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A STUDY ON TRENDS IN THE MANAGEMENT OF CHRONIC LIVER DISEASE PATIENTS

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ABSTRACT

Chronic liver disease (CLD) is a progressive deterioration of liver functions. The generation of clotting factors and other proteins, the detoxification of toxic metabolic products and the excretion of bile are all liver functions. This continuous inflammation, destruction, and regeneration of liver parenchyma led to fibrosis and cirrhosis. These are leading causes of morbidity and mortality in the country, majorly attributed to excessive alcohol consumption, viral hepatitis, or non-alcoholic fatty liver disease. The study aimed to understand the recent trends in managing chronic liver disease. The liver function tests were assessed in all subjects with a history of CLD complications, and treatment was initiated. Patients were re-examined with LFTs to note the efficacy of the treatment. The study showed that CLD is more prevalent in males due to their lifestyle and social habits. The primary drug prescribed was ursodeoxycholic acid (18.7%), with the best advisable diet restrictions of water and salt (17.4%). Follow-up was conducted regarding LFTs and observed improvement with treatment. With the best management plan, liver functioning can be reverted to normal. Management of CLD and its complications is vital to maintaining hepatic function and the quality of life of patients. With a note on progress, the best non-pharmacotherapies can be advised to improve patients' quality of life. The study provides an idea to physicians regarding the recent trends and ways of planning a therapy.

Keywords: Chronic Liver Disease, Liver Function Tests, Ursodeoxycholic Acid, Management of Liver diseases, Cirrhosis

INTRODUCTION

Chronic liver disease (CLD) is a long-term degradation of liver processes, such as the manufacture of clotting factors and other proteins, the detoxification of toxic metabolic products, and the excretion of bile. CLD is chronic inflammation, destruction, and regeneration of the liver parenchyma that leads to fibrosis and cirrhosis. Cirrhosis is the last stage of chronic liver disease, characterised by disturbance of hepatic architecture, the creation of extensive nodules, vascular reorganisation, neo-angiogenesis, and extracellular matrix deposition. The underlying mechanism of fibrosis and cirrhosis at a cellular level is the recruitment of stellate cells and fibroblasts, resulting in fibrosis, while parenchymal regeneration relies on hepatic stem cells.[1]

MATERIALS AND METHODS

A prospective observational study was designed to assess 99 patients with liver diseases and complications. Patients admitted to the Gastroenterology department of Sagar Hospitals, Jayanagar, Bengaluru, were studied for six months. The study was conducted following the International Conference on Harmonization- Good Clinical Practice guidelines. Institutional Ethical Committee clearance (dated 02 July 2021) was obtained from the board for the protocol to conduct a study in the hospital, the study procedure, and the patient's the informed consent form.

Patients above or equal to 30 years with previously and newly diagnosed CLD were recruited for the study. The patients in the Obstetrics and Gynecology department were excluded. Patients below 30 years of age were excluded from the study as these groups have different physiological behavior and treatment options. While conducting this prospective study, the patients were explained the treatment regimen, and possible ADRs and the effects of drug interactions that may occur were explained. Their consent was obtained after an explanation.

The patient's blood samples were withdrawn and sent to the laboratory for liver function tests. Liver functions were tested by noting the serum level of total bilirubin, direct bilirubin, protein, albumin, alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (AST), and gamma-glutamyl transpeptidase (GGT) and these were assessed to understand the severity of the liver condition.

Based on the severity, treatment was started. LFTs were re-tested after 15 days to check the improvement in liver functions, and the recovery rate was even noted to understand the best treatment choice. Treatment with both therapeutic and non-therapeutic approaches was initiated based on LFT parameters. Treatment with drugs like Ademetionine, Albumin, Chlordiazepoxide, Entecavir, L-ornithine L-aspartate, Metadoxine, Rifaximin, S-adenosyl L-methionine disulfate, Silymarin, Tenofovir, Ursodeoxycholic Acid and an ayurvedic drug (composition of *Capparis spinosa* (Himsara), *Cichorium intybus* (Kasani), Mandur bhasma, *Solanum nigrum* (Kakamachi), *Terminalia arjuna* (Arjuna), *Cassia occidentalis* (Kasamarda), *Achillea millefolium* (Biranjasipha), and *Tamarix gallica* (Jhavaka)) and various non-pharmacological approaches included both diet and lifestyle modifications were advised following the patient's condition. The patient's treatment chart was checked for interactions. Appropriate steps were taken to prevent or reduce the effects of the interactions.

