



Interrelationship of Polypharmacy, Drug Utilisation and Medication Adherence in Chronic Liver Disease: Evidence From a Tertiary Care Hospital

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Abstract

Background/Aim: Management of chronic liver disease (CLD) often involves multiple medications, increasing the risk of polypharmacy, drug–drug interactions (DDIs) and food–drug interactions (FDIs), which may influence medication adherence. This study aimed to evaluate medication use patterns and adherence among patients with CLD at a tertiary care hospital and to examine associations between polypharmacy, DDIs, FDIs and medication adherence.

Methods: A prospective observational study was conducted over six months at a tertiary care hospital in Haryana, India. Data were collected from 200 patients with CLD through medical record reviews and patient interviews. Prescriptions were analysed according to the Ministry of Health Prescription Audit Guidelines. Medication adherence was assessed using the Medication Adherence Rating Scale (MARS). Polypharmacy, DDIs and FDIs were identified and their associations with adherence were statistically analysed.

Results: The majority of patients were male (79 %) and 52.5 % were aged 41–60 years. Polypharmacy was present in 92 % of patients. DDIs were identified in 84.5 % of prescriptions, predominantly of moderate severity, while FDIs were observed in 43.5 % of cases. Medication adherence was classified as poor in 10 %, moderate in 48 % and strong in 42 % of patients. A statistically significant association was observed between polypharmacy and DDIs ($p < 0.001$). Medication adherence showed a significant negative association with FDIs ($p = 0.002$). No significant association was found between medication adherence and either polypharmacy or DDIs.

Conclusion: Polypharmacy and DDIs were highly prevalent among patients with CLD; however, they were not significantly associated with medication adherence. FDIs were the only interaction type significantly associated with reduced adherence, highlighting the importance of dietary counselling and patient education in this population.

Key words: Liver disease, chronic; Polypharmacy; Drug interactions; Medication Adherence Rating Scale; Medication adherence.

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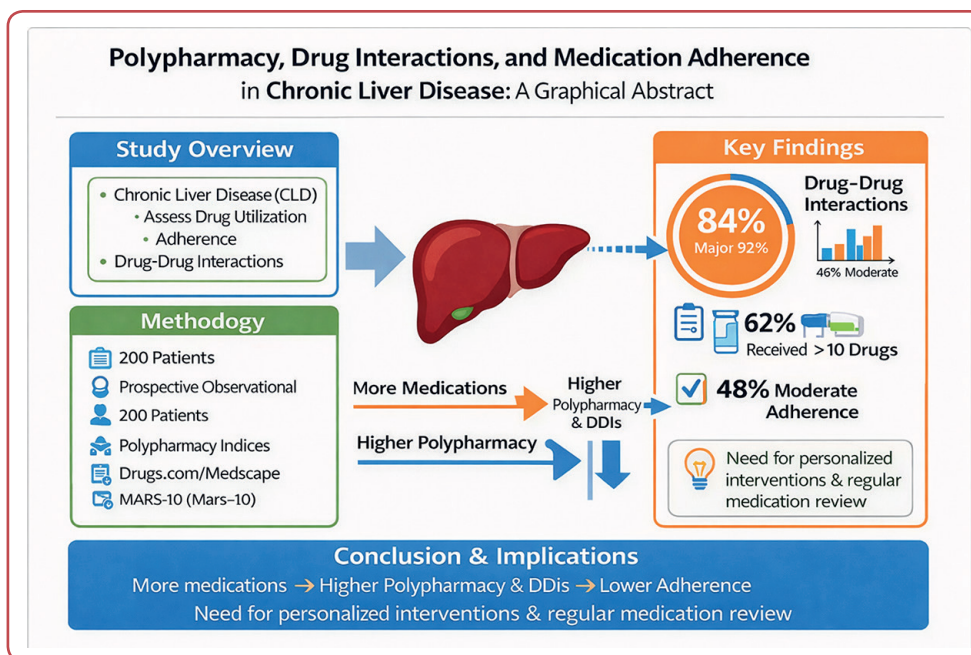
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Graphical abstract

