Alcoholic Liver Disease: Alfa Fetoprotein Alteration, Hematological & Biochemical Characteristics

Aswad Al.Obeidy * (FICMS) (FICMS GE & Hep)

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Summary:

Background: *Alcohol remains the single most significant cause of liver disease throughout the Western world, responsible for between 40 and 80% of cases of cirrhosis in different countries. Many of the factors underlying the development of alcoholic liver injury remain unknown, and significant questions remain about the value of even very basic therapeutic strategies.*

Patients and Methods*: In a cross sectional study, 113 alcoholic patients with evidence of liver disease in the absence of other significant etiology attending the Gastoenterorology and Hepatology Teaching Hospital between December 2001 and December 2003 were studied for the hematological and biochemical spectrum of alcoholic liver disease including Alfa fetoprotein (AFP) and gamma glutamyl transpeptidase alteration.*

Results: *The serum aminotransferase was mildly elevated and the AST/ALT ratio often exceeds 2.The serum bilirubin and PT positively correlated with the severity of ALD. The GGT was commonly elevated irrespective of liver damage. AFP was bellow normal in (80%) and was negatively correlated with the severity of ALD.*

Conclusion: *The hematological profile of ALD was macrocytosis and neutrophile leukocytosis. The serum aminotransferase was mildly elevated. The GGT was commonly elevated irrespective of liver damage. AFP was bellow normal in the majority and is negatively correlated with the severity of ALD.*

Key wards: *Alcoholic liver disease, Alfa fetoprotein, gamma glutamyl transpeptidase.*

Statistical analysis: *Chi square tests and the mean value with SD for each value were determined using ANOVA. A p value of <0.05 was considered to be positive.*

Introduction:

The incidence of cirrhosis among alcoholics is about 10-15 %[1], require 80 gm of ethanol daily for 10-20yrs. Cofactors in the development of alcoholic liver disease (ALD) include: inherited differences in ethanol metabolism [2], female gender [4], coexistence of hepatitis C and B virus infection [4], malnutrition [6], obesity [6], H pylori infection and gastritis [7], concurrent exposure to hepatotoxins, cigarette smoking [8] and iron overload [9]. There are currently four major theories concerning the mechanism by which alcohol damage the liver :(1) Centrilobular hypoxia[10]. (2)Neutrophil infiltration and activation [11]. (3) Inflammatory cell infiltration and activation. [12] (4) Antigenic adduct formation. [13]. The laboratory parameters that are most useful in predicting the severity of alcoholic liver injury are bilirubin level, prothrombin time (PT), and albumin level. The first two have been used to formulate a discrimination function (DF), defined as 4.6 x (PT-control

In second) +bilirubin (mg/dL); when the result is greater than 32, a mortality rate of 50% can be predicted within one month [14].

The mainstays of treatment for ALD are:1.Abstinence.2.Nutritional Supplement.3.Antiinflammatorydrugs.(Glucocorticoids)4.Antioxidants.5.LiverTransplantat The prognosis of patient with alcoholic liver disease (ALD) depend upon several variables including: The clinical severity of liver injury at diagnosis, the extent of irreversible liver damage at diagnosis and the subsequent drinking behavior. Patient with fatty liver or equivalent have had the best outcome (70% to 80% survival rate at 4 to 5 years); those with alcoholic hepatitis or cirrhosis, an intermediate outcome (50% to 75% survival rate at 4 to 5 years); and those with cirrhosis combined with alcoholic hepatitis, the worst outcome (30% to 50% survival rate at 4 to 5 years) [15].

* *Gastroenterology & Hepatology Teaching Hospital*

Patients and Methods:

A total number of 113 patients with ALD attending the Gastroenterology and Hepatology teaching hospital were studied. All consumed 80 Gms of ethanol or its equivalent for 10-20 years with evidence of liver disease in the absence of other significant etiology. Each patient was interviewed, detailed history, general medical examination was done and a study protocol paper was filled. Blood sample was taken for complete blood count, liver function test, serum iron, total iron binding capacity (TIBC), serum ferritin, serm copper, ceruloplasmin, lipid profile, Alfa fetoprotein (AFP) and gamma glutamyl transpeptidase (GGT). The aim of the study is to determine the hematological and biochemical profile of ALD including Alfa fetoprotein, gamma glutamyl transpeptidase alteration with the prevalence of HBV, HCV and hepatocellular

carcinoma.

Results:

Macrocytic anemia was found in (70%) with a mean of mean corpuscular volume (MCV) 103.6 fl. Leucocytosis was common with a mean white blood count (WBC) of 11600 cells/mm^3. The serum aminotransferase was mildly elevated and the AST/ALT ratio often exceed 2 in all stages of ALD.The serum bilirubin and PT positively correlated with the severity of ALD.There was a negative correlation between serum albumin the severity of ALD. The serum alkaline phosphatase (ALP) was moderately elevated (2-3 times) and the level of GGT was commonly elevated in alcoholics irrespective of liver damage. The prevalence of HBV was (17.7%) and HCV (11.5%). Triglyceride (TG) was mildly elevated while serum cholesterol was normal. The serum ferritin exceed 332 microgram/L in 60% as in table (1)