Data management and statistical analysis were performed using SPSS software version 21.0. The variables were analyzed using paired T-test and Chi-square test.

RESULTS AND DISCUSSION

From the total recovered subjects, we observed that 45.5% of them had SGOT in the range of 5-40 units/L; 67.7% of them had SGPT in the range of 7-55units/L; 63.6% had ALP in the range of 44-147 IU/L; 48.5% had Albumin in the range of 3.4-5.4 g/dL; 52.5% had Total Protein in the range of 6-8.3 g/dL; 43.4% had Total Bilirubin level more than 1.2 mg/dL; 57.6% had Direct Bilirubin level more than 0.3%; 55.6% had GGT level more than 38 units/L.

In our study, patients were assessed for the liver parameters to note the abnormalities in the functioning of the liver even after treatment. We observed that 53.5% of the patients had their SGOT levels more than 40 units/L; 26.3% had SGOT level more than 55 units/L; 22.2% had their ALP levels more than 147 IU/L; 6.1% had their Albumin levels more than 5.4 g/dL, and 60.6% had less than 3.4 g/dL; 6.1% had their Total Protein level more than 8.3 g/dL and 27.3% had less 6 g/dL; 58.6% had Total Bilirubin level more than 1.2 mg/dL; 75.8% had their Direct Bilirubin level more than 0.3 mg/dL; 73.7% had their GGT level more than 38 units/L. [Table 1]

The study showed a significant difference between the liver variables before and after the treatment showing that treatment improved liver function. In the total enrolled subjects with CLD, the recovery rate was observed in the patients and found that 21% of patients did not recover with pharmacotherapy and non-pharmacotherapy, and 79% of patients showed good response and recovery with pharmacotherapy and non-pharmacotherapy. [Figure 1]

From the subjects distributed according to treatments based on the outcome, with pharmacotherapy, 69 patients were majorly advised with ursodeoxycholic acid, out of which 55 (13.89%) patients showed recovery with this treatment option. With non-pharmacotherapy, 74 patients were advised with water restrictions up to 800-1000ml, out of which 64 patients (15.15%) showed recovery with this advice. [Table 2 (a and b)]

In the study findings, we have observed that a higher rate of moderate potential drug-drug interactions was identified in 109 male genders (60.9%), a higher rate of minor drug interactions was identified in 20 male genders (11.2%), and a higher rate of significant interactions was identified in 10 male genders (5.6%). [Figure 2]

Table 1: Distribution of subjects according to the Liver parameters (N= 99)

Parameter	Range	Before	After
SGOT (4-55 U/L)	>40	69.7%	53.5%
	5 to 40	30.3%	46.5%
	Total	100.0%	100.0%
SGPT (7-55 U/L)	>55	60.6%	26.3%
	7 to 55	39.4%	73.7%
	Total	100.0%	100.0%
ALP (4-147 IU/L)	<44	3.0%	1.0%
	>147	61.6%	22.2%
	44 to 147	35.4%	76.8%
	Total	100.0%	100.0%
Albumin (3.4-5.4 g/dL)	3.4 to 5.4	21.2%	33.3%
	<3.4	52.5%	60.6%
	>5.4	26.3%	6.1%
	Total	100.0%	100.0%
Total Protein (6-8.3 g/dL)	<6	23.2%	27.3%
	>8.3	36.4%	6.1%
	6 to 8.3	40.4%	66.7%
	Total	100.0%	100.0%
Total Bilirubin (0.3-1.2 mg/dL)	<0.3	1.0%	3.0%
	>1.2	85.9%	58.6%
	0.3 to 1.2	13.1%	38.4%
	Total	100.0%	100.0%
Direct Bilirubin (<0.3 mg/dL)	<0.3	10.1%	24.2%
	>0.3	89.9%	75.8%
	Total	100.0%	100.0%
GGT (8-38 U/L)	>38	87.9%	73.7%
	8 to 38	12.1%	26.3%
	Total	100.0%	100.0%

