IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 9 Ver. 12 (September. 2018), PP 01-12
www.iosrjournals.org

A Prospective Study on The Pattern of Hepatic Enzymes After Abstinence In Alcohol Dependence Patients

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Abstract
BACKGROUND*: All patients who present with clinical features of hepatitis or chronic liver disease or who have elevated serum elevated transaminase levels should be screened for an alcohol use disorder.Typical laboratory findings in ALD include transaminase levels with aspartate aminotransferase greater than alanine aminotransferase as well as increased mean corpuscular volume, gamma-glutamyltranspeptidase, and A:G ratio .*
AIM*: To study the pattern of Hepatic enzymes after abstinence among alcohol dependent patients*
MATERIALS AND METHODS: *: A prospective study on all patients with alcohol dependence attending de addiction centre.A total of 118 patients have been enrolled in the study. Serum biomarkers SGOT {AST} and SGPT (ALT) were analysed at 0,15,30, 60 90 and 180 days*
RESULTS: *Mean age in years of the study population is 38.5 years. Mean age of alcohol intake is 21.3 years. Mean duration of alcohol intake is 17.2 years The mean value of AST/ALT ratio was found to be 1.09 with a range of 0.59 to 1.62. In the present study the mean AST levels come down with the increase in the duration of abstinence.*
CONCLUSIONS*: Majority of the subjects reached normal range of AST levels after 30 days of abstinence. Nearly 60% of them reached normal ALT levels after 60 days of abstinence. The AST levels will reach earlier to normal levels when compared to ALT levels in abstinence of Alcohol.*
Keywords*: serum biomarkers AST (SGOT) , ALT (SGPT), Abstinence of alcohol*

Date of Submission: 14-09-2018 Date of acceptance: 29-09-2018

I. Introduction

Alcohol is a hepatotoxin that is commonly consumed worldwide and is associated with a spectrum of liver injury including simple steatosis or fatty liver, alcoholic hepatitis, fibrosis and cirrhosis.

Excessive alcohol consumption is a risk factor for a multitude of adverse health consequences and is indeed one of the leading causes of preventable morbidity and mortality worldwide with a significant burden attributable to ALD. Excessive or harmful alcohol use is ranked as one of the top five risk factors for death and disability globally and results in 2.5 million deaths and 69.4 million annual disability adjusted life years.

There is a strong correlation between the prevalence of ALD, specifically cirrhosis, and a country's annual per capita alcohol consumption. Levels of alcohol consumption vary geographically with Eastern European countries having the highest annual per capita consumption (15.7 L per person).

Rates of ALD are highest in countries with the highest rates of alcohol consumption including Eastern Europe, Southern Europe and the United Kingdom. In 2010, ALD resulted in 493300 deaths worldwide and 14.5 million disability adjusted life years with alcoholic cirrhosis comprising 47.9% of all liver cirrhosis deaths.

While alcohol is a well established hepatotoxin with higher levels of consumption associated with increased risk of development of ALD, no absolute threshold of alcohol consumption is necessary for the development of liver injury, and no direct linear correlation between level of alcohol consumption and severity of ALD has been established.

Approximately 60%-90% of individuals who drink more than 60 g of alcohol per day have been shown to have hepatic steatosis. However, less than half of individuals with alcoholic steatosis, who continue to drink alcohol, will progress to fibrosis and only 10%-20% will eventually progress to cirrhosis. Nonetheless, once steatohepatitis has developed, the risk of development of cirrhosis is increased compared with simple steatosis.

In addition, individuals who have demonstrated steatohepatitis who continue to drink alcohol or who develop symptomatic alcoholic hepatitis have higher rates of progression to cirrhosis compared with those who subsequently abstain from alcohol consumption or who have never had an episode of symptomatic alcoholic

hepatitis. Alcoholic cirrhotics who abstain from alcohol consumption for at least 1.5 years have improved survival rates compared to those that continue to drink.

AIMS and OBJECTIVES: To study the pattern of liver enzymes after abstinence among alcohol dependent patients attending a Tertiary Care Hospital in Andhra Pradesh

OBJECTIVES

- To study the socio demographic profile of patients attending for de addiction treatment at a tertiary mental care hospital, Visakhapatnam.
- To study the pattern of Liver Enzymes after abstinence from Alcohol

II. Materials And Methods

A prospective study on all patients with alcohol dependence attending de addiction centre at a Tertiary Care Hospital, Visakhapatnam for a period of 1 year .A total of 118 patients have been enrolled in the study.

HYPOTHESIS Elevated Liver enzymes level will decline with abstinence from alcohol.

Inclusion criteria

- Patients meeting ICD-10 criteria for alcohol dependence syndrome
- Age group between 20-60 years.

Exclusion criteria

- Patients with co morbid medical illness
- Intellectual disability cases
- Age<20 years and more than 60 years
- Other substance dependence except nicotine.

Sample size: All the patients attending de addiction centre at Tertiary Care Hospital Visakhapatnam who are willing and given consent to participate in the study who have met the inclusion and exclusion criteria ,were included. Patients were followed up for 6 months from the date of admission. Serum biomarkers SGOT {AST} and SGPT (ALT) were analysed at 0,15,30, 60 90 and 180 days..A total of 118 patients were involved in the study. All the patients were tested for serum bio markers at 0,15 and 30 days as they are under inpatient care during that period. As the patients are on inpatient care all the enrolled patients have been followed up for 30 days. Counselling was done for all the patients attending de addiction centre at Tertiary Care Hospital, Visakhapatnam, highlighting the importance of abstinence and liver enzymes returning to normal levels. Out of them 34 patients did not follow the abstinence and were lost to follow up.

Socioeconomic classification: Socioeconomic status of the study subjects was analysed using the modified Kuppuswamy classification .

