

A Study to Assess Prevalence and Drug Utilization Pattern in Hepatic Impairment Patients with or without Comorbidities in a Tertiary Care Teaching Hospital

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ABSTRACT

Background: The liver is the core of metabolic activity in the body. Around 50% of the classes of drugs are known to be hepatotoxic. Thus prescribing medications in patients with liver disease is indeed a challenging task.

Objectives: To study the prevalence and to carry out the drug utilization evaluation of the therapy prescribed among hepatic impairment patients.

Methodology: A prospective observational study was carried out for six months among inpatients of the medicine department of Chigateri district hospital. Patients were enrolled on the basis of inclusion criteria; data was collected using a data collection form and results were analyzed using MS Excel. **Results:** A total of 160 patients were enrolled, the most prevalent condition was alcoholic liver disease ($n=66$, 41.25%) followed by chronic liver disease ($n=47$, 29.38%) and hepatic encephalopathy ($n=12$, 7.5%). Out of 1466 drugs been prescribed, 795 drugs were used specifically for hepatic impairment. Drugs used to treat oedema (diuretics) were most

commonly prescribed ($n=198$, 25%) followed by gall stone dissolution agents ($n=124$, 16%) and sugars ($n=97$, 12%). **Conclusion:** Alcoholic liver disease was the most prevalent hepatic condition, followed by chronic liver disease. The diuretics were the most widely used hepato-specific drugs among the patients.

Key words: Drug utilization pattern, Hepatic impairment, Abstinence, Diuretics.

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INTRODUCTION

Chronic Liver Disease (CLD) is an umbrella term for the disease of the liver that occurs due to prolonged exposure to various immunological, mechanical, or metabolic injury for six or more months without complete subsiding or termination of the abnormal disease condition.¹ According to the European Association for the Study of the Liver, approximately two million deaths per year worldwide are due to liver diseases, and one million are due to cirrhosis, viral hepatitis and hepatocellular carcinoma.² As 50% of the class of drugs in physician's desks are known to be hepatotoxic, prescribing medications in patients with liver disease is indeed a challenging task.³ Drug utilization studies are significant for obtaining information about the patterns of drug use, quality, characteristics and the results of drug use.⁴⁻⁶ These studies can help in understanding the drug prescribing and utilization trends in the institution and allow to get a better insight into the therapy.⁷ Prescription pattern and drug evaluation studies are even more important as the majority of drugs are metabolized in the liver.¹ Majority of liver diseases mostly originated from alcohol abuse, obesity and long-term administration of various hepatotoxic drugs like anti-epileptics, anti-tuberculosis and antiretroviral drugs.² Thus, the patient needs the safest and effective therapy with proper patient counselling and dosage adjustment while the administration is at its peak. The clinical pharmacist can educate the patient regarding the safe use of medicine after knowing the trends in the hospital.⁸ Hence, the purpose of this prospective study is to find out the most prevalent type of hepatic impairment and assess the drug utilization pattern among hepatic impairment patients.

MATERIALS AND METHODS

Study site, design and duration: This was an observational and prospective study conducted in the medicine department of Chigateri District Hospital, Davangere (Tertiary care teaching hospital) for a period of six months from November 2019 to April 2020.

Sample size: Proposed sample size was calculated by using the formulae,

$$\text{Sample Size} = \frac{Z_{1-\alpha/2}^2 \times p(1-p)}{d^2}$$

Where,

$Z_{1-\alpha/2}$ = standard normal variant (at 5% type I error ($p < 0.05$), it is 1.96)

P = expected proportion in the population-based on previous studies.

D = absolute error

Prevalence (p) was found to be 11%. So, taking this value, we got:

$$\text{Sample Size} = \frac{1.96^2 \times 0.11(1 - 0.11)}{0.05^2}$$

= 150.43

So, a minimum required sample size was 151 patients, 160 was the achieved sample size.

Study criteria: Inpatients of the general medicine ward of either sex above 18 years of age and diagnosed with any type of hepatic diseases with or without comorbidities were enrolled in the study. Patients who were pregnant or having a terminal illness or whose complete information was missing were excluded from the study. Informed consent was taken from enrolled patient.

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Study procedure: Patients were enrolled based on the inclusion and exclusion criteria by obtaining consent from each. All the relevant data were entered into a well-designed data collection form. The collected data were analysed for further investigation on prescribing trends in hepatic impairment of the patients admitted in the medicine department and also to study the most prevalent type of hepatic impairment among the study patients. Data were analysed using Microsoft Excel (descriptive analysis) and results were presented in graphs and tables.