ALP: Alkaline Phosphatase; GGT: Gamma- Glutamyl Transferase; SGOT: Serum Glutamic Oxaloacetic Transaminase; SGPT: Serum Glutamic Pyruvic Transaminase

{Legends: This table explains the liver parameters of patients (n=99) before and after treatment. 69.7% of patients who had their SGOT more than 40U/L was reduced to 53.5%; 60.6% of patients who had their SGPT more than 55U/L was decreased to 26.6%; 61.6% of the patients who had their ALP more than 147 IU/L, was reduced to 22.2%; 26.3% of the patients who had their Albumin more than 5.4 g/dL was decreased to 6.1%; 36.4% of the patients who had their Total Protein more than 8.3 g/dL was reduced to 6.1%; 85.9% of the patients who had their Total Bilirubin more than 1.2 mg/dL, was reduced to 58.6%; 89.9% of the patients who had their Direct Bilirubin more than 0.3 mg/dL, was reduced to 75.8%; 87.9% of the patients who had their GGT more than 38 U/L, was reduced to 73.7%. We can see that there is a significant difference seen with the treatment provided.}

Table 2(a): Distribution of subjects according to Liver parameters based on outcome

Pharmacotherapy Management	Outcome		Total
	Not Recovered	Recovered	
Ademetionine	3 (0.76%)	7 (1.77%)	10 (2.53%)
Albumin	0 (0.00)	2 (0.51%)	2 (0.51%)
Chlordiazepoxide	3 (0.76%)	3 (0.76%)	6 (1.52%)
Entecavir	0 (0.00)	1 (0.25%)	1 (0.25%)
L-ornithine L-aspartate	4 (1.01%)	18 (4.55%)	22 (5.56%)
Liv. 52	0 (0.00)	1 (0.25%)	1 (0.25%)
Rifaximin	14 (3.54%)	44 (11.11%)	58 (14.65%)
Silymarin	0 (0.00)	4 (1.01%)	4 (1.01%)
Tenofovir	1 (0.25%)	0 (0.00)	1 (0.25%)
S-adenosyl L-methionine disulfate	0 (0.00)	4 (1.01%)	4 (1.01%)
Ursodeoxycholic Acid	14 (3.54%)	55 (13.89%)	69 (17.42%)
Metadoxine	0 (0.00)	1 (0.25%)	1 (0.25%)
Other drugs for co-morbidity	45 (11.36%)	172 (43.43%)	217 (54.80%)
Total	84 (21.21%)	312 (78.79%)	396 (100%)

{Legends: Total study subjects (n=99) were provided with various pharmacotherapeutic agent and outcome were broadly divided into recovered (78.79%) and non-recovered (21.21%). Recoveries were seen with patient with various drugs, Ademetionine (1.77%); Albumin (0.51%); Chlordiazepoxide (0.76%); Entecavir (0.25%); L- ornithine L- aspartate (4.55%); Liv. 52 (0.25%); Rifaximin (11.11%); Silymarin (1.01%); tenofovir (0.00); S- adenosyl L- methionine disulfate (1.01%); Ursodeoxycholic acid (13.89%); Metadoxine (0.25%). And patients who were yet to recover with the drugs, Ademetionine (0.76%); Albumin (0.00%); Chlordiazepoxide (0.76%); Entecavir (0.00%); L- ornithine L- aspartate (1.01%); Liv. 52 (0.00); Rifaximin (3.54%); Silymarin (0.00%); Tenofovir (0.25%); S- adenosyl L- methionine disulfate (0.00); Ursodeoxycholic acid (3.54%); Metadoxine (0.00)}.

