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Assessment of prescribing pattern in chronic liver disease (CLD) patients and rational use of medication in a tertiary care teaching hospital: A uni-centric prospective study

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***Abstract*---**Background: Chronic liver disease (CLD) is a condition of liver damage that includes cirrhosis and fibrosis of liver. It is a progressive destruction of liver functions due to inflammation,

exertion of bile and detoxification of harmful products of metabolism. Objective : To assess the prescribing pattern in chronic liver disease patients and to facilitate rational use of medication. Method : A uni-centric prospective (observational) study was conducted for a period of 6 months for analyzing the prescribing pattern used in treating Chronic Liver Disease (CLD) patients. All the patients (both male and female) diagnosed with CLD visited to gastroenterology department were included in the study. Patients with pregnancy, age below 18 year and above 80 year were not involved in the study. Result: It was observed that the number of males accounted for the 64% of the total patients and rest 36% were females. CLD affected the age group of 48 – 58 years and the common causes were hepatitis C virus (55.55%) and alcohol consumption (26.19%). Most of the patients commonly presented with abdominal pain (89%) and anasarca (63%), however, the common complications included ascites (50%), PHTN (50%), and esophageal varices (43.65%). It was found that 19.71% of the total drugs prescribed were in the fixed dose combination and 18.30% of antibiotics were prescribed in a total of 1420 drugs. However, only 9.29% of the generic drugs were prescribed. The commonly prescribed drugs included antibiotics, laxatives, antacids and multivitamins. The most prescribed antibiotics were rifaximin, metronidazole, cefotaxime and ceftriaxone. Lactulose and Lactitol were the frequently prescribed laxatives. Conclusion: The study concluded that the tendency of prescribing generic medicine remained low.

***Keywords*---**hepatic encephalopathy, ascites, anasarca, hepatitis C virus, PHTN, oesophageal varices.

Introduction

Chronic liver disease (CLD) is a condition of liver damage that includes cirrhosis and fibrosis of liver. It is a progressive destruction of liver functions due to inflammation, exertion of bile and detoxification of harmful products of metabolism [1-2]. Hepatic encephalopathy, ascites, and coagulopathy are the most common and deadly consequences of CLD [3]. In patients with liver cirrhosis, these alterations may lead to greater medication concentrations, which may result in undesired side effects and toxicity. Patients with liver cirrhosis face a unique set of challenges when it comes to prescribing medication [4]. It has also reported that drug's metabolism and excretion may be affected by the changed liver condition. Hepatotoxic effects make up 10% of all adverse drug reactions, and about 50% of pharmaceutical drugs have been linked to liver damage. More than 100 drugs have been linked to full-blown hepatic failure. In order to treat CLDs and its accompanying problems, including cirrhosis of the liver, patients need to be given the correct medication [2].

For clinical and economic goals, medication usage assessment is critical. With the help of recommendations from national and international bodies, prescriptions must be written sensibly so that an appropriate drug can be selected from a vast range of treatment options [5]. WHO has provided guideline-based approach for

the care and treatment of liver disease based on aetiology and complications. Prescription pattern monitoring studies are therefore focused on the extent and profile of drug prescribing, dispensing and use [6]. These studies form a link between various sectors like pharmacoeconomic, pharmacogenetics, and evidence-based medicine [7]. It promotes healthy discussion among the health care professionals to improve the practice of rational use of medicines. On observing the patients who consulted the gastroenterology department, it was found that majority of them presented with CLD. Since no earlier study was done on the prescription analysis of CLD patients, the present study was designed and conducted to get the right choice of drug in CLD. This is, as far as we know, the first study of its kind to be published. Patients with chronic liver disease at the Tertiary Care Teaching Hospital were enrolled in this study to make a note on pharmacotherapy in line with evidence-based guidelines and drug formulary recommendations.