RESULTS

Age and Gender-Wise Distribution of Study Population

In our study, the age group between which there were most hospital admissions was 31-40 ($n=51$, 32%) among males and 41-50 ($n=5$, 3%) among females followed by 41-50 ($n=39$, 24%) in males and 51-60 ($n=4$, 2.5%) in females. The complete information is depicted in Table 1.

Prevalence of Various Liver Impairments

Out of a total of 160 patients, the most prevalent hepatic impairment was alcoholic liver disease ($n=66$, 41.25%) and chronic liver disease ($n=47$, 29.38%) followed by hepatic encephalopathy ($n=12$, 7.5%), and the least common were alcoholic hepatitis ($n=4$, 2.5%), drug induced hepatitis ($n=4$, 2.5%) and cholelithiasis ($n=4$, 2.5%). The details are shown in Table 2.

Occurrences of Comorbidities among Hepatic Impairment Patients:

Patients being admitted with hepatic impairment may or may not be present with comorbidities. They have been categorized based on the presence or absence of comorbidities and the number of comorbid illnesses. Out of 160 patients, ($n=98$, 61.25%) of hepatic patients were with comorbid illness, whereas ($n=62$, 38.75%) of them were without comorbidities. Among patients having comorbid conditions, hepatic patients with one comorbidity accounted for ($n=69$, 43.12%), and two comorbidities accounted for ($n=29$, 18.12%) of the total hepatic impairment patients. The details are shown in Table 3.

Distribution on the Basis of Child-Pugh and Discriminant Score

Based on the Child-Pugh score, ($n=20$, 12.5%) of the 160 patients were observed to be underclass A, ($n=103$, 64.38%) as class B, and ($n=37$, 23.13%) as class C and based on discriminant score, ($n=117$, 73.13%) of the total cases showed good prognosis and ($n=43$, 26.88%) showed poor diagnosis.

Drug Utilization Pattern of Drugs Being Used Specifically for Hepatic Impairment

Out of 1466 drugs been prescribed, 795 drugs were used specifically for hepatic impairment. Drugs used to treat oedema (diuretics) were most commonly prescribed ($n=198$, 25%) followed by gall stone dissolution agents ($n=124$, 16%) and sugars ($n=97$, 12%) and the least prescribed was anti-viral drugs ($n=1$, 0.1%) as shown in Table 4.

Drug Utilization Pattern of Non-Hepatospecific Drugs

Among 1466 drugs been prescribed, 671 drugs were non-hepatospecific. The most commonly used class of drug is antibiotics ($n=164$, 24%), followed by antiulcer agents ($n=158$, 24%) and vitamin supplements ($n=111$, 16.5%) and the least prescribed were corticosteroids and anti-viral ($n=2$, 0.30%) as illustrated in Table 5.

Most Commonly Observed Drug-Related Problems and Medication Errors

Out of 160 prescriptions, 36 prescriptions showed various types of drug-related problems, out of which indication without drugs ranks the most ($n=25$, 62.5%) followed by drugs without indication ($n=6$, 15%) and the least observed was inappropriate medication ($n=5$, 12.5%).

DISCUSSION

Hepatic impairment can be predisposed by many factors. One of the major is alcohol abuse. Alcohol abuse is now becoming the leading cause of morbidity and mortality and also has become one among the socioeconomic burden.⁹ In the study majority of the patients being admitted among males were between age group 31-40 years ($n=51$, 32%) and among females were between 41-50 years ($n=5$, 3%) in contrast to results found in Mangalagiri, Guntur,¹⁰ where 51-60 years were predominant among males ($n=26$). In this study, the most prevalent hepatic impairment observed in the six months study was alcoholic liver disease ($n=66$, 41%) due to the excessive consumption of alcohol among individuals, but it doesn't coincide with the study conducted at Nigeria, where hepatocellular carcinoma ($n=289$, 44.3%) was prevalent.¹¹ In this study, both one and two comorbidities were observed; portal hypertension was the most occurring comorbidity (10%), which is similar to the study conducted at Andhra Pradesh ($n=5$, 30.35%), but in contrast hypothyroidism in a study conducted at Mangalagiri Guntur ($n=6$, 27.7%).^{9,10} In this study, patients falling in class B of Child-Pugh Score is most observed ($n=103$, 64.38%), this may be due to the earlier hospital admissions due to the emergence of various clinical manifestations in contrast to the study conducted at Kochi, Kerala

Table 1: Age and Gender Wise Distribution.