TOOLS

- A semi structured questionnaire was used to collect data from the patients.
- Investigations like SGOT, SGPT and Serum Bilirubin will be done on day 1, repeated at 15 ,30 ,60,90,120 and 180 days of abstinence from alcohol.
- Follow up of the patient up to 6 months &laboratory investigations after 2,4 and 6 months.

Estimation of Biomarkers: Estimation of biomarkers was done in clinical laboratory, Tertiary Mental Care Hospital ,Visakhapatnam. For estimation of ALT and ALT International Federation of Clinical Chemistry (IFCC) method was used. It utilizes a semi auto analyser CHEM-7 , "ERBA" Mannahelm make. It reads the absorptivity at a wavelength of 340 nm.

Reagents used for SGOT estimation:2 Oxoglutarate 12mmol/L ,L-aspartate 200mmol/L, MDH >545IU/L,LDH>909U/L,NADH >0.018 mmol/L.

Reagents used for SGPT estimation: 2-oxyglutarate 12mmol/L ,L-Alanine 500mmol/l,LDH_>1820 IU/L ,NADH_>0.18 IU/L.

PROCEDURE:500 micro litres of reconstituted reagent and 50 micro litres of serum are mixed in attest tube and presented to the semi auto analyser and the result is read after 4 minutes which is displayed on the reading monitor.

Reference range for SGOT:5-34 IU/L at 37 degrees centigrade.

Reference range for SGPT: 0-40 IU/L AT 37 degrees centigrade.

DATA ANALYSIS

Data collected was analysed using MS EXCEL and SPSS software version 21 was used and appropriate statistical tests will be applied.

ETHICAL ISSUES

Prior permission was taken from the Institutional Ethics Committee Andhra Medical College before the start of the study.
Consent was taken from every patient who participated in the study.

III. Results

The study was conducted in a tertiary care hospital at Visakhapatnam. A total of 118 subjects have been involved in the study. All the subjects are males. Mean age in years of the study population is 38.5 years. Mean age of alcohol intake is 21.3 years. Mean duration of alcohol intake is 17.2 years

Table 1: Distribution of study populations according to age

Age in years	Frequency	Percent
11-20 yrs	1	0.8
21-30 yrs	17	14.4
31-40 yr	58	49.2
41-50 yrs	38	32.2
51-60 yrs	4	3.4
Total	118	100.0

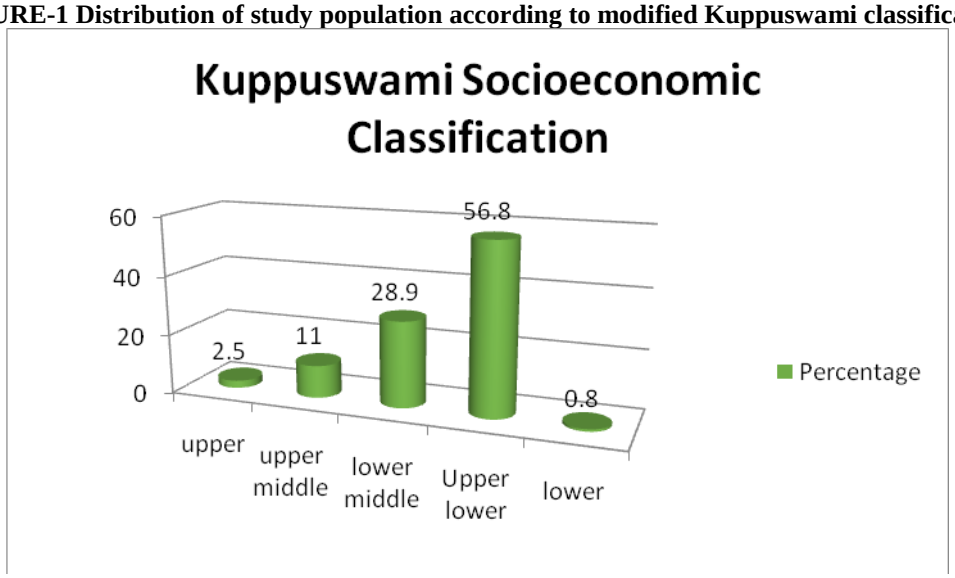
In the present study majority of the study subjects (49.2%) belong to 31-40 years age group, followed by age group between 41 and 50 years (32.2%).

TABLE-2 DISTRIBUTION OF STUDY SUBJECTS ACCORDING TO INCOME

Income Per Month	Frequency	Percent
>36017	4	3.4
1800-36016	15	12.7
13495-17999	13	11.0
8939-13494	36	30.5
5387-8988	39	33.1
1803-5386	11	9.3
Total	118	100.0

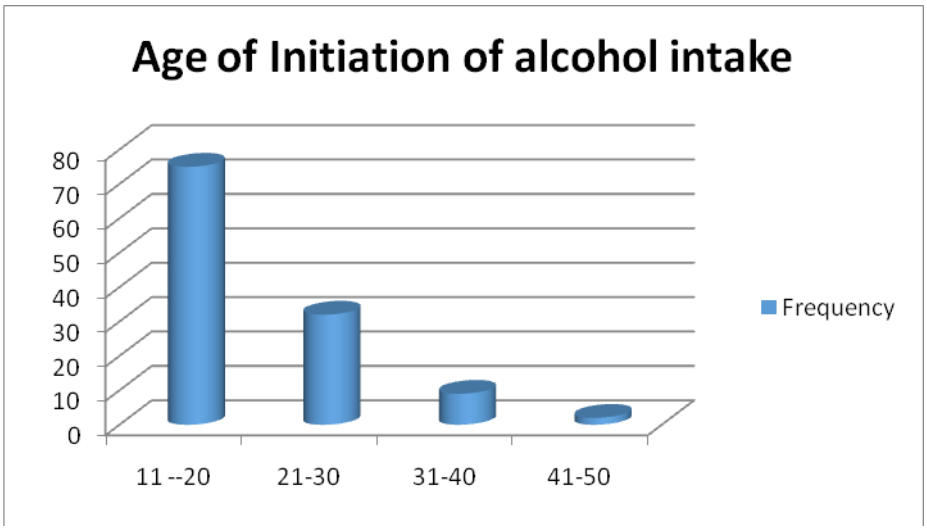
Majority of the subjects (33.1%) are in income group 5 followed by 30.5% in the income group 4.