Table 2(b): Distribution of subjects according to Liver parameters based on outcome

Non- Pharmacotherapy Management	Outcome		Total
	Not Recovered	Recovered	
Antioxidant-rich food like berries and fish	8 (2.02%)	35 (8.84%)	43 (10.86%)
Breathing exercises	4 (1.01%)	16 (4.04%)	20 (5.05%)
Consume soft food	4 (1.01%)	5 (1.26%)	9 (2.27%)
Consumed properly cooked food	2 (0.51%)	2 (0.51%)	4 (1.01%)
Diabetic diet	4 (1.01%)	30 (7.58%)	34 (8.59%)
Eat unsalted nuts and seeds	0 (0.00)	1 (0.25%)	1 (0.25%)
High energy and high protein diet	3 (0.76%)	12 (3.03%)	15 (0.06%)
High energy moderate protein diet	7 (1.77%)	23 (5.81%)	30 (7.58%)
Knee exercises	5 (1.26%)	11 (2.78%)	16 (4.04%)
Intake of iron-rich food	0 (0.00)	3 (0.76%)	3 (0.76%)
Low-fat diet	3 (0.76%)	7 (1.77%)	10 (2.53%)
Low protein and low-calorie diet	1 (0.25%)	2 (0.51%)	3 (0.76%)
Low salt and sugar intake	9 (2.27%)	48 (12.12%)	57 (14.39%)
Meditation and breathing exercises	0 (0.00)	1 (0.25%)	1 (0.25%)
Probiotics intake	3 (0.76%)	7 (1.77%)	10 (2.53%)
Regular exercises	3 (0.76%)	10 (2.53%)	13 (3.28%)
Stop alcohol consumption	8 (2.02%)	15 (3.79%)	23 (5.81%)
Use MCT oil for cooking	2 (0.51%)	8 (2.02%)	10 (2.53%)
Water restrictions 800 – 1000 ml	14 (3.54%)	60 (15.15%)	74 (18.69%)
None	4 (1.01%)	16 (4.04%)	20 (5.05%)
Total	84 (21.21%)	312 (78.79%)	396 (100%)

{Legends: Total study subjects (n=99) were provided with various non-pharmacotherapeutic suggestions and outcome were broadly divided into recovered (78.79%) and non-recovered (21.21%). Recoveries were seen with patient, suggested with various non-pharmacotherapeutic advice, Antioxidant-rich food like berries and fish (8.84%); Breathing exercises (4.04%); Consume soft food (1.26%); Consumed properly cooked food (0.51%); Diabetic diet (7.58%); Eat unsalted nuts and seeds (0.25%); High energy and high protein diet (3.03%); High energy moderate protein diet (5.81%); Knee exercises (2.78%); Intake of iron-rich food (0.76%); Low-fat diet (1.77%); Low protein and low-calorie diet (0.51%); Low salt and sugar intake (12.12%); Meditation and breathing exercises (0.25%); Probiotics intake (1.77%); Regular exercises (2.53%); Stop alcohol consumption (3.79%); Use MCT oil for cooking (2.02%); Water restrictions 800 – 1000 ml (15.15%). And patients who were yet to recover with the non-pharmacotherapeutic suggestions, Antioxidant-rich food like berries and fish (2.02%); Breathing exercises (1.01%); Consume soft food (1.01%); Consumed properly cooked food (0.51%); Diabetic diet (1.01%); Eat unsalted nuts and seeds (0.00); High energy and high protein diet (0.76%); High energy moderate protein diet (1.77%); Knee exercises (1.26%); Intake of iron-rich food (0.00);Low-fat diet (0.76%); Low protein and low-calorie diet (0.25%); Low salt and sugar intake (2.27%); Meditation and breathing exercises (0.00); Probiotics intake (0.76%); Regular exercises (0.76%); Stop alcohol consumption (2.02%); Use MCT oil for cooking (0.51%); Water restrictions 800 – 1000 ml (3.54%)}.