Introduction

Chronic liver disease (CLD) refers to a slow decline in liver function, which includes the production of clotting factors and various proteins, the detoxification of harmful substances and the removal of bile. This condition is marked by a persistent cycle of inflammation, tissue damage and regeneration, which can eventually lead to serious complications like fibrosis and cirrhosis.¹ The causes of CLD are quite varied and include several factors. These range from viral infections like Hepatitis B and C to alcoholic liver disease (ALD),² non-alcoholic fatty liver disease (NAFLD),³ autoimmune liver diseases and various metabolic disorders.² When it comes to the clinical signs of CLD, they can change depending on how far the disease has progressed. In the early stages, you might notice symptoms like fatigue, nausea, a loss of appetite and some mild abdominal discomfort. However, as the disease advances, symptoms can become more severe, including jaundice, ascites (which is the buildup of fluid in the abdomen), hepatic encephalopathy (leading to confusion and cognitive issues), gastrointestinal bleeding and signs of portal hypertension.⁴

The treatment of CLD depends on its underlying cause and severity. The formulation of treatment mixtures involves addressing the underlying causes of illnesses while also alleviating the as-

sociated painful symptoms. However, there exists no standardised protocol for creating these mixtures, as this process largely hinges on the perspective of the prescribing physician and the specifics of the patient's case. The prescription of medication has become an essential component of medical care, with accurate decision-making in this area crucial in preventing errors.⁵ Prescription analysis plays a significant role in identifying errors and facilitating improvements in performance.⁶ Effective management of CLD often involves complex treatment regimens, which may include multiple medications to address the underlying liver disease, associated complications and comorbid conditions. This complexity increases the risk of polypharmacy, which is further associated with challenges such as adverse drug interactions and reduced medication adherence.¹ The prevalence of polypharmacy is high in patients with chronic diseases like CLD. Assessing medication adherence is crucial for preventing negative clinical outcomes, including hospitalisations and disease progression. Tools like the Medication Adherence Rating Scale (MARS) are essential for evaluating patient adherence behaviour, showing barriers and easing tailored interventions.⁷ Also, polypharmacy can significantly increase the risk of drug interactions in patients with CLD. Since the liver plays

a central role in drug metabolism, patients with CLD are more vulnerable to adverse drug reactions (ADRs) and drug-drug interactions (DDIs). Drug-food interactions (DFIs) can be particularly significant in CLD, too, due to impaired drug metabolism and altered nutrient absorption.⁸ By analysing prescriptions, we seek to enhance the understanding of medication management in CLD patients.

This study aimed to assess drug utilisation patterns and medication adherence in patients with CLD in a tertiary care hospital.

Methods

Sampling

A prospective observational study took place at a tertiary care hospital in Mullana, Ambala, Haryana, spanning six months from December 2024 to May 2025. This research followed the guidelines set out in the Declaration of Helsinki and received approval from the Institutional Ethics Committee of MM College of Pharmacy, Maharishi Markandeshwar Deemed to be University, located in Mullana, Ambala, Haryana, India. The study included individuals aged 18 and older who had been diagnosed with CLD, regardless of its cause, after obtaining their written informed consent. However, those with mental health issues, incomplete data, pregnant or breastfeeding women and individuals involved in surgical or accidental cases were not eligible to participate. With a confidence level of 95 %, a prevalence rate of 50 % and a margin of error of ± 6.9 %, the necessary sample size was determined to be 202. Ultimately, data from 200 patients were gathered for the study based on this sample size calculation.

Data collection

Considering the criteria for inclusion and exclusion, participants for the study were recruited after they signed the written informed consent form. Data were gathered by reviewing the medical records of patients in the ward and conducting personal interviews with them. Before they joined the study, the research objectives were explained and patients were assured that their information would be kept confidential. Once they were enrolled, data were collected using a structured patient proforma.