FIGURE-1 Distribution of study population according to modified Kuppuswami classification



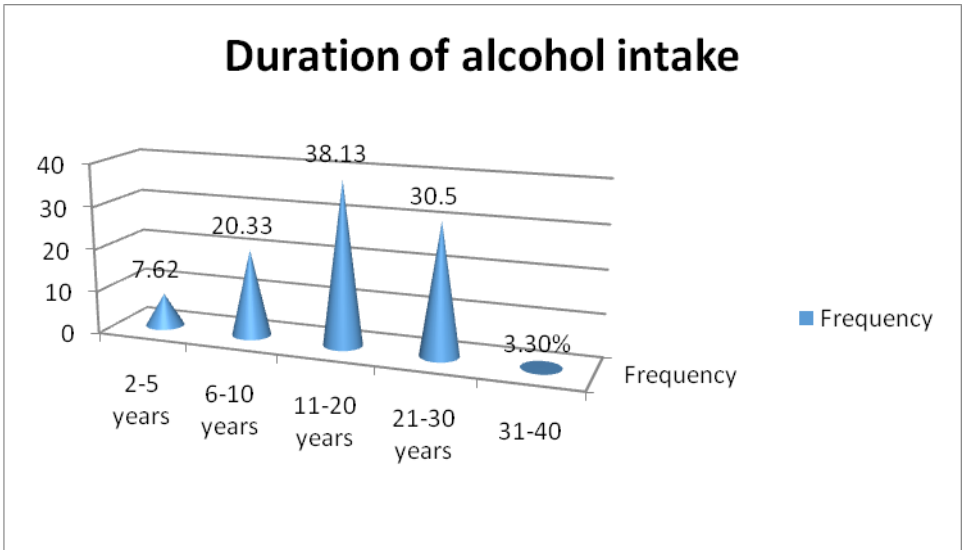
According to modified Kuppuswami classification majority of the subjects belong to Upper lower class(67) followed by Lower middle class(34).

FIGURE-2 DISTRIBUTION ACCORDING TO AGE OF ALCOHOL INTAKE



In our study it was observed that the age of initiation of alcohol intake majority were in the age group of 11-20 years i.e 63.6% followed by 27.1% in the age group of 21-30 years.

FIGURE-4 DISTRIBUTION ACCORDING TO DURATION OF ALCOHOL INTAKE



Majority of the subjects (65%)in our study consume alcohol for more than 10 years.
In the present study 38% of the subjects consume alcohol for between 11-20 years and 30.5% of the subjects consume between 20-30 years

TABLE-3 DISTRIBUTION ACCORDING TO QUANTITY OF ALCOHOL INTAKE

QUANTITY OF ALCOHOL INTAKE	Frequency	Percent
<90ml	6	5.1
91-180	16	13.6
181-360	10	8.5
361-540	23	19.5
541-750	23	19.5
>750	40	33.9
Total	118	100.0

The above table shows the quantity of alcohol consumed per day. Majority of the subjects consume more than 500 ml per day.

TABLE-4 DISTRIBUTION OF SUBJECTS ACCORDING FREQUENCY OF ALCOHOL INTAKE

Frequency	No of subjects	Percent
Daily	106	89.8

< 5 days/week	12	10.2
Total	118	100.0

Majority of study subjects (89.8) have history of daily intake of alcohol followed by 10.2% who had history of intake of alcohol at less than 5 days per week

AST/ALT Levels

The mean value of AST/ALT ratio was found to be 1.09 with a range of 0.59 to 1.62.

TABLE-5 Duration of alcohol intake vs AST levels

Duration of Alcohol intake	N	Mean	Std Deviation
2-5 years	9	82.44	21.4
6-10 years	24	85.08	22.06
11-20 years	45	80.93	23.075
21-30 years	36	76.89	16.374
31-40 years	4	73.25	12.312

In our study it was observed that the mean levels of AST are decreasing with duration of alcohol intake .As the duration is increasing beyond 20 years the mean levels of AST are coming down. Maximum levels are found in those study subjects having history of alcohol consumption for 6-10 years.

TABLE-6 Duration of alcohol intake vs ALT levels

Duration of Alcohol intake	N	Mean	Std Deviation
2-5 years	9	76.2	16.9
6-10 years	24	79.8	21.7
11-20 years	45	72.8	15.1
21-30 years	36	71.9	16.7
31-40 years	4	64.5	10

It was observed that the mean levels of SGPT levels are high (79.8) in those subjects who had history of consumption of 6-10 years of duration.

TABLE-7 Quantity of alcohol intake vs ALT levels

Quantity of alcohol intake	N	Mean	Std Deviation
< 90 ml	6	76.00	21.27
90-180 ml	16	80.56	15.98
181-360	10	81.20	16.89
361-540 ml	23	73.13	14.78
541-750 ml	23	68.65	15.00
>750 ml	40	72.13	19.24

