a predictor for ALD (Masson et al., 2014), as old age (i.e. 65 and above) is more susceptible to ALD and show higher degree of ethanol-induced injuries than young age people (Meier and Seitz 2008). Other influential factors are specific genetic markers (i.e., single-nucleotide polymorphisms) that have identified by various studies associated by Genome-wide that shows the genes encoding alcohol-metabolizing enzymes, cytokines, and antioxidant enzymes are linked to the advancement of ALD (Stickel & Hampe 2012).

Dietary fat is a macronutrient and it is also the modifier for ALD. In rodents, dietary saturated fat appears to guard against alcohol-induced liver damage, whereas dietary unsaturated fat enriched in linoleic acid reportedly promotes such damage (Kirpich et al., 2016). Various population-based studies have showed a significant relationship between the risk of liver damage and alcohol consumption in people having body mass index greater than normal values (Ruhl &Everhart 2005). Smoking is linked with higher risk of alcoholic cirrhosis in humans (Klatsky & Armstrong 1992).

Alcohol-abused patients show the worsened conditions in the course of hepatitis C (HCV) and hepatitis B (HBV) viral infections, triggering fastdevelopment to fibrosis, cirrhosis, and even hepatocellular carcinoma (Szabo et al, 2006). Numerous common mechanisms of viral infection and alcohol-induced damage have been suggested (Zakhari 2013).

Material and Method

Study population:

Total 60 males suffering from ALD were taken to study the risk factors leading the progression of liver disease.

Inclusion criteria: Willing male patients having ALD were included.

Study design: Descriptive and cross-sectional study.

Tools used:

Questionnaire (both open and close ended) with interview schedule were used to know the risk factors affecting the patients.

Statistical analysis:

Statistical analysis was performed with SPSS 16 statistical package. A logistic-regression model was used in the multivariate modeling of associations. Odds ratios (ORs) and 95% confidence intervals (CI) were also calculated.

Results

Study Population: Total 953 patients, all males,
having alcohol from minimum five years age, were taken. Out of the 953 drinkers, 60 were ALD patient. None of the were taking any medicines since last 2 months. Anti-HCV and HBsAg were negative in all patients. Various risk factors were studied like average daily alcohol intake, duration of drinking, type of alcohol beverage and drinking habits etc.

**Daily alcohol consumption and duration of drinking as risk factors for ALD:**

Analysis of data investigated that daily alcohol consumption higher than 20gm is significant with progression of ALD and serve as a major risk factor for this condition (table 1). It was also found that the mean duration of drinking longer than 5 years also may be the reason for ALD and it was found significant in results. Above this threshold, the OR for ALD increased proportionally with consumption of alcohol daily. The highest OR (10.68, P<0.01) occurred when daily consumption exceeded 160 gm/day. It was observed that when alcohol intake is at highest level, the percentage of ALD patients (18.7%), were significantly higher than that of the lowest level of alcohol intake having less than 20gm/day. Only those subjects were found to be suffering from ALD, whose daily alcohol consumption was above 20 gm and the duration was also above 5 years. So, it can be concluded that daily intake of 20 gm alcohol for 5 years is the risk threshold. In case of ALD patients who were drinking less than 20gm/day from 10-15 years (longer duration), the percentage of morbidity was very less i.e. 2.2% only.

**Table 1: Average daily alcohol intake and duration of drinking**

<table>
<thead>
<tr>
<th>Alcohol intake</th>
<th>N</th>
<th>&lt;5Yr</th>
<th>&gt;=5-9Yr</th>
<th>&gt;=10-14Yr</th>
<th>&gt;=15-19Yr</th>
<th>&gt;=20 Yr</th>
<th>Total</th>
<th>OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(g/d)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>585</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>13(2.2%)</td>
<td>-</td>
</tr>
<tr>
<td>&gt;=20-39</td>
<td>163</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>4</td>
<td>8</td>
<td>18(11.4%)</td>
<td>5.43</td>
</tr>
<tr>
<td>&gt;=40-79</td>
<td>112</td>
<td>1</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td>15(13.5%)</td>
<td>7.02</td>
</tr>
<tr>
<td>&gt;=80-159</td>
<td>57</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>8(14.6%)</td>
<td>8.24</td>
</tr>
<tr>
<td>&gt;=160</td>
<td>36</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>6(18.7%)</td>
<td>10.68</td>
</tr>
<tr>
<td>Total</td>
<td>953</td>
<td>3(1.5%)</td>
<td>9(4.0%)</td>
<td>11(6.3%)</td>
<td>12(11.2%)</td>
<td>25(9.8%)</td>
<td>60(6.3%)</td>
<td></td>
</tr>
</tbody>
</table>

P<0.01, vs group of alcohol intake <20g/d.