The socio-demographic details, including patients' age, gender, addiction, area, diet, education, co-morbidities and medication history, were documented in the data collection form. Further physical examination and laboratory investigations (like liver function test (LFT), complete blood count (CBC) and renal function tests (RFT)) were recorded. Patients' prescriptions were thoroughly analysed according to the Ministry of Health and Family Welfare Prescription Audit Guidelines.⁹

Patients' medical records before and after discharge were assessed to check the presence of polypharmacy and drug interactions. Based on the information about the number of medications being used by patients, polypharmacy status was determined and categorised as no (< 2 drugs), minor (2–4 drugs), moderate (5–9 drugs) and major (> 9 drugs).¹⁰ Drug interactions were assessed using *Drugs.com*¹¹ and *Medscape* interaction checkers.¹² Drug duplication occurs because of prescribing more than one medication for the same indication. Self-report instrument, the MARS, was used to measure medication adherence. In this study, patients' prescription was analysed for drug utilisation patterns and medication adherence in patients with CLD in a tertiary care hospital.

The Prescription Audit Guidelines by the Ministry of Health and Family Welfare aim to enhance prescription quality, minimise errors and ensure the rational use of medicines in healthcare settings. They emphasise structured prescriptions containing essential patient details, diagnosis and medications, preferably written using generic names for affordability. To reduce errors, hospitals are encouraged to adopt electronic prescribing systems and perform regular audits to identify discrepancies. The guidelines advocate against polypharmacy, promote responsible antibiotic usage to combat antimicrobial resistance and require institutions to establish audit committees to monitor prescribing trends using predefined indicators. These measures collectively improve patient safety and ensure effective medical treatment.⁹

The MARS is a ten-item yes/no self-report instrument. Originating from the combination of two existing scales, the 30-item Drug Attitudes Inventory and the 4-item MARS was designed to create a more reliable and valid tool for assessing medication adherence behaviour in individuals. The

total scores on the MARS range from 0 (indicating a low likelihood of adherence) to 10 (indicating a high likelihood). This scale reflects the understanding that adherence is a continuum, with individuals capable of making decisions anywhere along the spectrum from complete adherence to complete non-adherence, such as only taking medication when experiencing symptoms.¹³

Assessment of DDIs and FDIs

DDIs and FDIs were identified using *Drugs.com* and *Medscape Drug Interaction Checker* databases. All prescribed medications were assessed, including regular, PRN, over-the-counter drugs, vitamins, minerals and documented dietary supplements. Each patient’s complete medication list was independently screened in both databases. In case of discrepancies, the higher severity classification was retained and interactions reported by either database were included. Final validation was performed by a clinical pharmacist.

DDIs and FDIs were classified as major, moderate, or minor based on database definitions, with only clinically relevant FDIs included in analysis. For statistical analysis, the presence of at least one DDI or FDI per patient was used for association and correlation analyses, while the total number of interactions per patient was recorded for descriptive purposes only.

Statistical analysis

The study population’s characteristics were outlined using descriptive statistics. For continuous data, mean and standard deviation were used, while for categorical data frequency and percentage were used. To evaluate the differences between groups, the Independent T-Test, One-Way ANOVA, Two-Way ANOVA and the Pearson Correlation Coefficient were applied. All analyses were performed with SPSS version 25 and p-value of less than 0.05 was considered to be significant.

