Assessment and Comparison of Outcome in Different Treatment Groups of Alcoholic Liver Cirrhosis Patients

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Abstract - In worldwide(2010), alcohol liver cirrhosis causes half a million deaths accounting for 50% of all cirrhosis related mortality. In India leading cause of liver cirrhosis is excess alcohol consumption. Survival rate of liver cirrhosis can be increased through abstinence. Abstinence reduces the liver complications like Ascites, Hepatic encephalopathy, Portal Hypertension. Abstinence can achieve through counseling and deaddiction therapy. A Prospective observational study was carried out for a period of six months in gastroenterology department and a counseling centre located in Telangana state to find out how far the counseling and deaddiction therapy maintained abstinence. The main aim of the study was to assess and compare the outcomes in alcoholic liver cirrhosis patients in different treatment groups. A total of 150 patients were divided into three groups; group1,group 2, group 3 according to treatment regimen. Group1received only symptomatic treatment. Group2 received symptomatic treatment + counseling and group3 received symptomatic treatment, counseling and deaddiction therapy using Baclofen. Outcome was assessed by the improvement of child Pugh score after 3 months of treatment. We found that compared to group 1 and group2, group3 have shown highest improvement of child Pugh score and had highest expected survival rate. It concluded that only counseling may not be effective to maintain the abstinence. Counseling along with deaddiction therapy (Baclofen) is effective in maintaining the abstinence and reducing the relapse rate in alcoholic liver cirrhosis patients.

Key Words: Alcoholic liver cirrhosis, Child Pugh score, Survival rate

I. INTRODUCTION

Liver cirrhosis is an irreversible damage to liver causing parenchymal necrosis, regeneration and fibrosis diffusion resulting in lobular architecture disorganization through the liver .The normal lobular architecture is lost and form islands and nodules called pseudo lobules1. It is diagnosed by examination or laboratory parameters such as coagulopathy, hypoalbuminaemia and hyperbilirubinaemia. Coagulopathy occur normal function of liver is lost to produce the clotting factors.Hypoalbuminaemia occurs when hepatocytes decreased the synthesis of albumin. Hyperbilirubinaemia occurs when there is an insufficient conjugation of bilirubin; unconjugated bilirubin rises in blood stream. Ultrasound imaging of liver may show features of cirrhosis[2]. Alcoholic liver cirrhosis has the complications like portal hypertension, varices, ascites and hepatic encephalopathy3. The most important clinical feature of portal hypertension are the development of varices due to the alternative routes of blood flow from the portal to the systemic circulation; bypassing the liver. Ascites is the pathological accumulation of lymph fluid with in the peritoneal cavity. Hepatic encephalopathy can be defined as central nervous system disturbance with a wide range of neuropsychiatric symptoms associated with hepatic insufficiency and hepatic failure3. Alcohol is a legal drink, readily available and cheap. Its consumption is well entrenched in the social fabric of many adult populations and virtually consumed as a behavioral norm[4]. Alcohol is consumed in most regions of the world; two billion people worldwide consume alcoholic beverages. It is estimated that 76.3 million have a diagnosable alcohol use disorders by World Health Organization[5]. It is a leading cause of liver disease. It is responsible for over 2.5 million deaths every year and alcoholic liver disease (ALD) accounts for a large portion of alcohol related morbidity and mortality[6]. Data showed, in France mortality rate for ALD was 14.3 per 100 000 population and in United States 7.9 per 100 000[4]. Liver cirrhosis mortality in the world is 23.54% and it ranks 27th as a cause of death in the world[1].In 2010, alcohol cirrhosis caused half a million deaths worldwide, accounting for 50% of all cirrhosis-related mortality[6]. In United States, cirrhosis caused 26,000 deaths; among them 44% deaths are from alcoholic cirrhosis. Recent data reveals that alcohol cirrhosis