Materials and Methods

Study protocol

Review of literature was done in accordance with the designed inclusion criteria before enrollment of the subject for the study to ensure participants eligibility. These included age, sex, medication, family and social history, smoking, alcohol consumption and demographic details.

Study site and approval

The study was conducted at Department of Gastroenterology, Teerthanker Mahaveer Medical College and Research Centre, Bagadpur, Delhi Road, Moradabad. The protocol of the study was designed to evaluate the prescribing pattern of CLD in a tertiary care teaching hospital and study was approved by Institution Ethical Committee (IEC), Teerthanker Mahaveer Medical College and Research Centre, Bagadpur and Medical Council of India. The hospital has complete facilities for investigations and treatment of gastroenterology problems in adult, pediatric and geriatric patients. The duration of the study was six months from January 2019 to June 2019.

Data collection

The data was collected by the examination of patient's medical record directly.

Sample size

The sample size for study had been calculated by using n Master 2.0 software at 95% confidence interval and 7.5% margin of error, the minimum sample size required for the study was 126.

Study population

Patients visited in– and outpatient departments of gastroenterology who fulfill the inclusion criteria were included in the study.

Inclusion criteria

1. Patient with chronic liver disease
2. Patients of either sex
3. Age group (18-80 years)

Exclusion criteria

1. Patient not willing to participate
2. Pregnant women

Results

Comparison of demographic data

Out of 126 patients of CLD from in- and outpatient departments of gastroenterology; 64.28% patients were found males (81 patients) and 35.72% were females (45 patients). The patients fell under different age groups i.e., 18-28 (8 patients), 28-38 (14 patients), 38-48 (30 patients), 48-58 (37 patients), 58-68 (27 patients), 68-78 (8 patients), and 78-88 (2 patients). Age group of 78 – 88 years had least number of patients.

Frequency of etiological factors

There were various factors responsible for chronic liver disease in which hepatitis C virus pertaining to alcohol intake were the prominent ones as compared to hepatitis B viral infection and fatty liver. The number of alcohol intake patients was 33(26.20%), patients for hepatitis C, hepatitis B and fatty liver were 70 (55.55%), 29 (23.01%) and 28 (22.20%), respectively.

Distribution of patients based on complications and symptoms

Out of 126 patients, majority were suffering from ascites 63 (50%) and portal HTN 63 (50%) followed by esophageal varices 55 (43.65%) and hepatic encephalopathy 57 (43.23%) (Figure 1). Gastric varices 16 (12.69%) and jaundice 15 (11.90%) were the least common complications of CLD. Anasarca 63 (50%), hematemesis 18 (14.28%), melena 34 (26.98%) and abdominal pain 89 (70.63%) were the common symptoms of CLD (Figure 2). Among all the patients, abdominal pain was the most common symptom followed by anasarca. Hematemesis was the least commonly observed symptom.