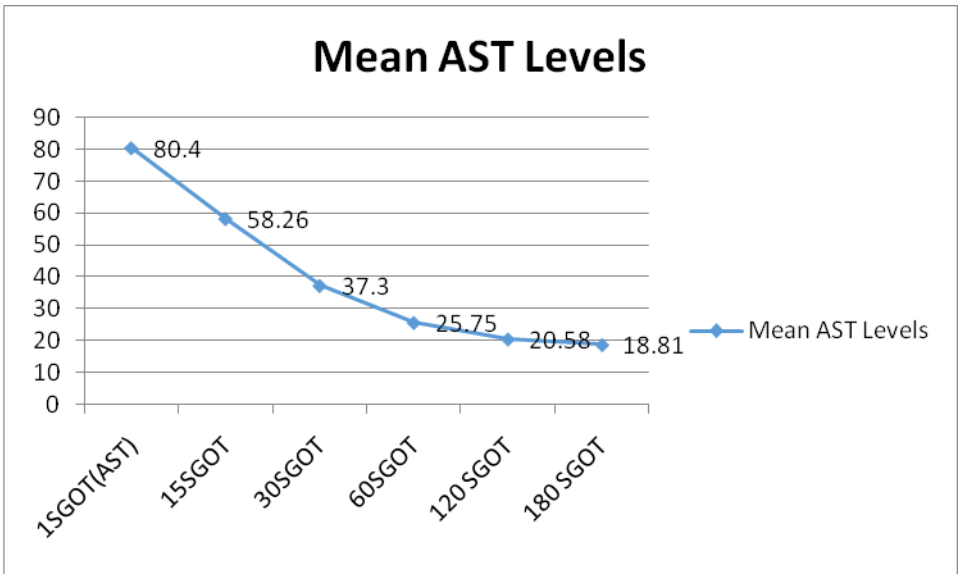
In the present study the mean ALT levels are maximum in those subjects who consume more than 180 ml per day.

TABLE-8 QUANTITY OF ALCOHOL INTAKE VS AST LEVELS

Quantity of alcohol intake	N	Mean	Std Deviation
< 90 ml	6	84.67	26.38
90-180 ml	16	87.13	23.60
181-360	10	89.1	21.18
361-540 ml	23	78.83	15.61
541-750 ml	23	77.04	22.18
>750 ml	40	77.73	19.66

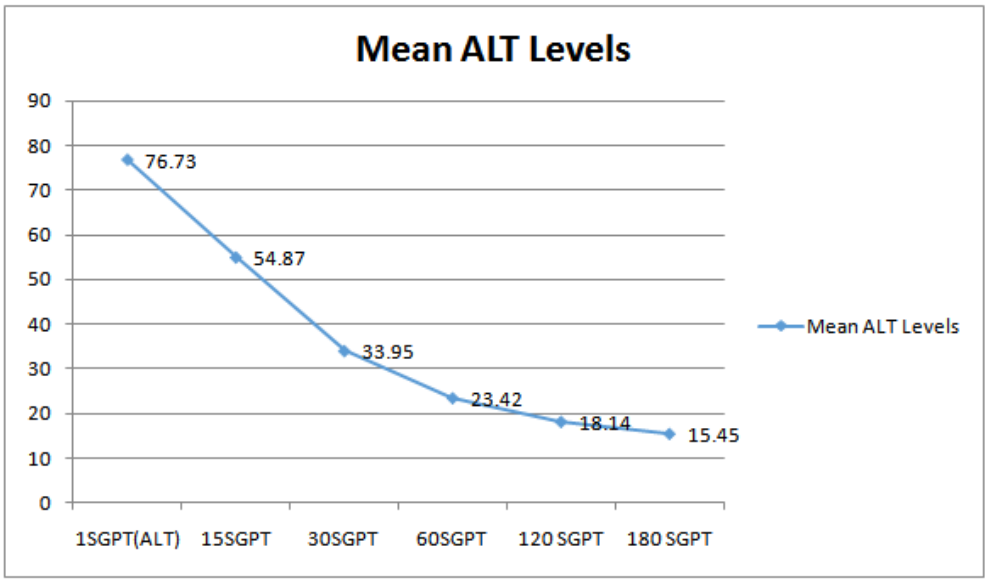
In the present study majority of the subjects consume more than 500ml of alcohol per day .Nearly 30% of the subjects consume more than 750 ml per day.

FIGURE-4 ANALYSIS OF AST LEVELS AT Various intervals after abstinence of alcohol.



In the present study the mean AST levels come down with the increase in the duration of abstinence. When multivariate analysis was done to to test whether there is statistical significance in between the means and it was found to be statistically significant with F value of 173.457(Wilks Lambda).

FIGURE-5 Analysis Of Alt Levels At Various Levels Of Abstinence Of Alcohol



In the present study the mean ALT levels come down with the increase in the duration of abstinence. When multivariate analysis was done to to test whether there is statistical significance in between the means and it was found to be statistically significant with F value of 200.358(Wilks Lambda).

TABLE-9 SGOT levels reaching normalcy in the study subjects

SGOT Levels	Frequency	Cumulative Frequency	Cumulative percent
SGOT 0	0	0	0
SGOT 15	1	1	1.2
SGOT 30	38	39	46.4
SGOT 60	37	76	90.5
SGOT 120	5	81	96.4
SGOT 180	1	82	97.6

AST levels were analyzed at various intervals .In the present study it was observed that nearly 46% of the subjects reached normal values after 30 days of abstinence. By 60 days more than 90% of the subject have attained normal AST levels. In the present study 38 (45.2%) subjects have attained within normal levels of SGOT after 30 days of abstinence. Majority of the study subjects(90.5%) reached normal AST levels by 60

days. 97.6 % of the subject attained normal levels by 180 days .2 subjects did not attain the normal levels by 180 days.

TABLE-10 Distribution of subjects according to attaining normal ALT Levels

SGPT Levels	Cumulative frequency	Cumulative frequency	Cumulative Percent
SGPT 0	15 (17.8)	15	17.8
SGPT 15	6 (7.14)	21	25
SGPT 30	9 (10.71)	30	82.1
SGPT 60	50 (59.52)	80	95.2
SGPT 120	3 (3.57)	83	98.8
SGPT 180	0	83	98.8

In the present study majority (95%) of the study subjects attained normal ALT levels. However one subject did not attain normal levels even after 180 months. Nearly 60% of the subjects attained normal levels on 60th day of abstinence.

