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Management of Alcohol Associated Liver Diseases by Using Aldactone and Ursokem.

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ABSTRACT:
Liver is the largest organ that aids in digestion and removes waste products. As it also helps in filtering out toxins ,where alcohol abuse will be the major cause for liver diseases. Alcohol accounts for approximately 1,00,000 deaths each year with nearly 20% of deaths attributable to Cirrhosis. Pathogenesis depend on factors such as variations in alcohol-metabolism etc…Diagnosis is based on raised serum markers such as gamma-glutamyl transferases, liver-biopsy. "Abstinence" is most vital aspect for treatment. The therapy includes Corticosteroids, antioxidants etc…In this study, we observed management of ALD using "Aldactone" and "Ursokem".As,Spiranolactone is an Aldosterone-receptor antagonist and K+ sparing diuretic, aldactone which plays a major role to relieve from symptoms.Spiranolactone has been linked to rare cases of clinically apparent drug-induced liver diseases also.As,Ursodeoxycholic-acid has multiple hepatoprotective activities,it therefore increases proportion of non-toxic hydrophilic bile acids.Prolong use of Ursokem has survival benefit of primary biliary cirrhosis and delay liver transplantation.Therefore,in this study risk factors and symptoms subside after using aldactone and ursokem drugs.

KEYWORDS: Alcoholic Liver Disease, Abstinence, Aldactone, Ursokem, Cirrhosis.

I. INTRODUCTION:

Alcoholic liver disease is a term that encompasses the liver manifestations due to alcohol over consumption which cause the liver to become inflamed and swollen. The liver is the largest solid organ in the body and is also considered as gland because among its many functions, it makes and secretes bile. Liver functions include filtering out blood toxins, storing energy, making hormones and proteins, and regulating cholesterol and blood sugar[(1)]. Some of the most common types of liver diseases include: Alcohol-related liver disease- Chronic alcoholism, Non-alcoholic fatty liver disease - Increased BMI, Hepatitis - HAV,HBV,HCV Virus, Hemochromatosis - Gene hereditary, Primary biliary cirrhosis - Caused by a improper functioning of immune system[(2)]. Causes include Idiopathy, Genetics, Polymorphisms in the enzymes ADH, CYP2E1, and ALDH, Acetaldehyde a toxic chemical that is produced by the body's break down of alcohol. Viral Liver Disease, Hepatotoxic Exposure, Hepatotoxins may act synergistically or additively with alcohol. This is especially true with acetaminophen and vitamin A overdose. Epidemiology is alcohol is used by approximately 75% of the population of the United States, with a 7% incidence of alcoholism. In addition, alcohol accounts for approximately 100,000 deaths in the U.S. each year, with nearly 20% of those deaths attributable to cirrhosis. Alcohol dependence and or abuse rates are higher for men than women and for non-blacks than blacks. Several factors have been proposed to explain the pathogenesis of alcoholic liver injury. These include variations in alcohol metabolism, Centrilobular hypoxia, Inflammatory cell infiltration and activation , Antigenic adduct formation. Signs and symptoms in early stage -Pain in the abdomen ,Nausea, vomiting ,Diarrhoea, loss of appetite are observed. At late stage –Jaundice, Edema of the lower limbs, Ascites, Clubbing, Loss of weight, Hematochezia(Bleeding in stools) ,Hematemesis.

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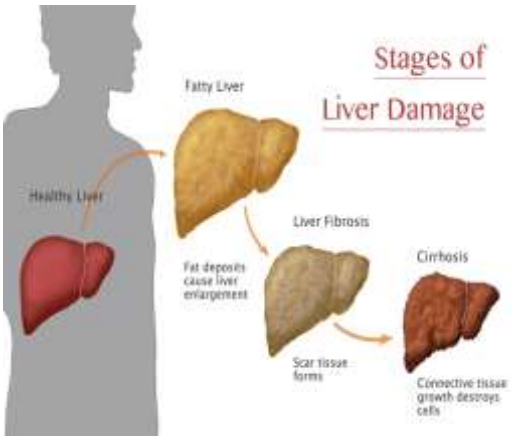