Results

Demographic characteristics of patients

In presented study, it was found (Table 1) that a significant portion of the participants were male, making up 79 % of the group. Most of them were between the ages of 41 and 60 years, account-

ing for 52.5 % and a majority hailed from rural areas, at 57.5 %. Almost half of the participants had completed high school or achieved a higher

Table 1: Demographic and clinical data of patients with chronic liver disease (CLD)

Characteristics	N	%
Demographic characteristics		
Gender		
Male	158	79.0
Female	42	21.0
Age		
20-40	41	20.5
41-60	105	52.5
61-80	54	27.0
Area		
Urban	85	42.5
Rural	115	57.5
Education		
Uneducated	51	25.5
Primary	4	2.0
Middle	3	1.5
High	83	41.5
Graduated	59	29.5
Diet		
Vegetarian	73	36.0
Non-vegetarian	127	64.0
Addiction		
Alcohol	88	44.0
Smoking	6	3.0
Both	43	21.5
Tobacco chewing	2	1.0
All three	1	0.5
None	60	30.0
Clinical characteristics		
Co-morbidities		
Hypertension	86	43.0
Diabetes	64	32.0
COPD	55	27.5
GERD	38	19.0
Cardiovascular diseases	22	11.0
Thyroid	8	4.0
UTI	7	3.5
Tuberculosis	6	3.0
CKD	3	1.5
Medications prescribed		
< 5	16	8.0
> 5	184	92.0

COPD: Chronic obstructive pulmonary disease; GERD: gastroesophageal reflux disease; UTI: urinary tract infection; CKD: chronic kidney disease;

level of education and a large number followed a non-vegetarian diet, which was 64 %. Addictions were prevalent, particularly to alcohol, which affected 44 % of the participants, while 21.5 % struggled with both alcohol and smoking. Interestingly, 30 % reported having no addictions at all. The most common co-morbidities were hypertension, affecting 43 % and diabetes, which impacted 32 %. Additionally, a striking 92 % of the participants were prescribed more than five different medications.

Association between various demographic parameters

Figure 1 provides a snapshot of the participants' demographics, revealing that most were male, aged between 41 and 60 and hailing from rural

areas. The educational background was predominantly high school and graduate-level, with only a small number lacking formal education or having just completed primary or middle school. A significant portion followed a non-vegetarian diet and many reported struggles with addictions, especially alcohol, often combined with smoking, although some indicated they had no such issues.

Analyses of prescription-questionnaire-based approach

A strong adherence to prescription standards was found (Figure 2). The majority of records included essential patient information, clear handwriting, diagnoses, generic medication names, signatures and compliance with STG/EML, which was over 98 %. While clinical histories, examina-