survival rate is between 23 to 50%[7].In India leading cause of liver cirrhosis is excess alcohol consumption. The exact prevalence of alcohol cirrhosis is not known because the disease is often silent1. A review of Indian studies of biopsy-proven cases of liver cirrhosis from 1933-1975 found cumulative mean of 16% of patients with alcohol dependence. However, in recent prevalence of alcohol related cirrhosis is increasing.In recent study conducted inKerala, alcohol consumption was the major cause for cirrhosis in 60% patients2.According to WHO, alcohol percentage in different types of alcoholic beverages are: Brandy 40-50%, Whisky 40-55%, Rum 40-55%, Wine 10-22%, Beer 4-8%, country liquor 50-55%.Fibrosis diffusion starts in perivenular area and is influenced by amount of alcohol ingested. Periventricular fibrosis and deposition of fibronectin occurs in 40-60% of patients who ingest more than 40-80g/day for average of 25years7.Although alcohol dependence and development of liver cirrhosis depends upon the genetic and dietary habits[2], even lesser amount of alcohol and lesser duration of alcohol consumption can cause alcohol cirrhosis , this has been thought to be the genetic polymorphisms of genes responsible for alcohol metabolism like ADH, ALDH, CYP2E1 and gene responsible for inflammatory cytokine production like TNF-α and IL-10[8]. Although alcohol liver cirrhosis is an irreversible damage to the liver9, survival rate can be increased through abstinence10,11,12. Abstinence is the corner stone of the therapy13.Abstinence can be achieved through brief interventions like counseling14 and deaddiction therapy like baclofen15,16.The survival rate of the alcoholic liver cirrhosis can be estimated by the prognostic factor like child Pugh score. It is used in the survival prognosis in the liver cirrhosis condition before and after treatment.The score evaluates five parameters: ascites, encephalopathy, bilirubin, prothrombin time and albumin as shown below17.

Table 1 : Child Pugh scoring[3]:

Score:	1	2	3
Bilirubin(mg/dl)	1-2	2-3	>3
Albumin(mg/dl)	>3.5	2.8-3.5	<2.8
Prothrombine Time	1-4	4-6	>6
Ascites	None	Mild	Moderate
Encephalopathy	None	1 and 2	3 and 4

Classification of child Pugh used to evaluate the degree of liver failure in patients with cirrhosis. It has three stages according to the score from the points on continuous 5-15 points scale.The total score classifies patients into grade A, B, C which depend upon the ascites, encephalopathy, jaundice, serum albumin, and prothrombin time17

Table 2 : Classes of child Pugh score

	One year survival	Two year survival
Class A :<7 points	100%	85%
Class B :7-9 points	81%	57%
Class C:10-15 points	45%	35%

II. AIM AND OBJECTIVES

Aim: To assess and compare the outcomes of Alcoholic liver cirrhosis patients in different treatment group by using child Pugh score.

Objectives: To determine the prevalence of alcoholic liver cirrhosis.

To assess the pattern of experience in Alcoholic liver cirrhosis.

To study the therapeutic management of Alcoholic liver cirrhosis patients.

To assess and compare the outcomes of Alcoholic liver cirrhosis in different treatment groups.

To assess the life expectancy of different treatment groups by using Child Pugh score.

III. METHODOLOGY

A prospective observational study was conducted in two individual clinics. One is a private gastro clinic consists of out-patient department only and OP strength is 50-100 patients/day. Second clinic is a psychiatric counseling centre located at Warangal which provides the counseling and treatment for alcohol, smoking, chewed tobacco addicted patients and psychiatric patients. It also an out-patient department with the OP strength of50-60 patients/day.The study has been carried out for 6 months. Patients diagnosed with Alcoholic Liver cirrhosis, with the age >18yeras and both genders were considered for inclusion, Alcohol intake of >30g/day for males and >20g/day for females were considered for inclusion criteria. Patients along with other liver disease like viral hepatitis are excluded from the study. The data was collected from the patients review records and from direct communication with patients and their care takers. Data collected includes demographics, other pertinent clinical data like past medical history, laboratory data for serum bilirubin, albumin levels and Prothrombin time. Patients who filled and signed informed consent forms were only included in the study. Complete data was collected in a specially designed data collection form. Study population

was dividedinto three groups (50 patients in each group) according to their treatment regimen as mentioned below.

Group: 1 Patients receiving treatment of drugs like Ursodeoxycholic acid 300mg, Propranolol 40 mg, Diuretics (Spironolactone 50 mg and Furosemide 20 mg) without counseling and deaddiction therapy.

Group:2 Patient receiving treatment of drugs like Ursodeoxycholic acid 300mg, Propranolol 40 mg, Diuretics (Spironolactone 50 mg and Furosemide 20 mg) along with counseling.

Group:3 Patient receiving treatment of drugs like Ursodeoxycholic acid 300mg, Propranolol 40 mg, Diuretics (Spironolactone 50 mg and Furosemide 20 mg) + counseling +deaddiction therapy of Baclofen 30mg.