Alcoholic liver disease has four main stages: 1.Alcoholic Fatty Liver Disease **:**Steatosis, is an abnormal accumulation of fat in the parenchymal cells of the liver and can occur within hours of significant alcohol intake. Drinking a large volume of alcohol can cause fatty acids to collect in the liver. This stage of the disease is often reversible if the individual abstains from alcohol. 2. Alcoholic hepatitis**:** Continued alcohol use will lead to ongoing liver inflammation. This can occur after many years of heavy drinking. If the individual abstains from alcohol on a long-term basis, Alcoholic hepatitis is usually reversible[(4)]. 3. Fibrosis: It is a build-up of certain types of protein in the liver, including collagen. Mild-to-moderate forms of fibrosis may be reversible. Continuous fibrosis and inflammation can lead to liver cancer. 4..Cirrhosis : It occurs when the liver has been inflamed for a long time, leading to scarring and loss of function . As the liver no longer processes toxins properly, it will be more sensitive to medications and alcohol. Risk factors includes quantity of alcohol**,** Gender**,** Hepatitis–C Virus**,** Obesity, Malnutrition, Genetic profiles of particular enzymes such as ADH, ALDH and CYP4502E1 -- they will have a higher chance of developing alcoholic liver disease. Complications includes Smoking , high blood pressure, Internal bleeding, Encephalopathy, Ascites with associated kidney failure, Liver cancer. Diagnosis includes Biochemical Tests, Aminotransferases Levels**,** Gamma glutamyl transpeptidase levels**,** Hematologic and electrolyte abnormalities**,** Liver Biopsy, Ultrasound **,**Computerized Tomography[(5)]. Medications include Corticosteroids, Calcium Channel Blockers, Insulin, Antioxidant supplements, and S-adenylyl-L-methionine (SAMe). Liver Transplant is a treatment option for end-stage liver disease and acute liver failure, although availability of donor organs is a major limitation[(6)]. Aldactone is a aldosterone antagonist spironolactone, 17-hydroxy-7α-mercapto-3-oxo-17α-pregn-4-ene-21carboxylic acid γ-lactoneacetate. Tablet: 25mg, 50mg, 100mg .Oral suspension : 5mg/ml[(7)]. Spiranolactone is a renal competitive aldosterone antagonist that inhibits the effects of aldosterone.As,aldactone is effective in lowering the systolic and diastolic blood pressure in patients with primary hyperaldosteronism. It is also effective in most cases of essential hypertension [(8)]. Spironolactone is known as a "water pill" (potassium-sparing diuretic).Used to treat high blood pressure , heart failure and oedema. Used to treat hypokalaemia and conditions in which the body is making too much of a natural chemical (aldosterone)[(9,10)]. Side effects includes Drowsiness, Dizziness ,Stomach upset, Signs of kidney problems, Mental/mood changes, Unusual fatigue/ weakness, muscle spasms ,Menstrual period changes ,Breast pain, Gynecomastia in men [(11)]. Ursodeoxycholic acid is an epimer of chenodeoxycholic acid. Ursodiol is a synthetically-derived form of ursodiol produced by the liver and secreted and stored in the gallbladder. This agent dissolves or prevents cholesterol gallstones by blocking hepatic cholesterol production and decreasing bile cholesterol[(12)]. Tab: 250mg, 500mg.Cap:300mg. It reduces elevated liver enzymes by increasing bile flow. Ursokem is concentrated in bile and decreases biliary cholesterol by inhibiting intestinal absorption → Results in reduced cholesterol from gall stones→ Results in dissolution of gall stones. Used in Primary biliary cirrhosis, Alcoholic liver disease, Non-alcoholic steato hepatitis, Hepatic diseases, Used to relieve itching in pregnancy who suffer from obstetric cholestasis. Side effects includes Diarrhoea, Indigestion, Headache, Nausea or Vomiting, Back pain , Bloody and cloudy urine[(13)].

II. MATERIALS AND METHODS

STUDY DESGIN: A Prospective Observational study.

STUDY DURATION: The study was conducted in following six months duration that is from September 1st 2018.

STUDY SITE: The study was conducted at government hospital in Eluru, West Godavari district.

STUDY POPULATION: Study population size – 60.

SOURCE OF DATA AND MATERIALS:

Method of collecting data:

- Patient interview.

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- Patient Case note and Prescription.

Method of collection of material:

- Patient concert form.
- Patient Data collection form.