Table 3: Paired t-test showing the significance of the treatment on the Liver variables

Liver variables	Paired differences		t	Degrees of freedom	P-value
	Mean	SD			
Albumin	0.74	0.95	7.69	98.00	0.000
ALP	0.52	0.54	9.47	98.00	0.000
D. Bilirubin	0.67	0.49	13.40	98.00	0.000
GGTP	0.58	0.52	11.08	98.00	0.000
SGOT	0.55	0.50	10.84	98.00	0.000
SGPT	0.42	0.52	8.17	98.00	0.000
T. Bilirubin	1.27	0.98	12.96	98.00	0.000
T. Protein	0.79	1.02	7.71	98.00	0.000

{Legends: Paired T-test was performed on the subjects' (n=99) liver function parameters where the before and after treatment liver parameters were compared. A greater significance level (p-value < 0.05) was found with the treatment given on liver parameters.}

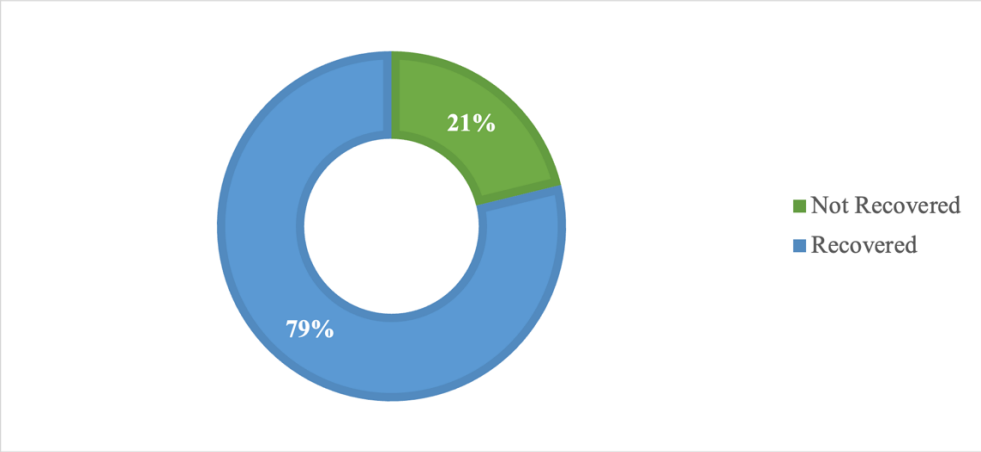

Figure 1: Frequency distribution showing recovery

{Legends: In the total enrolled subjects (n=99) with CLD, the recovery rate was observed in the patients and found that 21% of patients did not recover with pharmacotherapy and non-pharmacotherapy, and 79% of patients showed good response and recovery with pharmacotherapy and non-pharmacotherapy.}

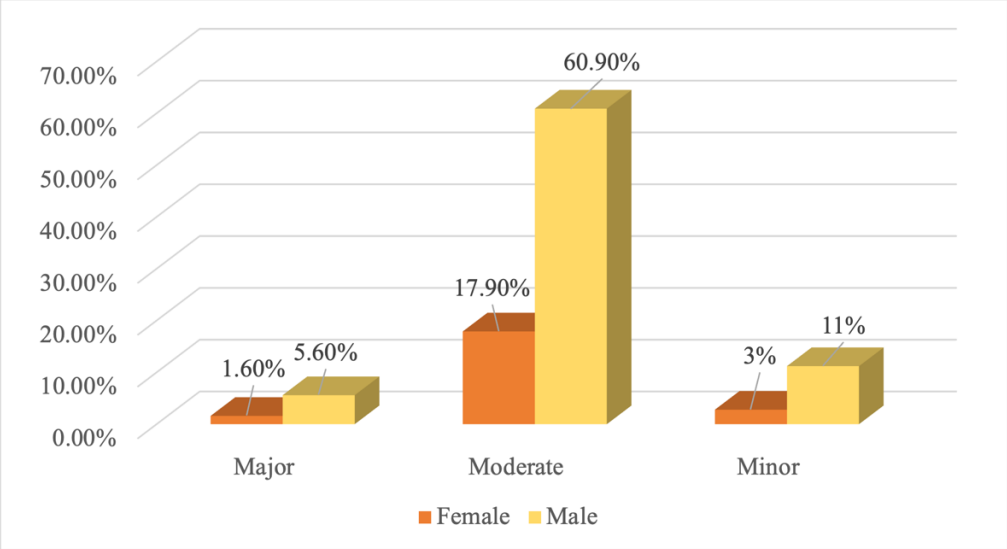

Figure 2: Distribution of severity of drug interactions based on gender

{Legends: Various potential drug interactions were studied. The data was analysed, and a bar graph was drawn. Various drugs were prescribed, amongst which, moderate potential drug-drug interactions were identified in 60.9% (male) and 17.90% (female), some minor drug interactions were identified in 11.2% (male) and 3% (female) and a few major interactions were identified in 5.6% (male) and 1.60% (female)}