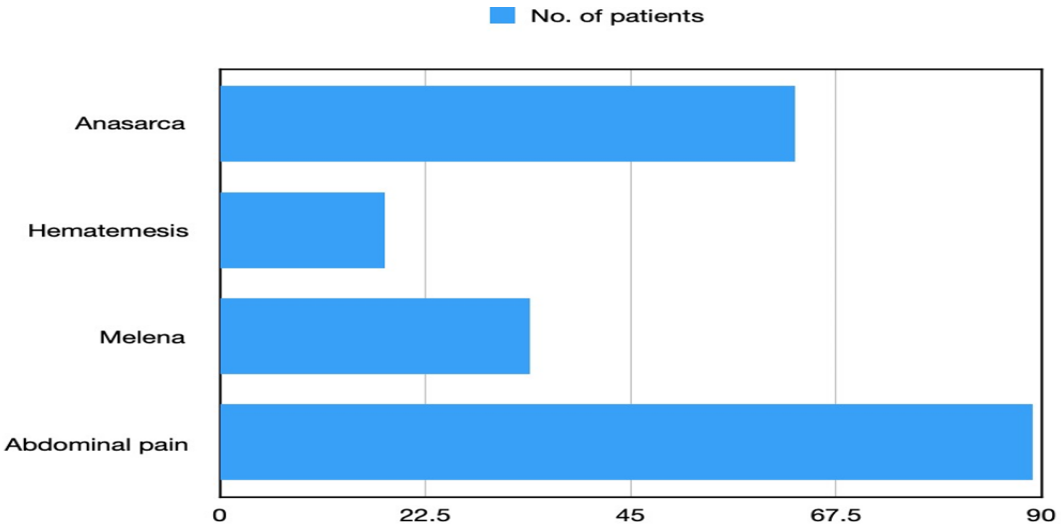

Figure-1 Distribution of patients based on symptoms

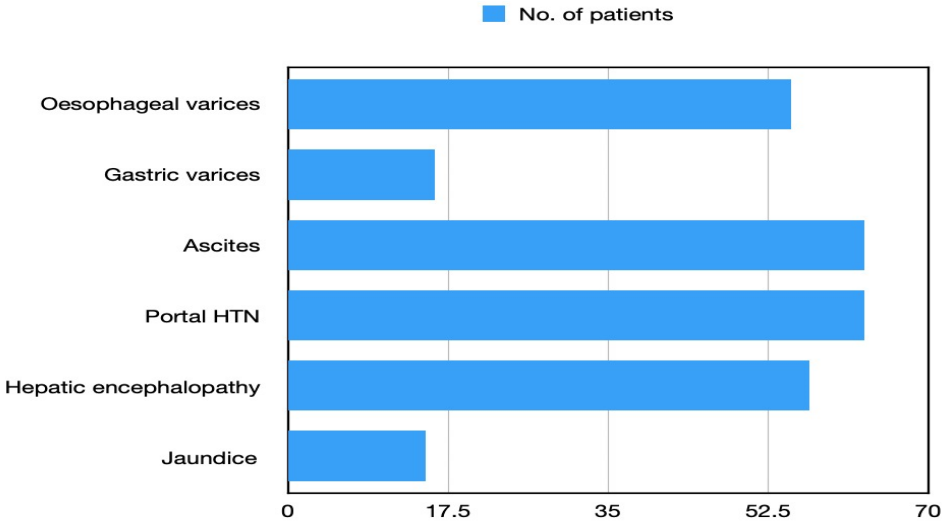

Figure-2 Distribution of patients based on complications

Class of drugs prescribed commonly in CLD

The common class of drugs prescribed in CLD are antibiotic, antihypertensive, diuretic, proton pump inhibitors, antidiabetic, laxative, antiviral, multivitamin and minerals. Antibiotics were the most used class of drugs and had been prescribed in 81.74% of prescriptions followed by laxatives 80.15%. Anti-hypertensives, antidiabetics and diuretics were also used to treat complications. Antivirals were prescribed only in 42.85% of prescriptions.

Table 1 Prescribing pattern of drugs for CLD

Class of drugs	Number of prescription	Number of drugs prescribed	Percentage
Antibiotics	11	0	8.73
	17	1	13.49
	51	2	40.47
	47	3	37.30
Antihypertensive	71	0	56.34
	46	1	36.50
	7	2	5.55
	2	3	1.58
Diuretics	58	0	46.03
	53	1	42.06
	15	2	11.90
PPIs	44	0	35
	65	1	52
	15	2	12
	2	3	1
Antidiabetic	104	0	82
	11	1	9
	10	2	85
	1	3	3
Laxatives	25	0	20
	68	1	54
	31	2	25
	2	3	1
Antiviral	72	0	57
	27	1	21
	25	2	20

	2	3	2
Multivitamins and minerals	33	0	26
	38	1	30
	33	2	26
	14	3	11
	3	4	3
	5	5	4
Other drugs	15	0	12
	27	1	21
	31	2	25
	26	3	21
	12	4	9
	15	5	12