Statistical analysis: All the results were analyzed by using Microsoft excel 2007 and graph pad prism. Statistics used were Mean, Standard deviation, P- value and child Pugh score.

Data Analysis: For the assessment of outcome in alcoholic liver cirrhosis,childPugh score and laboratory parameters were considered.The mean ± SD child Pugh score of 50 patients before treatment and after treatment was calculated in each group and compared the mean ± SD child Pugh score of three

groups.Assessment was done and the most effective group was determined by comparison of mean ± SD child Pugh score before and after treatment. The group which had least mean± SD child Pugh score was determined. The most effective group where in patients benefited by drugs; drugs and counseling; drugs, counseling and deaddiction therapy which were categorized as group 1, group 2, and group 3 respectively. Weestimated the expected Survival rate and life expectancy in three groups by child Pugh score before and after treatment.Effective group is analyzed which had more percentage of expected survival rate after treatment compared to before treatment.

Effective group was also analyzed by the calculating the mean ± SD and p-value of laboratory parameters of albumin, bilirubin, and prothrombin time before treatment and after treatment in each group

During the study period of 6 months a total of 200 patients data was collected. Among them 70 patients belongs to group1, 62 patients belongs to group2 and 68 patients belong to group3. We have excluded 20 patients from group 1 ,12 patients from group2,18 patients from group3 because of lack of follow up and insufficient data. We have included 50 patients in each group and a total of 150 patients

IV.RESULTS

Table 3:Age wise distribution of groups:

Age group	Group 1 n (%)	Group 2 n(%)	Group 3 n(%)
31-39	11 (22%)	0(0%)	8(16%)
40-49	19(38%)	21(42%)	17(34%)
50-59	16(32%)	24(48%)	20(40%)
60-69	4(8%)	5(10%)	5(10%)

Of 150 patients, we found that the age group of 40-49 years in group 1, 50-59 years in group 2, and 50-59years in group 3 were more prevalent with the percentage of 38, 48 and 40 respectively. As shown in table 3.

Table 4: Signs and symptoms in different groups suffering with alcoholic liver cirrhosis.

Signs and symptoms	Group 1 n (%)	Group 2 n(%)	Group 3 n(%)
Weight loss	13(26%)	17(34%)	20(40%)
Malaise	15(30%)	13(26%)	12(24%)
Jaundice	50(100%)	49(98%)	50(100%)
Abdominal pain	25(50%)	25(50%)	23(46%)
Fatigue	3(6%)	6(12%)	6(12%)
Ascites	23(46%)	35(70%)	30(60%)
Encephalopathy	1(2%)	1(2%)	0

As shown in table 4, of 150 patients, more common symptoms were jaundice (98-100%) followed by Ascites (46-70%) in all groups.

Table 5: Types of alcoholic beverages consumption

Type	Group 1 n (%)	Group 2 n(%)	Group 3 n(%)
Whisky	42(84%)	44(88%)	46(92%)
Brandy	5(10%)	4(8%)	2(4%)
Toddy	2(4%)	1(2%)	1(2%)
country liquor	1(2%)	1(2%)	1(2%)

Of 150 patients, most of the patients consumed whisky with the percentage of 84,88 and 92 followed by brandy with the percentage of 10 ,8 and 4 in group:1,group:2 and group:3 respectively. As mentioned in table 5.

Table 6: Amount of alcohol consumed per day in different groups.

Amount consumed per day	Group 1 n(%)	Group 2 n(%)	Group 3 n(%)
60-90ml	0(0%)	2(4%)	3(6%)
100-200ml	12(24%)	11(22%)	12(24%)
201-300ml	7(14%)	17(34%)	18(36%)
301-400ml	19(38%)	12(24%)	13(26%)
401-500ml	5(10%)	3(6%)	2(4%)
501-600ml	1(2%)	1(2%)	0(0%)
601-750ml	6(12%)	4(8%)	2(4%)

As mentioned in table 6, most of the patients (of all three groups) consumed 300-400ml of alcohol per day with the percentage of 38, 24 and 26 in group 1, group 2 and group 3 respectively.

Table 7:Duration of alcohol consumption in year in each group

Consumption in years	Group 1 n(%)	Group 2 n(%)	Group 3 n(%)
1-5	3(6%)	0(0%)	0(0%)
5-10	16(32%)	8(16%)	9(18%)
11-15	7(14%)	4(8%)	4(8%)
16-20	14(28%)	30(60%)	27(54%)
21-30	10(20%)	7(14%)	9(18%)
31-40	0(0%)	1(2%)	1(2%)

Of 150 patients, we found majority of the patients were consuming alcohol for the 16-20years with the percentage of 28, 60 and 54 in group 1, group 2 and group 3 respectively. As mentioned in table 7.