STUDY CRITERIA:

INCLUSION CRITERIA:

- Patients diagnosed with alcohol related liver diseases.
- Patients who are on Ursokem.
- Patients who are on Aldactone.
- Patients who are willing to participate in the study.

EXCLUSION CRITERIA:

- Women patients are excluded.
- Non alcoholic liver disease cases are excluded.

STATASTICAL ANALYSIS:

- Descriptive statistics such as frequencies and percentages were calculated for categorical variables.
- Mean (±) Standard Deviation were computed for continuous variables.
- Graphic representation like line graph and pie chart were used for visual interpretation to analyse the data.

III. RESULTS :

During the six months of study period from September 2018 to February 2019, we have evaluated 60 patients with diagnosis of alcohol associated liver diseases in male medical ward in government hospital, Eluru .In this study risk factors like age , diseases state , drug action and about symptoms subsided after drug action are collected from the 55 patients. They were analyzed and the following demographic details were obtained. The study composed of n=55 alcohol associated liver diseases patients the various observations are made as follows:

Table 1: Age factor of patients who are involved in the study.

Age	No. of patients	(%)percentage of Pts
21-30	3	5%
31-40	18	33%
41-50	18	33%
51-60	14	25%
61-70	1	2%
71-80	1	2%

•MEAN VALUE: 9.16

•STANDARD DEVIATION: 34.02

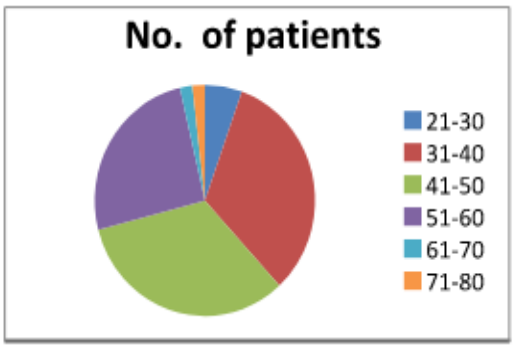

Fig 1: Out of 55 patients were 5% were in between age of 20-30,33% were in between age of 31-40%.33% were in between 41-50.25% were in between age of 51-60.2% were in between age of 61-70.And another 2% were in between age of 71-80 and the mean deviation value is 9.16 and standard deviation value is 34.02.The most prominent age group was effected due to alcohol associated liver diseases is 31-50years.

Table 2: Diseased state of the patients considered in the study.

	In COL pts	%COL	In ALD pts	% ALD	In ALH pts	%ALH
Jaundice	7	21%	2	12%	3	60%
Ascites	25	75%	6	35%	1	20%
Portal hypertension	6	18%	0	0%	0	0%
Hepatic encephalopathy	3	9%	4	23%	1	20%
Pedal edema	5	15%	3	18%	2	40%
Hepatomegaly	4	12%	5	29%	2	40%
Splenomegaly	6	18%	5	29%	1	20%
Hepatic renal syndrome	4	12%	1	5%	0	0%

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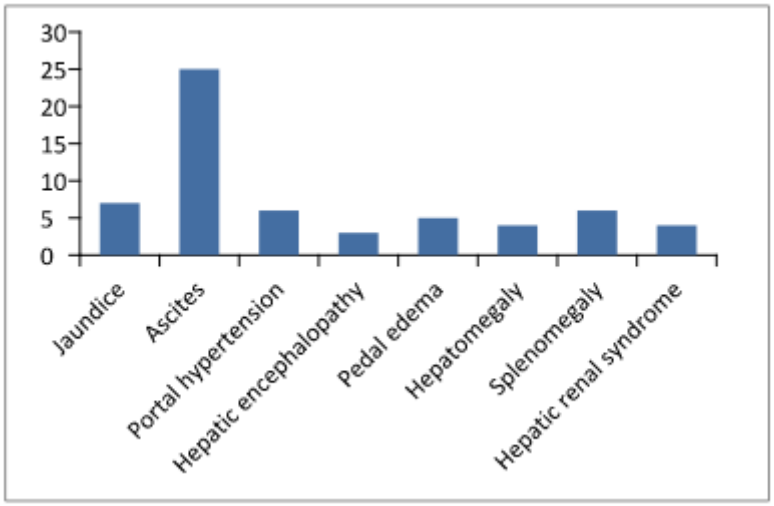