IV. Discussion

The present study was conducted at a Tertiary care centre, Visakhapatnam. The institute has been maintaining a de addiction ward. It is a referral centre for surrounding districts of Andhra Pradesh. With increase in number of alcohol dependent patients attending the de addiction centre for treatment, a study was planned to assess the biomarker levels of alcohol dependant patients attending this centre.

A total of 118 subjects who met both inclusive and exclusive criteria following ICD -10 criteria have been included in the study.The study was done for a period of one year.During the first 6 months all new patients attending the de addiction centre have been enrolled and were followed up for the next 6 months. Biomarkers were analysed at 0, 15, 30, 60,120 and 180 days and the results have been tabulated.

On visit to de addiction centre all new patients will be admitted and retained in the ward for a period of 30 days. In our study all the 118 patents enrolled were tested for liver enzymes on 0, 15 and 30 days and then followed up further after they were discharged . Counselling during admission was done and all the subjects were followed up by taking the contact mobile numbers of the individuals as well as the relatives of the subjects. Out of 118 finally 84 patients regularly came to de addiction centre and were analysed for liver enzymes. The remaining subjects were lost to follow up.

In the present study the mean age in years of the study population is 38.5 years. Mean age of initiation of alcohol intake is 21.3 years. Mean duration of alcohol intake is 17.2 years. (Table-1,Fig 2 & 3) Our study coincides with the results in a study on associates of severity of alcohol dependence by **Ranjana Tiwari et al**[1] it was observed that early drinking onset was found to be associated with increased severity of alcohol dependence .Their mean age is 38.5 years. In a study on analysis of patients admitted with alcohol dependence syndrome in a tertiary care hospital in a calendar year by **Nishanth J et al**[2] the mean age of the patients was 44.34 years.According to **Unnikrishnan ,Reghukumaran Nair, K. Vidhukumar, Anil Prabhakaran**[3] there was a significant linear decline in the age at onset of alcohol use and use disorder. The mean age at onset of alcohol use and alcohol use disorder declined from 24 to 17 years and 46 to 21 years, respectively, from the pre‐ 1950 birth cohort to the post‐ 1985 birth cohort.

AGE Nearly 50% of the subjects belong to 30-40 years age group, followed by age group between 40 and 50 years(32.2%)(Table-2) . In a study conducted by **Vineykumar et al**[4] on alcohol dependence in Rohtak Haryana observed that majority of the subjects are from rural background and are in the age group of 26-45(63%) years of age. In a study on Socio demographic psychosocial aspects of male alcoholics in a suburban area of Nagpur conducted **by Deshmukh Deepanjali et al (2014)**[5] out of total participants 42% of the patients were in the age group of 35-45 years of age, 26 %of the participants were of the age more than 45 years age group. In a study conducted by **R. CHANDRASEKARAN, B. SIVAPRAKASH & V. CHITRALEKA**[6] where 800 patients (796 (99.5%) men and 4 (0.5%) women] with alcohol dependence were treated in the de-addiction centre over a period of 5 years from 1995 to 1999. Mean age was 39.7 (8.66) years. Majority (44.4%) of the patients belonged to the 35-44 yr. age group.

Socioeconomic Classification: When occupation of the subjects were analysed according to modified Kuppuswami classification majority(34.7%) of them were semiskilled workers and majority of them had income more than Rs 10,000 per month.67 subjects belong to Upper lower class(fig- 1). Our results were similar to a study conducted by **R.Chandrasekharan et al**[6],based on the socio-economic status scale (Kuppusamy), majority of patients belonged to the upper lower (IV) and lower (V) socio-economic classes (35.9% and 29.1% respectively). 42.5% of the patients had been referred by physicians, while 52.5% were brought by family members and friends.

In a study conducted by **Ruma Dutta et al (2014)**[7] the mean age of the study participants was 37.20 years. The current study show that most of the adults belonging to low socio-economic status showed a higher rate (46%) of alcohol consumption compared to adults belonging to medium and high socio-economic status (31%). There was also a higher consumption rate among the less educated (39%) when compared to higher educated adults (28%).The results of the present study showed that the mean age of the consumers at the initiation of consuming alcoholic beverages was 20.5±5.7 years, which is considerably low. Overall, the age range at initiation of drinking was 20-29 years as found in different studies, despite the wide differences among regions, populations, and years of studies

Initiation of alcohol intake : As in many studies the age of initiation of alcohol intake was 64% in subjects less than 20 years of age(fig-2). Nearly 90 % of the subjects had initiation of alcohol in less than 30 years age group. In a study conducted by **Unnikrishnan et al**[3] had shown a significant linear trend in the decline of age at onset of alcohol use and alcohol use disorder. The mean age at onset after 1985 cohort was 17 years. This was comparable to the Global Burden of Disease Study in 2010, which showed a decline in the average age of initiation of alcohol use from 28 in 1980s to 17 in 2007, in terms of absolute time periods. The changing social norms and growing acceptability of alcohol, increased accessibility and availability, and continuous growth in disposable income (per capita income) might have contributed to the declining trend in the age of initiation and alcohol dependence. A younger age of alcohol initiation was strongly related to a higher level of alcohol misuse at the age of 17–18, although this transition is mediated by the effects of parent drinking, proactive parenting, peer alcohol initiation, and ethnicity.

Quantity of alcohol intake; Consumption of alcohol was found to be high among the study subjects (Table-3). Majority of the subjects (more than 50%) were consuming more than 500 ml per day. On analysis of frequency of alcohol intake it was observed that 90% of the subjects had the habit of daily consumption of alcohol. In the present study nearly 73% of the subjects consume more than 500 ml of alcohol per day. Out of them nearly 34% of the subjects consume more than 1 full bottle i.e > 750 ml per day.