S. no	Age group	Gender		Total no of patients, n (%)
		Male, n (%)	Female, n (%)	
1	<20	3 (2%)	0 (0%)	3 (2%)
2	21-30	18 (11%)	2 (1%)	20 (12%)
3	31-40	51 (32%)	2 (1%)	53 (33%)
4	41-50	39 (24%)	5 (3%)	44 (28%)
5	51-60	24 (15%)	4 (3%)	28 (18%)
6	61-70	7 (4%)	0 (0%)	7 (4%)
7	71-80	3 (2%)	0 (0%)	3 (2%)
8	>80	1 (1%)	1 (1%)	2 (1%)
	Total	146 (91%)	14 (9%)	N=160 (100%)

Table 2: Prevalence of Various Liver Impairments.

S. no	Diseases	No. of patients, n (%)
1	Alcoholic liver disease	66 (41%)
2	Chronic liver disease	47 (29%)
3	Hepatic encephalopathy	12 (8%)
4	Pancreatitis	11 (7.5%)
5	Non-alcoholic hepatitis	7 (4%)
6	Hepatocellular carcinoma	5 (3%)
7	Alcoholic hepatitis	4 (2.5%)
8	Drug-induced hepatitis	4 (2.5%)
9	Cholelithiasis	4 (2.5%)
	Total	N=160 (100%)

Table 3: Occurrences of Comorbidities among Hepatic Impairment Patients.

Hepatic diseases	One comorbidity, n (%)		Two comorbidities, n (%)	
Chronic liver disease	CLD+Anaemia	6 (3.75)	CLD+HE+PH	2 (1.25)
	CLD+HE	3 (1.9)	CLD+PH+Cystitis	1 (0.63)
	CLD+CKD	3 (1.9)	CLD+HTN+T2DM	1 (0.63)
	CLD+PH	16 (10)	CLD+HRS+Anaemia	2 (1.25)
	CLD+Bronchitis	1 (0.63)	Total	6 (3.76)
	CLD+T2DM	2 (1.25)		
	Total	31(19.43)		
Alcoholic liver disease	ALD+Pancreatitis	4 (2.5)	ALD+HCC+HBV	1 (0.63)
	ALD+Anaemia	14 (8.75)	ALD+HE+Anaemia	4 (2.5)
	ALD+CKD	2 (1.25)	ALD+HE+PH	4 (2.5)
	ALD+RVD	1 (0.63)	ALD+PH+Anaemia	5 (3.13)
	ALD+HTN	1 (0.63)	Total	10 (8.76)
	ALD+PH	7 (4.38)		
	ALD+Gastritis	2 (1.25)		
	ALD+Psoriasis	1 (0.63)		
	ALD+cellulitis	1 (0.63)		
	ALD+TB	1 (0.63)		
	Total	34(21.28)		
Hepatocellular carcinoma	HCC+PH	1 (0.63)		
	HCC+Anaemia	1 (0.63)		
	Total	2 (1.26)		
Cholelithiasis	Cholelithiasis+Anaemia	2 (1.25)		
	Total	2 (1.25)		
Drug induced liver injury			DILI+TB+RVD	3 (1.88)
			DILI+RVD+Anaemia	1 (0.63)
			Total	4 (2.51)
Alcoholic hepatitis			AH+AGE+Anaemia	1 (0.63)
			AH+T2DM+PE	3 (1.88)
			Total	4 (2.51)
Total [n (%)]	69 (43.12%)		29 (18.12%)	98(61.25)
	Only hepatic diseases (without co-morbidities) [n (%)]			62 (38.75)
Total				N=160(100)

CLD: Chronic Liver Disease; ALD: Alcoholic Liver Disease; CKD: Chronic Kidney Disease; PH: Portal Hypertension; HE: Hepatic Encephalopathy; T2DM: Type 2 Diabetes Mellitus; HTN: Hypertension; HRS: HepatoRenal Syndrome; RVD: RetroViral Disease; TB: Tuberculosis; HCC: Hepato Cellular Carcinoma; AKI: Acute Kidney Injury; DILI: Drug-Induced Liver Injury; AH: Alcoholic Hepatitis; AGE: Acute Gastro Enteritis; PE: Pleural Effusion

where class C (50%) of Child-Pugh Score is most admitted as they are providing the reason that most are referred cases.¹² In a Turkish study, patients scoring ≥ 32 are considered as poor prognosis (>50%) were observed to be more compared to ≤ 32 , which is regarded as a good

prognosis.¹³ Whereas our study showed most patients in ≤ 32 , that is good prognosis category only ($n=117$, 73%). In a study conducted in Andhra Pradesh showed the drug utilization of diuretics preponderantly compared to other class of drugs ($n=220$), which is similar to our study,

Table 4: Drug Utilization Pattern of Drugs Used Specifically for Hepatic Impairment.