Fig 2 : With respective to the disease state of patient were diagnosed with icterus, out of 55 patients in case of cirrhosis 21.2% were effected, in case of ALD 12% were effected and in alcoholic hepatitis 60% were effected. In case of ascites condition 75% were effected in cirrhosis of liver 35% were affected in ALD and 20% were effected in alcoholic hepatitis. In case of portal hypertension 18% were affected in cirrhosis of liver. In case of hepatic encephalopathy 9% were effected in cirrhosis of liver 24% were affected in ALD and 20% in alcoholic hepatitis. In case of pedal edema 15% were effected in cirrhosis of liver 18% were effected in ALD and 40% were effected in alcoholic hepatitis. In case of hepatomegaly 12% were effected in cirrhosis of liver 30% were effected in ALD and 40% were effected in alcoholic hepatitis. In case of splenomegaly 18% were effected in cirrhosis of liver 29% were effected in ALD and 20% were effected in alcoholic hepatitis. In case of hepatorenal syndrome 12% were effected in cirrhosis of liver 5% were effected in ALD.

Table 3: Action of drugs prescribed for the selected patients.

Disease	URSOKEM	URSOKEM %	ALDACTONE	ALDACTONE%	BOTH	BOTH%
COL	6	18%	7	21%	17	52%
ALD	6	35%	4	24%	3	18%
ALH	1	20%	3	60%	0	0%

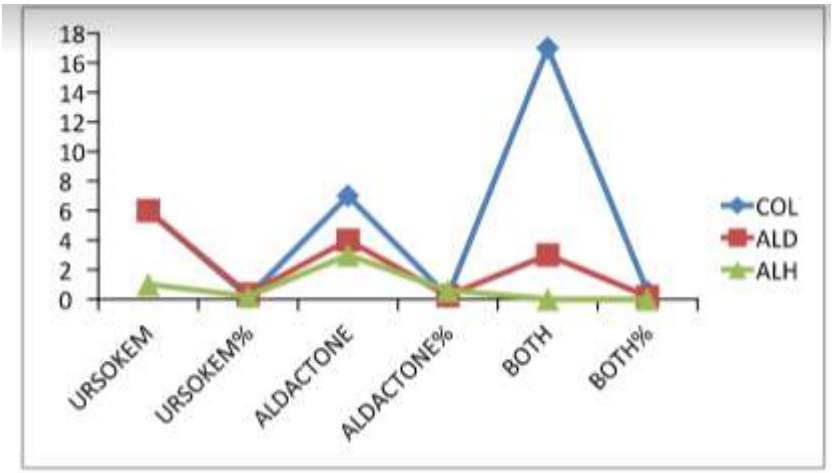

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Fig 3: In case of cirrhosis of liver 18% were using ursokem, 21% were using aldactone and 52% were using both. In case of alcoholic liver disease 35% were using ursokem, 24% were using aldactone and18% were using both. In case of alcoholic hepatitis 20% were using ursokem 60% were using aldactone.

Table 4: Symptoms subsided after drug use.

SYMPTOMS	COL pts	COL %	ALD pts	ALD %	ALH pts	ALH%
ICTERUS	4	57%	1	50%	3	100%
ASCITES	10	40%	4	67%	0	0%
PEDAL EDEMA	4	80%	3	100%	2	100%
SPLEENOMEGALY	4	67%	4	80%	0	0%
HEPATOMEGALY	2	50%	4	80%	1	50%