Frequency of alcohol intake: In the present study analysis was done pertaining to frequency of intake of alcohol per day and it was observed that nearly 90% of the subjects consume alcohol daily and remaining 10% consume more than five days per week (Table-4). On further analysis of alcohol intake according to number of occasions per day 28% of the subjects consume for more than five occasions per day followed by 46 % who consume 2-5 occasions per day. In a study conducted by **Nishanth et al**[2] 100% of the sample reported high frequency of drinking more than 5 days per week or 7 days in most of the patients. These results show that majority of the patient have the habit of heavy drinking.

Duration of alcohol consumption.

Majority of the subjects (65%)in our study consume alcohol for more than 10 years.

It was observed that 38% of the subjects consume alcohol for between 11-20 years and 30.5% of the subjects consume between 20-30 years (fig-3) .In the study conducted by **Nishanth et al**[2] majority of the subjects(54.4%) consume alcohol for 10-30 years.

Our study results were nearer to the study conducted by **Dr Walter A**[8] where 60% of the patients were consuming for a period of 10 – 14 years and 40 % of the subjects were consuming for a period more than 14 years. In a study conducted by **Dr R.Chandrasekharan et al**[6] the mean duration of daily intake of alcohol was 9.7+ 7.6 years. Evaluation of coagulation parameters and liver enzymes among alcohol drinkers in Port Harcourt, Nigeria International Journal of General Medicine 2013:6 489–494.Two hundred adults (120 alcoholics and 80 age and gender matched non Alcohol) aged 25–65 years (mean age 45.25 ± 11.50) were enrolled in this study. Of the 120 chronic alcohol drinkers, 37 were dependent on local dry gin while 83 were dependent on other alcoholic beverages. Duration of alcohol intake among the subjects ranged from 3–30 years.

Liver enzymes:

The most common enzymes analysed in alcohol dependant patients are ALT,AST and GGT. In our hospital the biomarkers analysed for alcohol de addiction patients were AST and ALT.

AST: ALT ratio The ratio of AST to ALT is of use in Wilsons disease ,CLD and alcohol liver disease. Abstinence from alcohol improves this ratio.

As various studies have shown that AST and ALT were better indicators of alcohol dependent patients which were found to be liver specific have been analysed in our study. The mean AST/ALT ratio was found to be 1.09 with a range of 0.59 to 1.62. The normal values considered in our laboratory are AST levels of 5-34IU/l and ALT levels are 0-50IU/L.When duration of alcohol intake was analysed in relation to liver enzymes it was

observed that with the increase in duration of alcohol intake i.e subjects with more than 10 years of alcohol intake the mean levels of AST are coming down.

In the study group 55% of the subjects had AST:ALT ratio more than 1.The distribution value of AST:ALT ratio was found to vary according to the drinking pattern of the study subjects. In a study conducted by **Dr Walter et al**[8] it was observed that most of the patients (40%) had a SGOT/ SGPT of more than 2. This was followed by 36% of the patients having SGOT/SGPT ranging between 1 and 2. Only 24% of the patients had SGOT/SGPT below 1.

According to **Robert Oshea**[9] No single laboratory marker definitively establishes alcohol to be the etiology of liver disease .Furthermore, alcohol may be one of a number of factors causing liver injury, and the specific contributory role of alcohol alone may be difficult to assess in a patient with multifactorial liver disease. A number of laboratory abnormalities ,including elevated serum amino transferases, have been reported in patients with alcoholic liver injury, and used to diagnose ALD. Serum Aspartate amino transferase (AST) is typically elevated toalevelof2-6 times the Upper limit.

So normal in severe alcoholic hepatitis .Levels of AST more than500IU/L or an Alanine aminotransferase (ALT) 200 IU/L are uncommonly seen with alcoholic hepatitis (other than alcoholic foamy degeneration, or concomitant acetaminophen overdose), and should suggest another etiology. In about 70% of patients, the AST/ALT ratio is higher than 2, but this may be of greater value in patients without cirrhosis. Ratios greater than 3 are highly suggestive of ALD.

In a study conducted on male alcoholism-Biochemical diagnosis and effect of abstinence by **R.Ray et al**[10], revealed that mean values of GGT, GOT and GPT were significantly higher among the alcoholics as against the controls. GGT was elevated (above lab. normal range) among 47% of alcoholics and 3% of controls, GOT was elevated among 60% of alcoholics and 40% of controls and GPT was high among 35% of alcoholics and 16% of controls. Values of biochemical tests after one month's abstinence showed that , GOT, GPT, and GGT which were elevated admission showed significant decline.

According to **Gavin Artee et al**[14] for habitual alcohol consumption (more than 50 g/day with liver injury), aspartate transaminase (AST) is more sensitive (50% sensitivity) than alanine transaminase (ALT) (35% sensitivity) but ALT elevation is a little more specific (86% specificity) than AST elevation (82% specificity). Almost all patients will have elevation of AST ,ALT with both below 300 IU/ml. When the AST:ALT ratio is greater than two, the most likely diagnosis is ALD; in some studies, more than 80% of patients reach this ratio. Elevation of g glutamyltransferase (GGT) is more sensitive (70%) but less specific (65–80%) than elevation of AST or ALT for excessive alcohol consumption. Because GGT is ubiquitous in many organs and drugs that induce the microsomal enzymes cause GGT elevation, the specificity of GGT elevation is limited.