DISCUSSION

The distribution of subjects according to liver parameters based on the outcome explains the different parameters used to diagnose chronic liver disease with their outcomes. Here, the table implies that a more remarkable recovery was seen with treatment by observing theirs before and after treatment liver parameters. Similar findings were found in the study conducted by Garrido M., Pereira Guedes T, Alves Silva J, Falcão D, Novo I, and Archer S, *et al*.[2]

Paired t-test shows a significant difference between the liver variables before and after the treatment showing that treatment improved liver function. [Table 3]

A study by Ru Gao, Feng Gao, Guang Li, and Jian Yu Hao showed similar results: patients with chronic liver diseases showed statistically significantly decreasing levels of albumin, white blood cells, haemoglobin, and platelet levels.[3] The patients with chronic liver diseases also showed statistically considerably increased levels of alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, γ- glutamyl transferase, total bilirubin, blood urea nitrogen, and prothrombin time.

By studying the recovery rate of the patients, one can understand the impact of the recent trends of treatment regimens used in a hospital setup. Similar findings were seen in the study conducted by Baba Sulemana Mohammed and Matthew Aidoo.[4]

In pharmacotherapeutic treatment, 69 patients were majorly advised with ursodeoxycholic acid, out of which 55 (13.89%) patients showed recovery with this treatment option. With non-pharmacotherapy, 74 patients were advised with water restrictions up to 800- 1000 ml, out of which 64 patients (15.15%) showed recovery with this advice. A similar finding is also seen in a study by Miguel A. Lalama and Yasser Saloum.[5]

Ursodeoxycholic acid is now the solely established medicine for treating persistent cholestatic liver disorders, according to a study published by D Kumar and R K Tandon.[6] Its properties include cytoprotection, anti-apoptosis, membrane stabilisation, anti-oxidation, and immunomodulation. In patients with primary biliary cirrhosis (PBC), long-term therapy of ursodeoxycholic acid is linked to improved survival and a postponement of liver transplantation. According to another study conducted by Paul Angulo, significant improvement of abnormal liver tests may be achieved during ursodeoxycholic acid therapy in patients with primary sclerosing cholangitis, intrahepatic cholestasis of pregnancy, cystic fibrosis-associated liver disease, non-alcoholic fatty liver disease, graft-versus-host disease of the liver, total parenteral nutrition-induced cholestasis, and some paediatric cholestatic liver diseases.[7] We discovered that 109 times male genders (60.9 %) had a higher incidence of moderate probable medication-drug interactions, 20 out of that (11.2 %) had a higher rate of minor drug interactions, and 10 had a higher rate of serious interactions (5.6 %). Similar findings were found in research by Carmen C. Franz *et al.*, who discovered 132 pharmacokinetic drug-drug interactions (pDDIs) in 86 (21.5 %) individuals.[8] Seven of these pDDIs were directly responsible for 15 ADRs, most of which were related to Spironolactone, Torsemide, Furosemide, and Ibuprofen, with three resulting in hospitalisation.

CONCLUSION

We concluded that assessing the severity and complications is vital before arranging a therapy. The ageing of the organ makes it more sensitive to disease progression, necessitating careful consideration in medical treatment. Managing CLD and associated consequences are critical for maintaining liver function, everyday activities, and patient quality of life. In deciding on therapy strategies and dosages for accessible drugs, various newly developed medicines, and approaches, as well as ageing-related characteristics, must be considered. Physicians treating elderly patients will benefit from this information since they will better understand the body's and organs' changes as they age.

We found from this study that 79% of patients with CLD improved their liver parameters with treatment. This study concludes that a regimen with pharmacotherapy and non-pharmacotherapy combined shows the best lowering of the abnormal liver parameters that help in significantly improving the patient's quality of life.

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