Prescribing pattern based on class of drugs used

Results showed that out of 126 prescriptions, 47 had maximum of 3 antibiotics followed by 51 which had 2 antibiotics prescribed. However, 11 patients were not prescribed with any antibiotic (Table 1). It was found that Rifaximin was the most prescribed drug amongst all (25.69%) while Ceftriaxone was the least prescribed (7.30%) drug (Table 2). Interestingly, 36.50% prescriptions had only one antihypertensive drug prescribed while 56.34% prescriptions did not get any antihypertensive agents prescribed.

Maximum of two diuretics were prescribed in 15 prescriptions while 58 prescriptions had no diuretics. On analysis of 126 prescriptions, it was found that spironolactone was the most prescribed drug (56.62%) while Torsemide was the least prescribed drug (30.12%). Results showed that 52% prescriptions had only one PPI, and 1% prescriptions had 3 PPIs prescribed. Pantoprazole (95.04%) was the most prescribed agent among all PPIs used followed by Rabeprazole, which was found in 33.66% of prescriptions. Only 9% prescriptions were prescribed 1 antidiabetic while 85% of them had 2 antidiabetic agents prescribed. However, 82% prescriptions had no antidiabetic agents.

The maximum number of laxatives were as low as three and was seen only in two prescriptions. One laxative each was prescribed in 68 prescriptions among 126 prescriptions. Results exhibited that 38.97% of prescriptions contained the laxatives, however, lactulose closely followed by lactitol which were prescribed in 36.02% of prescriptions. Among the overall observations only 25 prescriptions had 3 antivirals prescribed. No antiviral drugs were prescribed in majority of

prescriptions accounting for 57%. Sofosbuvir (27.71%) was the most prescribed drug amongst all followed by Daclatasvir (14.45%) and Entacavir (14.45%), They were prescribed in equal frequency, while Tenofovir (8.43%) was the least prescribed drug.

It was observed that 30% of population were prescribed with only one supplement while 4% had five supplements. 26% of patients were not prescribed with any supplements. Various supplements of different ingredients were used in high frequency followed by vitamin K which accounted for 21.35% of prescriptions. Amongst all iron was the least prescribed agents (6.25%). Many drugs that did not belong to the commonly used classes were also prescribed. Antiemetics, analgesics and muscle relaxants were prescribed according to the clinical condition. Ondansetron (15.67%) and propranolol (14.92%) were majorly prescribed while drotaverine (4.85%) was least prescribed.

Table 2 Percentage of drugs prescribed

Class of drugs	Name of drugs	Drug prescribed
Antibiotics	Rifaximin	66 (25.69%)
	Cefotaxime	35 (13.40%)
	Ceftriaxone	19 (7.30%)
	Metronidazole	40 (15.38%)
	Others	59 (22.69%)
Diuretics	Furosemide	42 (54.21%)
	Torsemide	25 (30.12%)
	Spironolactone	47 (56.62%)
PPIs	Rabeprazole	34 (33.66%)
	Pantoprazole	96 (95.04%)
	Omeprazole	12 (11.88%)
	Others	5 (4.95%)
Laxatives	Lactulose	53 (38.97%)
	Lactitol	49 (36.02%)
	Others	31 (22.79%)
Antiviral	Sofosbuvir	23 (27.27%)
	Daclatasvir	12 (14.45%)
	Entacavir	12 (14.45%)

	Tenofovir	7 (8.43%)
	Velpatasvir	11 (13.25%)
Multivitamins and minerals	Vitamine K	41 (21.35%)
	Calcium	40 (20.83%)
	Iron	12 (6.25%)
	Others	78 (40.6250
Other drugs	Ondansetron	42 (15.67%)
	Drotaverine	13 (4.85%)
	Tramadol	17 (6.34%)
	Sucralfate	22 (8.20%)
	Propranolol	40 (14.92%)

Average number of generic drugs, injections and fixed drug combinations (FDCs)

The drugs prescribed by generic name were found to be 132 among overall 1,420 drugs prescribed and it accounted for 9.29%. The average number of generic drugs per prescription was found to be 1.04%. The drugs prescribed in injection form were found to be 427 from amongst the overall 1,420 drugs and it accounted for 30.07%. However, FDCs were found to be from 280 in number among the total of 1420 drugs and it accounted for 19.71%.