In a study conducted by **Subir Kumar Das and D.M.Vasudevan**[15] "BIOCHEMICAL DIAGNOSIS OF ALCOHOLISM" Department of Biochemistry, Amrita Institute of Medical Sciences, Kerala, Indian Journal of Clinical Biochemistry, observed that the ratio of Aspartate amino transferase (AST) to Alanine amino transferase (ALT) in serum may help in the diagnosis of some liver diseases. The entire study groups showed a significant alteration in comparison to normal healthy individual (1.04 ± 0.03). A significant reduction was observed in non alcoholic liver disease group (0.8 ± 0.02), whereas significant increases were observed in alcoholic liver disease groups with both moderate (1.16 ± 0.02) and heavy (1.5 ± 0.04) alcohol intake. Alcoholic liver disease group with heavy alcohol (ALDH) intake showed significant elevation in the AST/ALT ratio in comparison to alcoholic liver disease with moderate alcohol intake (ALD-M) group.

High AST, ALT suggest liver cell damage Both Aspartate aminotransferase (AST) and ALT are normally present in serum at low levels, usually less than 30 to 40 U/L. Although the actual values may differ from laboratory to laboratory, normal serum levels are usually less than 40 U/L for AST and less than 50 U/L for ALT. On the other hand, some experts have suggested lowering the upper limit of normal because of the increasing rate of obesity and associated non alcoholic fatty liver disease, which may not be detected using the traditional, higher normal values. Acceptance is growing for using ALT levels less than 40 U/L in men and less than 31 U/L in women, and AST levels less than 37 U/L in men and less than 31 U/L in women, as normal thresholds. Although ALT is present in several organs and in muscle, the highest levels are in the liver, which makes this enzyme a more specific indicator of liver injury. Both AST and ALT are released into the blood in greater amounts when Hepatocytes are damaged.

In a study correlating the quantity and duration of alcohol consumption with liver function tests' by **Dr. Walter A, Dr. Mohammed Ashraf**[9]. Father Muller Medical College Hospital 42% of the subjects had elevated SGOT levels and 8% of the subjects had elevated SGPT levels. The SGOT to SGPT ratio in the study group was more than 2 in 40% of the subjects, 1 to 2 in 36% of the subjects and 24% of the subjects had the ratio less than 1. There was a statistically significant correlation between quantity of alcohol consumption and SGPT levels. Serum ALP level was elevated in 12% of the subjects in the study group.

Similar results were seen when duration of alcohol intake in relation to AST was analyzed.

Quantity of alcohol intake in relation to liver enzymes :It was observed that mean value of ALT decreases with quantity of alcohol intake. Similarly the mean levels of AST decreases with quantity of alcohol intake.
Effects of Abstinence on the Ability of Clinical Laboratory Tests to Identify Male Alcoholics **MICHAEL J. ECKARDT**[16] Initial laboratory values for these patients (mean ± SD) 8 ± 8 days (range: 1 -60) after their last drink showed mild elevations above the reference range for alkaline phosphatase, AST, ALT, glucose, MCV, and MCH.. Repeated laboratory values 27 ±11 days (range: 5-55) later showed statistically significant (P • <. 0.05; Hotelling's T2) reductions in total protein, cholesterol, total bilirubin, alkaline phosphatase, AST, ALT, MCV, MCH, and increases in phosphorus, creatinine, chloride, potassium, and number of WBCs.
In a study conducted by **Ray et al**[10] it was observed that , GOT, GPT, and GGT which were elevated at admission showed significant decline. Levels of SGOT at the time of admission were 29.5 ± 18.6 after 30 days 17.7 ± 9.4, level of SGPT at the time of admission were 20.3 ± 18.8 and after 30 days 12.2 ± 9.4 .

Abstinence of alcohol: In the present study 118 patients who met the inclusion and exclusion criteria have participated in the study out of them 84 patients were followed up, upto 6 months remaining 34 patients were lost to follow up .On attending the de addiction centre at our institute all the patients will be admitted in the de addiction centre for a period of one month. Analysis of the patients were done for liver enzymes and all the 118 subjects enrolled in the study were followed up till 30 days as they were inpatients .So in our study 29% lost to follow up .Hence 84 subjects were analysed for AST,ALT levels and effect of abstinence as they are continuously followed up for 6 months.
According to ACG practice Guidelines: Abstinence is the most important therapeutic intervention for patients with alcoholic liver disease. Abstinence has shown to improve the outcome of histological features of hepatic injury. It improves the survival at all stages in patients with ALD. This improvement is relatively rapid and in 66% of the patients abstaining from alcohol, significant improvement was observed in 3 months
Treatment setting and follow up in alcohol dependence by **Suveera Prasad ,pratima murthy**[11] Indian journal of Psychiatry,2000,42(4),387-392 out of 134 patients enrolled in the study 48 subjects lost to follow up. At 6 months 52.9 % maintained abstinence and remaining lost to follow up.
In a study conducted by **N.Kar et al**[12] all the patients were followed up for at least one year. The follow up was once every month for first three months after discharge and then once every 2 to 3 months. Patients missing appointments were communicated by letters. At the end of one year, complete follow up data were not available for 6 (10.0%) patients, so the outcome of these patients could not be commented. Based on global outcome different groups are considered . (46.7%) had complete abstinence, 5 (8.3%) had occasional social drinking which was not pathological and 21 (35.0%) had pathological drinking with more than 50% of days in the follow up period spent in drinking.
When and how to evaluate mildly elevated liver enzymes in apparently healthy patient in a study conducted by **George Aragon MD Zobair M**[13].Younoss Centre for Liver Diseases, Inova Fairfax Hospital, Falls Church, Department of Gastroenterology, George Washington University, Washington, a cross-sectional study has investigated the effects of chronic alcohol consumption on the liver enzymes and coagulation parameters in Port Harcourt, Nigeria. Liver enzymes such as AST, ALT, and GGT, which remain vital indicators of hepato cellular injuries possibly due to long-term alcohol dependence, were considered in this study. Except for the mean value of the ALT (10. 5 ± 7.7), which did not show any significant change (P . 0.05), the mean values of the AST (23.4 ± 19.7) and GGT (42.3 ± 23.8) showed a dramatic rise among the chronic alcohol drinking subjects compared with their nondrinking counterparts (P , 0.05). These increases in the various enzymes are consistent with previous reports which found the liver as the prime target for alcohol induced diseases. Similarly, a previous report in Ghana among 60 total abstainers, 56 social drinkers, and 100 alcoholics indicated that GGT and AST are sufficiently sensitive to detect chronic alcoholics and that the serum GGT and AST showed progressive rise with increasing alcohol intake.
As per the study of **Robert OShea**[9] fatty liver develops in about 90% of individuals who drink more than 60 g/day of alcohol, but may also occur in individuals who drink less. Simple uncomplicated fatty liver is usually asymptomatic and self limited, and may be completely reversible with abstinence after about 4-6 weeks. This improvement can be relatively rapid and in 66% of the patients abstaining from alcohol , significant improvement was observed in 3 months. A 6 month period of abstinence has been recommended as a minimal testing criterion. This time period allows chemical dependency issues to be addressed .
In a study conductd by **Gavin Arteal, Luis Marsano**[14] , life style changes including abstinence ,nutrition, drug therapy, role of liver transplantation all play a vital role in restoring normalcy of liver. Abstinence from alcohol is vital in order to prevent further ongoing liver injury, fibrosis and possible hepato cellular carcinoma. Abstinence causes resolution of alcohol steatosis. Eventhough studies are few, many studies show beneficial effects of abstinence.
In a five year follow up study conducted by R**. Chandrashkharan et al**[6] in a tertiary care center, which is report based on 800 individuals with an ICD-10 diagnosis of alcohol dependence syndrome who utilised the