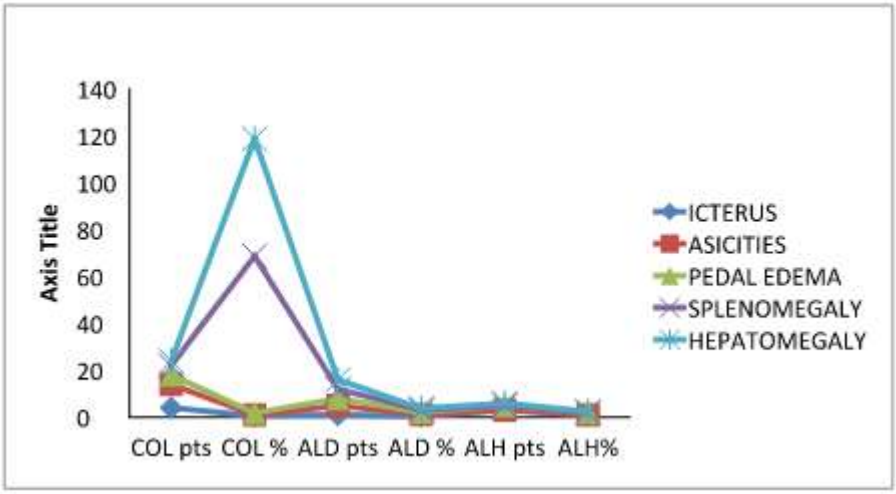

Fig 4: In case of cirrhosis of liver 57%, 50%in alcoholic liver disease and 100% in alcoholic hepatitis were relieved from icterus by using ursokem. In case of cirrhosis of liver 40%,67% in alcoholic liver disease were relieved from ascites by using spironolactone. In case of cirrhosis of liver 80%,100% in alcoholic liver disease and 100%in alcoholic hepatitis were relieved from pedal edema by using medication. In case of cirrhosis of liver 67%,80% in alcoholic liver disease were relieved from spleenomegaly by using medication. In case of cirrhosis of liver 50%,80% in alcoholic liver disease and 50% in alcoholic hepatitis were relieved from hepatomegaly by using medication.

IV. DISCUSSION

- We have evaluated 55 male patients for the study on alcohol associated liver diseases. The present study shows a much higher incidence rate of liver diseases in males than females.
- A hospital based study reported the age for onset of liver disease is 33 years which is comparable to our present study. The most prominent age group was 31-50years as high risk factor for liver disease. (according to table 1 & fig.1)
- Out of 55 patients selected for the study, 22% of COL patients had Jaundice 75% of COL patients of ascites, 18% COL patients of portal hypertension and splenomegaly each, 15% COL of pedal edema, 12% COL patients of hepatomegaly, 9% COL patients of hepatic encephalopathy. (Which are explained in table no. 2 & fig no.2)
- No patients were found to be having portal hypertension in alcohol liver disease.
- Drug of choice is Ursokem and Aldactone .

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- Among ALD patients, 35% were treated with Ursokem, 24% were treated with Aldactone and 18% were treated with both the drugs.(explained in table no. 3 & fig no.3)
- Among alcoholic hepatitis patients, 20% were treated with Ursokem, 60% were treated with Aldactone. Remaining 20% were treated with other than these drugs. (present in above table no. 3 & fig no.3)
- Among the COL patients 57% were relieved from the symptoms of jaundice, 40% were relieved from ascites, 80% were relieved from pedal edema, 505 were relieved from hepatomegaly, 66% were relieved from splenomegaly on using the drugs.(mentioned in table no .4 & fig no.4)
- In ALD patients, 50% were relieved from symptoms of jaundice, 66% were relieved from ascites, 80% were relieved from spleenomegaly and 80% from hepatomegaly and 100% were relieve from pedal edema.(Mentioned in above table no. 4 & fig no.4)

V. CONCLUSION

Over alcohol consumption is the leading cause of death, long term disability in adults worldwide and have a great impact on public health . Alcohol associated liver diseases is recurring and is more often disabling than fatal. Through our study we can conclude that the risk factors of liver diseases due to alcohol. The risk factors include jaundice, ascites, portal hypertension, hepatic encephalopathy, pedal oedema, hepatomegaly, splenomegaly, heapato renal-syndrome. The most prominent age group was found to be 31-50years. The drug management with aldactone and ursokem was observed in the conditions of alcohol associated liver diseases such as (cirrhosis of liver, alcoholic liver disease, alcoholic hepatitis) .And observing that weather symptoms are relieved by use of these drugs. As more than 50% of study subjects were not aware regarding common risk factors and warning symptoms of alcohol associated liver diseases, there is a need to develop health education modules, programs to improve awareness of alcohol associated liver diseases. The patient should be given proper counseling regarding over alcohol consumption.

Data Availability

Data were extracted from the clinical and treatment data base. Rare data can be supplied. The data used to support the findings of this study are available from the corresponding author upon request.

Ethical Approval

The study was approved by the local Institutional Ethics Committee .

Conflicts of Interest

The authors declare no conflicts of interest.

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