Discussion

It is the first time that pharmacoepidemiological methodologies and clinical data have been used together in one place, a Tertiary Care Teaching Hospital. We were able to conduct a thorough evaluation of the prescribing patterns and rational use of medicines in patients with Chronic Liver Disease (CLD) using this methodology. The study's design included prospective follow-up of all patients, ensuring the accuracy and objectivity of the data gathered through the use of a standard protocol. This study is a pragmatic investigation of changes in drug-prescribing procedures to follow the pharmacoepidemiological profile of liver care with a focus on the clinical, epidemiological, and institutional aspects of our target group.

Medicines are a critical component of high-quality health care. Everyone has the right to access safe, effective and cost-effective medications. It is the goal of the prescription pattern to look at several elements of medication use. Most cirrhotic individuals complained of abdominal pain as their primary ailment. A study by Kalaitzakis et al., 2006 demonstrated that increased severity of gastrointestinal symptoms was linked to weight loss and a decreased quality of life [8]. In most cases, stomach discomfort, Anasarca, portal hypertension, and ascites are present in CLD patients.

Antibiotics, laxatives, antacids, and multivitamins were among the most regularly recommended medications. Injectables accounted for 30.07% of all prescription dose forms, although only 9.29% of all medications were in generic form. However, fixed-dose combination accounting for 19.71%. Rifaximine, metronidazole, cefotaxime, and ceftriaxone were the most commonly administered antibiotics. Lactulose and lactitol were among the most commonly recommended laxatives.

Lucena et al., 2002 carried out a similar study to describe the prescribing patterns for the management of liver disease [9]. Non-evidence-based treatments, such as vitamin K and antiulcer medications, were reported to be used at a higher rate than expected. Prescription of anti-ulcer medicines for "gastric protection" in individuals with liver disease was an unexpected finding of this study. PPIs can be used to avoid stress ulcers in patients with fulminant liver failure and to prevent esophageal ulcers according to an evidence-based approach to this class of medicines in liver disease [10]. Notably, pantoprazole is at the top of the list of commonly prescribed medications. In addition, the fact that vitamin K is used by 41% of our study participants is intriguing. Vitamin K does not restore hepatic synthetic function in most patients with chronic liver illness, resulting in a decline in prothrombin activity [11]. The outcomes of this study may not be applicable to outpatients with mild liver disease because the study was conducted in hospitalised patients. However, despite the difficulties of comparing patients from different socioeconomic backgrounds, a similar number of medications were provided to patients with various chronic illnesses in the same hospitalised group [12].

Conclusion

As a result of these findings, it can be concluded that there is a wide range of prescribing practices for liver illness. As well as a widespread usage of medications was also observed that are not supported by evidences such as use of antibiotics, vitamin K, and antisecretory medicines. Clinical pharmacologists and doctors who deal with CLD patients may find these findings useful, since they point to the biggest obstacles that need to be overcome to improve standard of treatment.

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Ethics declarations

Competing interests and funding
No funding was received

Conflicts of interest
We declared no conflicts of interest.

Availability of data and material
Data can be made available on request

Code availability
Not applicable

Author contributions
All the authors equally to the contributed to the manuscript

Ethics approval
Yes.

Consent to participate
Not applicable.

Consent for publication
Not applicable.

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Legends to Figures

Figure 1 Complications found in patients visited to hospital
Figure 2 symptoms of disease found in patients visited to hospital