services of this centre over a period of 5 years from January 1995 to December 1999 Of these 800 patients, 321 (40.1 %) received in-patient care. Follow-up data of 607 cases seen between 1995 and 1998 was analysed. 28 (4.6%) had attended follow-up for more than one year, while 48 (7.9%) had come for follow-up visits for 6-12 months. 152 (25.1%) patients attended follow-up for 1-6 months, while 379 (62.4%) patients dropped out from the follow-up clinic in less than a month.

Level of Liver enzymes in relation to abstinence.

However in various studies the relapse rates or period of abstinence is lessened in many cases. On analysis of SGOT (AST) levels periodically it was observed that the mean values on the day of admission was 80.40 with a SD of 20.5 and at 180 days the value was found to be 18.8 with a SD of 7.14(Fig-4).When multivariate analysis(ANOVA) was done for AST levels the F value is 270.45 and it was found to statistically significant $p<0.05$.So there is a significant difference between the mean levels of AST(table-9).

In the present study 38(45.2%) subjects have attained within normal levels of SGOT after 30 days of abstinence. Majority of the study subjects (90.5%) reached normal AST levels by 60 days. 97.6 % of the subject attained normal levels by 180 days .2 subjects did not attain the normal levels by 180 days. The 2 subjects in whom the SGOT levels did not reach normalcy were sent to Department of Gastroenterology, King George Hospital Visakhapatnam for further evaluation.

Similarly the SGPT levels analyzed at the same intervals periodically the mean value on day 1 was 76.73 with an SD of 18.83 whereas at 180 days it was found to be 15.45 with SD of 6.59.F value was 275.9 and was statistically significant which shows there is a significant difference between the means of ALT levels .(table-10) .Abstinence in India ranges from 36% according to Desai et al to 50% as per Kuruvilla .

In the present study majority(95%) of the study subjects attained normal ALT levels. However one subject did not attain normal levels even after 180 months. Nearly 60% of the subjects attained normal levels on 60th day of abstinence. However one patient did not achieve normal SGPT levels even after 180 days of abstinence hence he was sent for further evaluation to Department of Gastroenterology King George Hospital Visakhapatnam. So abstinence is an effective tool in bringing the AST/ALT levels to normalcy. Longer the period of abstinence better will be the liver enzyme levels. In the present study with increase in duration there is reduction in the mean AST/ALT level

V. Conclusions

1 .A sample of 118 have been enrolled in the study. Out of them 84 subjects have regularly attended the hospital for follow up. Remaining 34 subjects were lost to follow up. Mean age 38.5 years. Mean age of alcohol intake 21.3 years. Mean duration of alcohol intake 17.2 years.

2.49.2% are in the age group of 31-40 years. According to Kuppuswamy Socio economic classification nearly 57% belong to upper lower class.

3. Age of initiation of alcohol was seen in 11-20yrs (63.6%) of the subjects .Nearly 70% of them consume alcohol for more than 10 years. Daily intake was seen in many of the subjects.

4. The mean value of AST/ALT ratio was found to be 1.09.

5. Majority of the subjects reached normal range of AST levels after 30 days of Abstinence. Nearly 60% of them reached normal ALT levels after 60 days of Abstinence.

6. With increase in duration of abstinence the mean AST/ALT levels are reaching normal levels.

VI. Limitations Of The Study

1.As the study is was conducted in a tertiary care hospital it cannot be extrapolated to the general population.

2. Study has not dealt into the problems secondary to alcoholism.

3. Although were also Gama Glutamyl Transferase, Mean Corpuscular Volume, Serum Albumin etc taken as biomarkers for assessing alcohol induced liver damage, we have taken AST and ALT only as these are the only tests being done in this institute.

4. Non Pharmacological modes of treatments has not been included in the de addiction treatment.

5. De addiction drugs have not been included in our study.

VII. Recommendations and Future Directions

1. As this is a hospital based study , community based study may be planned to understand the real problems associated with alcoholism.

2. The study may be continued further so as to include all the patients and a larger sample may be taken for analysis.

3. To include biomarkers like Gama Glutamyl Transferase(GGT), Mean Corpuscular Volume, Serum Albumin etc

4. Counselling and deterrent agent (Disulfiram) should be a part of the study as they are shown to have better impact on the abstinence.

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