Table 8: Laboratory parameters in different groups

	Group 1			Group 2			Group 3		
	BT± SD	AT ±SD	P	BT± SD	AT± SD	P	BT± SD	AT± SD	P
Bil	8.5±5.7	4.3±3.4	0.33	8.9±4.6	5.3±3.7	0.27	10.5±4.2	1.6±0.6	0.39
Alb	2.8±0.9	3.6±0.7	0.12	2.3±0.8	3.6±0.7	0.19	2.7±0.5	3.7±0.6	0.11
PT	5.3±1.3	4.3±0.9	0.04	5.8±1.1	4.3±0.8	0.09	5.6±1.2	4.0±0.7	0.09

BT-Before treatment, AT-After treatment, P-Value, Bil-Bilirubin, Alb-Albumin, PT-Prothrombin time

Bilirubin and prothrombine time values decreased significantly in group 3 > group 2 > group 1 whereas serum albumin increased significantly in group 3 > group 2 > group 1. As shownin table 8.

Table 9: Child Pugh score in three different groups before treatment and after treatment.

Groups	Child Pugh score		
	After treatment	Before treatment	Difference
Group 1	10.1 ± 1.4	8.86 ± 1.3	1.24
Group 2	10.9 ± 1.8	8.96 ± 1.7	1.94
Group 3	10.6 ± 1.2	7.18± 1.0	3.42

Child Pugh score in three different groups with a mean ± SD difference of 1.24, 1.94 and 3.42 decreased significantly in group 1, group 2, and group 3 respectively.

Table 10: Expected survival rate based on child Pugh score

Expected	One year		Two year	
survival rate				
	Before treatment	After treatment	Before treatment	After treatment
Group 1	45%	81%	35%	57%
Group 2	45%	81%	35%	57%
Group 3	45%	100%	35%	85%

Based on child Pugh score one year and two year expected survival rate was estimated.

For one year expected survival rate it was found in group 1 and 2 there was an improvement from 45 % to 81 % after treatment were as in group 3 there was an improvement from 45 % to 100 % after treatment.

For two year expected survival rate it was found in group 1 and 2 there was an improvement from 35 % to 57 % after treatment were as in group 3 there was an improvement from 35 % to 85 % after treatment. As mentioned in table 10.

V. DISCUSSION

In our study, we found majority of the patients belong to age group of 40-59 years which is similar to that of study conducted by Nitya nandh, et al.,[8] i.e 46±9.9 years. In our study majority of the patients (all groups) consumed branded spirit like whisky (84%-92%) than local country made spirit (2%) which is in contrast to the study by Nitya nandh, at el.,[8] where majority consumed local country made spirit (79%) than branded spirit (6.5%). It might be due to the financial status of our patients was better compared to their patients (i.eNityanandh, et al., [8]).

We found that 150 patients diagnosed with Alcoholic liver disease were consuming alcohol of 300-400ml/day and duration of drinking was 18-20years which is similar to the study conducted by Narawane, et al.,[18] and Nitya nandh, et al.,[8] In study by Narawane, et al.,[18] alcohol consumption is >200ml/day with the duration >14 years. Nitya nandh, et al.,[8] study found that alcohol consumption is 300-400U/month (1U approximately 30ml)[8] was found to be 17 years which is similar to our study. This might be due to the socio economic factors, environmental and, genetical factors (like based on peer pressure, culture norms and genetically tolerated patients.) to consume alcohol.

In our study, percentage of the patients presented with signs and symptoms like Jaundice 98-100, Ascites 40-70, Abdominal pain 40-50, Weight loss 26-40, Malaise 24 to 30 whereas Nitya nandh, et al.,[8] study they found that the percentage of patients presented with the symptoms like Jaundice, Ascites, Abdominal pain are 60,72 and 55 respectively. Tolerance and individual response to alcohol

could be the possible reason for different signs and symptoms.

In our study, we found that, almost all our patients 98-100% were suffering with hyperbilirubinemia but Nitya nandh et al., found that 85% of their study population were suffering with hyperbilirubinemia. In our study, mean bilirubin levels in all groups were found to be 8.5 to 10.5 mg/dl while Nitya nandh et al., study found 5.3±6.0 mg/dl. We found mean albumin levels in all groups 2.8 while Nitya nandh et al.,study found 2.8±.0.6 which is similar to the study. Tolerance and individual response to alcohol could be the possible reason for different laboratory parameters.