Table (1) Laboratory values in ALD

	GROUP 1 (n 43) Mild	**GROUP 2 (n 26) Moderate**	**GROUP 3 (n 44) Severe**	**Normal values**
Hematocrit (%)	38.6	34	33	31-37%
MCV (mic/mm^3	100	104	107	78-98
WBC (per mm^3)	8700	9300	11600	4-11000
AST U/L	62	89	66	10-35
ALT U/L	50	59	54	10-40
ALP (IU/Ml)	145	165	155	40-125
S.Bilirubin(mg/dl)	2.3	12.8	4.8	0.21-1
PT sec. Prolong	2.3	3.8	9.3	8-10.5 s
S. Albumin gm/dl	3.2	3.8	2.15	3.6-4.7
GGT u/l	62.3	75	58	10-55
S. Cholesterol	162	169	175	<200
S. TG mg/dl	134	147	177	53-150
HDL mg/dl	44	30	28	62
S.ferritin mic/l	457	417	326	17-300

Moderate disease was defined by bilirubin level >5mg/dl and severe disease by bilirubin level >5mg/dl and PT>4 seconds prolonged. [16] AFP was bellow normal in 80% and was negatively correlated although not significant with the severity of ALD as in table (3).

Table (3) Alfa fetoprotein alteration ALD

GROUP 1 (n 43) Mild	GROUP 2 (n 26) Moderate	GROUP 3 (n 44) Severe	P Value
8.04 ±2.7	7.37±3.5	5.8±2.3	> 0.05 (NS)

The prevalence of hepatocellular carcinoma (HCC) showed a statistically significant positive trend with severity of ALD, it increased from 4.7% among those with mild ALD to as high as 18.2% in those with severe disease their mean age was 58 years and the mean level of AFP was 15.5 ng/ml as in table (3).

Table (3): The prevalence of HCC according to the severity of ALD

		HCC	
Severity of ALD	**Total**	**N**	**%**
Mild	43	2	4.7
Moderate	26	2	7.7
Severe	44	8	18.2
Overall	113	12	10.6

P (trend) = 0.04

Discussion

Macrocytic anemia was common (70%) and the

mean WBC was 11600 /mm^3. Concurrent hematological abnormalities are common in moderate to severe alcoholic hepatitis. Macrocytosis indicates long-standing disease, and reflects poor nutritional status, the bone marrow toxicity of alcohol, decreased lipid deposition on red cell membrane and/or failure of congested spleen and liver to clear senescent RBC. Leukocytosis is a frequent and important abnormality in alcoholic hepatitis. Once other causes are excluded, the magnitude of the WBC elevation correlates closely with the severity of alcoholic liver disease [16]. The combination of raised MCV and serum GGT identify 90% of alcohol-dependent patients. [17]

The serum aminotransferase is only modestly elevated and does not correlate with disease severity. [18] The most common pattern of ALD is disproportionate elevation of AST compared to ALT, the ratio is usually greater than two and have been attributed to pyridoxine deficiency, which is a co-factor for the activity of ALT. According to this hypothesis the altered ratio, reflect a failure of appropriate increase in the ALT rather than a disproportionate elevation in AST. [19, 20] The severity of ALD is best correlated with serum bilirubin level and PT. Of notes in that the level of serum bilirubin, once a value of 5mg/dl has reached, does not correlate with disease activity whereas the PT increases progressively with worsening illness. [20]

The serum alkaline phosphatase (ALP) was modestly elevated (2-3 times) and GGT was commonly elevated. The level of ALP is often normal or minimally elevated in alcoholic fatty liver, and may be minimally elevated in alcoholic hepatitis and decompensated cirrhosis. In contrast, the GGT is usually elevated in heavy drinkers, irrespective of the presence of liver disease and is widely used as screening test for alcoholic abuse. The rise results mainly from enzyme induction, although hepatocellular damage and cholestasis may contribute and the level may return to normal within few weeks of abstinence, its 72% sensitive and 80% specific for the diagnosis of ALD.[21] The AFP value was bellow normal in 80%. This result is in consistence with Mendenhall who founded value bellow normal in 78% and 42% had undetectable level, clinically lowest AFP was observed in the more severely ill patients. Correlation analysis showed a significant relationship of AFP to visceral protein concentration, (i.e., albumin, transferrin). These finding suggest that AFP is a good index of disease prognosis. [22] The serum TG was mildly elevated while serum cholesterol was normal. Moderate alcohol intake is associated with an increase in serum TG level, and heavy alcohol may be associated with grossly elevated level caused by increased concentration of VLDL, these changes probably occur as a direct result of alcohol metabolism. Serum ferritin was above normal in 60% in this study. Bell found that serum ferritin was increased in 64 of 111 alcoholics (58%) and in 30 of 137 (22%) with chronic non-alcoholic liver disease (P >0.01). Serum ferritin is more frequently elevated in abusing patients with ALD than in patients with other chronic liver disease. [23]

Conclusion:

The hematological profile of ALD was macrocytosis and neutrophile leukocytosis. The serum aminotransferase was mildly elevated. The GGT was commonly elevated irrespective of liver damage. AFP was bellow normal in the majority and was negatively correlated with the severity of ALD.

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