**Type of alcohol beverage and drinking habits as risk factors for ALD:**

In present study population, it was observed that maximum subjects (38.61%) were drinking hard liquors followed by Beer (30.74%), Multiple alcohol beverage (20.25%) and wine (10.38%). 87.82% of the total subjects were drinking alcohol at meal time or with meals and the daily alcohol intake was significantly lower than that of the alcohol consumed at any time (means with and without meals) (p<0.05). It was also observed that the daily intake of hard liquor alcohol without meals was significantly higher than that of other categories of drinkers. Also, it was found that morbidity of ALD was much higher than that of drinkers who drink only wine or beer at mealtime. (Table 2)
### Table 2: Type of alcoholic beverage and drinking habits.

<table>
<thead>
<tr>
<th>Type of beverage</th>
<th>With meals only</th>
<th>At any time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>Daily intake (g)</td>
</tr>
<tr>
<td>Beer</td>
<td>293 (30.74%)</td>
<td>6.09±3.65</td>
</tr>
<tr>
<td>Wine</td>
<td>99 (10.38%)</td>
<td>10.69±5.28</td>
</tr>
<tr>
<td>Hard liquor</td>
<td>368 (38.61%)</td>
<td>44.97±14.90</td>
</tr>
<tr>
<td>Multiple</td>
<td>193 (20.25%)</td>
<td>29.50±12.0</td>
</tr>
<tr>
<td>Total</td>
<td>953 (100%)</td>
<td>837 (87.82%)</td>
</tr>
</tbody>
</table>

P<0.05, vs Beer.

### Discussions

Alcohol consumption is the major factor responsible for the progression of the chronic liver diseases (Crews; Rehm et al; Schuckit et al; Dal Maso 2002)\(^4,19,21,6\). The natural history of ALD ranges from different stages from asymptomatic to end stage liver disease. Specific clinical features are mostly absent in patients with ALD (Vaquero et al., 2003; Gordon 2001)\(^27,8\). The patients having different types of liver disease (fatty liver with alcoholic steatohepatitis, non-alcoholic fatty liver) without confirmatory lab tests, required the overall history of drinking pattern & habits, ultrasonography and liver biopsy (Skelly et al., 2001; Angelico et al., 2003; Jarque-López et al.,2001; Hourigan et al.,2001)\(^22,2,10,9\).

Various factors are responsible for progression of ALD including genetic and others like age, gender, BMI, body weight & type, frequency and duration of alcohol intake. The habit of consuming hard liquors without meals or at any time is other major factor (Thurman; Walsh et al., 2000)\(^26,28\). Study revealed that, there is no enough data to describe the risk threshold in terms of regular alcohol consumption in relation with years of alcohol intake and it was also observed that there is a wide range exists between 30gm/day to 80gm/day (Gordon 2001)\(^8\). Geographic dissimilarities also included due to great difference between eastern and western countries (Stewart 2002; Naveau et al., 2001)\(^23,18\).

In a study, the risk threshold of daily alcohol intake was 20 g; the duration was 5. Below the above-mentioned threshold, drinking rarely induced liver damage (Xiao et al., 2004)\(^31\). The present stud found same observations regarding risk factors of having daily alcohol consumption i.e. more than 20 g /day at least for 5 years. It was also found that the daily ingestion of alcohol more than 40 g and longer than 5 years, leads the liver damage easily. However, with a daily consumption more than 160 g, the frequency of alcoholic liver disease was only 18.7%. So, there is a significant difference in exposure among different individuals (Diehl 2002)\(^5\). It is normally believed that occurrence of ALD in general population is up to about 15% and increases with increased alcoholic consumption. One of the study showed the increased percentage due to only male patients in their study (Xiao et al., 2004)\(^31\). Same results are reported in present study. The forms of alcoholic drink and the different drinking and eating habits are closely related with ALD.
**Conclusion**

The present data concluded that the prevalence of alcoholic liver diseases is directly associated with the quantity of alcohol consumption and the frequency of alcohol. The dose related pattern and quantity of alcohol consumption also proves to be an important indicator for susceptibility to alcoholic liver. Consumption of hard liquors or multiple types of alcoholic drinks without food, in spite of the amount, is also related to increased incidence of alcohol-related liver diseases. In addition to above risk factors, there are many other factors involved like obesity, age, gender etc. Therefore, the study recommends to reduce the alcohol consumption, avoiding alcohol intakewithoutmealtimes.

**Conflict of Interest:** None

**Source of Funding:** Self

**Ethical Clearance:** Ethical clearance were taken from hospital authorities, concerned doctor. Consent was also taken from individual patients.

**References**