In a study conducted by Nitya nandh, et al.,[8] concluded alcohol that consumption is a dose dependent relation to the prognostic factor like childpugh score. The score was 10.29 with the 300-400 units/month (1U approximately 30ml) of 17years of alcohol consumption where as in our study chidpugh score is 10.92 to 11.0 with the 300-400 ml/day of >17 years 18-20 years. This might be due to the difference in alcohol consumption, tolerance, individual response to alcohol and their dietary habits which lead to the disease condition.

In a study conducted by Bartholomeus Johannes veddit, et al.,[19] they found that the patients who had abstained for three months showed improvement of child Pugh score. The patients, who are not abstained for three months, had no improvement of child Pugh score and underwent liver transplantation. In our study we found, that highest improvement of child Pugh score was seen in group 3 who had counseling and deaddiction therapy along with drug treatment. In group:3 child Pugh score before treatment was found to be 10±1 and after treatment the improvement of child Pugh sore significantly observed. It was found to be 7.18±1.00 compare to other groups. Two year expected survival rate was increased in group 3(85%) than other groups which was 57%.In our study the improvement of child Pugh score might be due to the baclofen, which decreases the cravings for alcohol and reduces the relapse rate in group 3 and thus maintained abstinence.

In a study of 156 patients conducted by Jonathan click, et al.,[20] that they found patients who are givencounseling showed significant improvement in the score for problems related alcohol and γ-glutamyltranspeptidase activity. This shows a greater mean fall of γ-

glutamyltranspeptidase(41%) for counseling patients than controls(14%).While in our study improvement of child Pugh score was not seen in group:2(counseling without deaddiction therapy) compared to group 3 (counseling with deaddiction therapy). After the treatment improvement of child Pugh score was superiorly seen in group 3(7.18±1.00) than group 1 and group 2(8±1) andthe percentage of expected survival rate significantly improved in group 3 than group 2 and 1. This suggest that more abstinence rate was seen in group-3 than group-2 and 1 and increased relapse rate was seen in group-1 and group-2 .Hence counseling along may not be effective to maintain the abstinence. Counseling along with deaddiction therapy like Baclofen is effective in maintaining the abstinence and decreasing the relapse rate in alcoholic liver cirrhosis patients.

Of all three groups, group:3 which consist of treatment with baclofen showed more improvement of child Pugh score than group:2. Expected survival rate was also superiorly increased in group:3 compare to group 2 and group 1.which is similar to that of study conducted by Giovanni Addolorato, et al.,[21] revealed that baclofen is effective at promoting alcohol abstinence in alcohol dependent patients with liver cirrhosis. They concluded that this drug is well tolerated and could have an important role in treatment of these alcohol liver disease patients. This reveals that abstinence rate was more in group-3 compare to group-2 and group-1.Relapse rate was lower in group-3 compare to group-2 and group-1. Hence our study also confirms that Baclofen is effective in promoting the alcohol abstinence in alcohol dependent patient with liver cirrhosis and without deaddiction therapy the improvement was low.

VI. CONCLUSION

Alcohol liver cirrhosis is more prevalent in the age group of 40-49 and 50-59 years and the individuals who consume alcohol (whisky and Brandy) > 200 ml/day over a period of 18-20 years were more prone to get alcoholic liver cirrhosis. Most of the patients were presented with jaundice and ascites followed by malaise and weight loss.

Group-3 had showed a significant improvement in child Pugh score. One year and two year expected survival rate was superior to Group 1 and Group 2.

Counseling alone may not be effective to maintain abstinence. Counseling along with deaddiction therapy using Baclofen is effective in maintaining the abstinence and reducing the relapse rate in alcoholic liver cirrhosis patients.

Baclofen was more effective in promoting the alcohol abstinence in alcohol dependent patient with alcohol liver cirrhosis and without deaddiction therapy the improvement was low.

Among three different treatment groups, group-3 treated with Deaddiction therapy using Baclofen 30mg along with

counseling and drugs like (Ursodeoxycholic acid 300mg, Propranolol 40 mg, Diuretics (Spironolactone 50 mg and Furosemide 20 mg) showed significant improvement in better patient outcome with very low relapse rate.

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