Sl. no	Class of drugs	Number of drugs n (%)
1	Liver protectants	70 (9)
2	Gall stone dissolution agents	124 (16)
3	Sugars	97 (12)
4	Laxatives	9 (1)
5	Enzymes	4 (0.5)
6	Drugs used to treat edema (diuretics)	198 (25)
7	Drugs used to treat portal HTN (β -blockers)	59 (7)
8	Antibiotics	73 (9)
9	Anti-hemorrhagic agents	83 (10)
10	Transfusions	72 (9)
11	Corticosteroids	5 (1)
12	Antivirals	1 (0.1)
	Total	N=795 (100)

Table 5: Drug Utilization Pattern of Non-Hepatospecific Drugs.

Sl no	Class of drugs	Number of drugs n (%)
1	Anti-ulcer drugs	158 (24)
2	Analgesics	42 (6)
3	Antibiotics	164 (24)
4	Antiemetics	39 (6)
5	Antidiarrheal	12 (2)
6	Antihypertensive	11 (2)
7	Cardiovascular Agents	5 (1)
8	Antidiabetics	5 (1)
9	Anti-convulsant	23 (3)
10	Antivirals	2 (0.3)
11	Vitamin Supplements	111 (16.5)
12	Nebulisations	8 (1)
13	Corticosteroids	2 (0.3)
14	Antihistamines	6 (1)
15	Miscellaneous	48 (7)
16	Transfusions	35 (5)
	Total	N=671 (100)

which showed utilization of diuretics like furosemide, spironolactone, amiloride and torsemide ($n=198$, 25%).⁹ This was in contrast with the other study conducted at Kochi, Kerala chologogues (92.66%) were prominent.¹² In the study of drug utilization of non-hepatospecific drugs, antibiotics were prominently prescribed ($n=164$, 24%) similar to the study conducted at Andhra Pradesh ($n=188$), in contrast, anti-ulcer drugs at Mangalagiri Guntur ($n=175$) were predominant.^{9,10} In a study conducted in Pakistan, the most commonly observed medication error was prescribing inappropriate medication ($n=48$, 49.48%).¹⁴ Whereas in our study, the most commonly observed medication error was indication without the drug ($n=25$, 62.5%), which is in contrast to their study. The study showed the incidence of drug-related problems and medication

errors; this can be minimized by using the bagging system in the hospital pharmacy.¹⁵

CONCLUSION

In our study majority of males were found to be suffering from hepatic impairment more compared to females. The most prevalent hepatic impairment observed to be was alcoholic liver disease accompanied by portal hypertension. The utilization pattern of diuretics was more among hepatospecific drugs and antibiotics were utilized more among non-hepatospecific drugs. Patients mainly fell into class B of Child-Pugh Score compared to the other two classes (A and C) and based on Discriminant Score; good prognosis overweighed poor diagnosis. Our study suggests that there are fair chances to ameliorate the drug utilization pattern among the health care system and minimizing the unwanted use of various medications, especially antibiotics. Patient counseling can make a good impact on patients for abstinence from alcohol and preventing further harm to the liver.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

CLD: Chronic Liver Disease; **ALD:** Alcoholic Liver Disease; **CKD:** Chronic Kidney Disease; **PH:** Portal Hypertension; **H&E:** Hepatic Encephalopathy; **T2DM:** Type 2 Diabetes Mellitus; **HTN:** Hypertension; **HRS:** HepatoRenal Syndrome; **RVD:** RetroViral Disease; **TB:** Tuberculosis; **HCC:** Hepato Cellular Carcinoma; **AKI:** Acute Kidney Injury; **DILI:** Drug-Induced Liver Injury; **AH:** Alcoholic Hepatitis; **AGE:** Acute Gastro Enteritis; **PE:** Pleural Effusion.

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