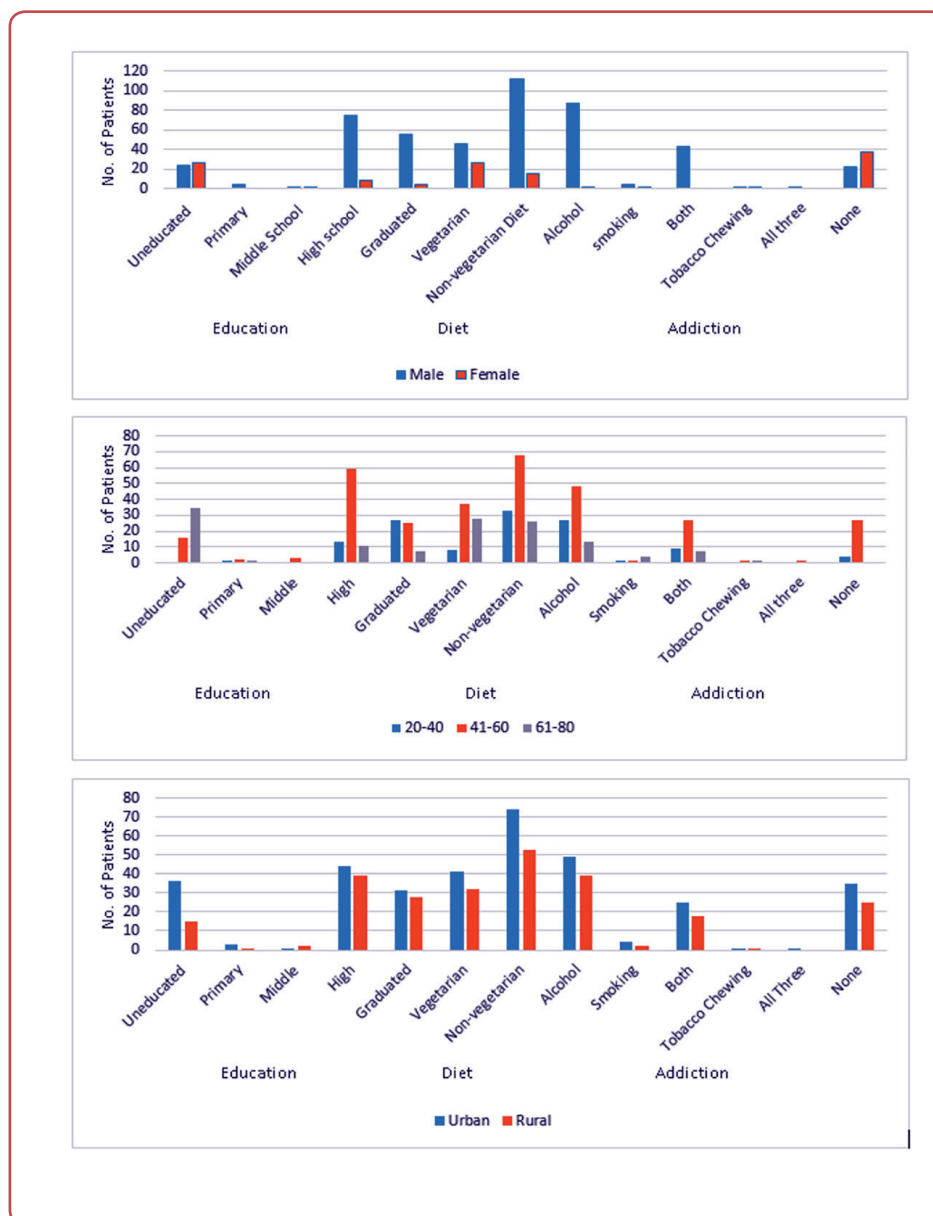


Figure 1: Association between various demographic parameters

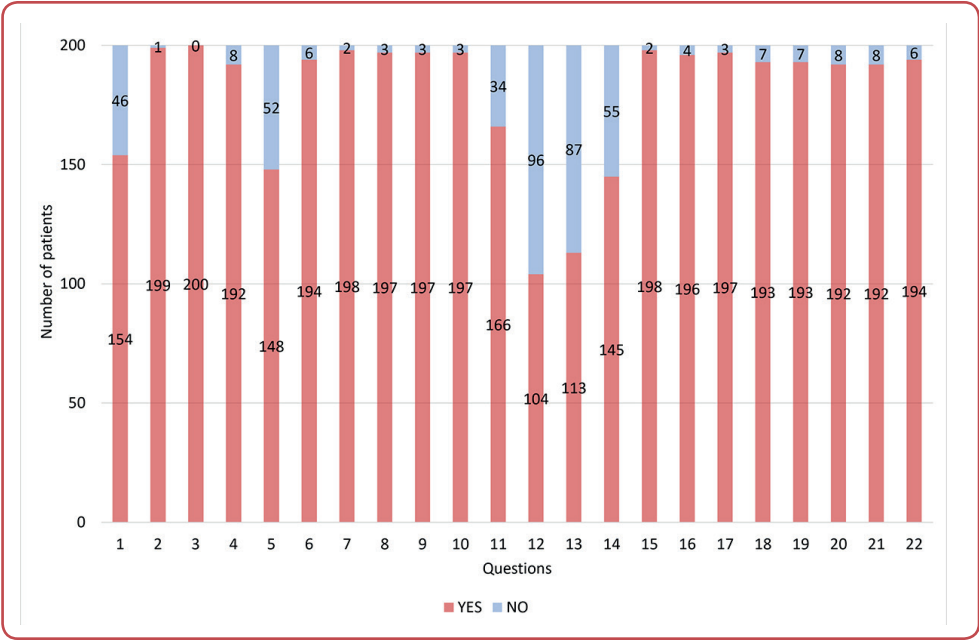


Figure 2: Prescription analysis

Questions:

1. OPD registration number mentioned?

2. Complete name of the patient is written?

3. Handwriting is legible in capital letter?

4. Brief history written?

5. Allergy status mentioned?

6. Salient features of clinical examination recorded?

7. Presumptive / definitive diagnosis written?

8. Medicines are prescribed by generic names

9. Medicines prescribed are in line with standard treatment guidelines (STG)?

10. Medicine schedule / doses clearly written?

11. Duration of treatment written?

12. Date of next visit (review) written?
13. In case of referral, the relevant clinical details and reason for referral given?

14. Follow-up advise and precautions (do's and don'ts) are recorded?

15. Prescription duly signed (legibly)?

16. Medicines prescribed are as per EML/ formulary?

17. Medicines advised are available in the dispensary?

18. Vitamins, tonics or enzymes prescribed?

19. Antibiotics prescribed?

20. Antibiotics are prescribed as per facility's antibiotic policy?

21. Investigations advised?

22. Injections prescribed?

tions and allergy statuses were mostly recorded, only 52 % of the next-visit dates were documented. Prescriptions frequently featured vitamins, antibiotics and injections, with more than 96 % of the medicines readily available in the dispensary.

Drug utilisation pattern

The most commonly prescribed medications included vitamins (427), antibiotics (317), proton pump inhibitors (PPIs) (195), laxatives (152), anti-hypertensives (88) and antiemetics (89) (Table 2). On the other hand, other categories like antivirals, hormones and speciality agents were prescribed much less often.

Drug interactions in CLD patients

DDIs were observed in 84.5 % of patients, with moderate interactions being the most frequent (46.0 %), followed by minor (25.0 %) and major (13.5 %) interactions, while 15.5 % of patients had no interactions. The presence DDIs was an-

alysed according to gender and age. Among participants with DDIs, 137 were male and 32 were female, compared to 21 males and 10 females without DDIs (p = 0.095). Regarding age, participants with DDIs were distributed as 35 (20–40 years), 88 (41–60 years) and 46 (61–80 years), while those without DDIs were 6, 17 and 8 in the respective age groups (p = 0.818). There was no statistically significant association between DDIs and either gender or age.

Out of the total patients, 87 patients (43.5 %) had FDI present, while 113 patients (56.5 %) did not have FDI. Among the 87 patients in whom FDI was present and the 113 patients in whom FDI was absent, no significant differences were observed with respect to gender or age distribution. In terms of gender, 69 males and 18 females were identified in the FDI-present group, compared with 89 males and 24 females in the FDI-absent group (p = 0.925). In a similar way, when we looked at the data by age, the group

Table 2: Most commonly drug classes prescribed

Drug class	N
Antibiotics	317
Laxative	152
Proton pump inhibitors (PPIs)	195
Antivirals	6
Beta-blockers	23
Hepatoprotectives	47
Vitamins	427
Analgesic	27
Antihypertensive	88
Nonsteroidal anti-inflammatory drugs (NSAIDs)	19
Gastrointestinal agent	59
Bronchodilators	23
Corticosteroids	26
Anti-adrenergic	24
Vasopressin receptor agonist	44
Antiemetic	89
Plasma volume expander	40
Health Supplements	44
Benzodiazepines	26
Anti -spasmodic	19
Angiotensin 2 receptor agonist	8
Mineralocorticoid receptor agonist	56
Dipeptidyl peptidase (DPP)-4 inhibitors	23
Biguanides	32
Diuretics	69
Digestive enzymes	9
Sodium-glucose transporter (SGL)-2 inhibitor	5
Immunity booster	6
Anti-arrhythmic	3
Topical emollients	6
Anta-acids	17
Somatostatin analogues	6
Probiotics	17
Local anaesthetics	3
Anti-psychotic	14
Anti-histaminic	7
Monosaccharides	7
Anti-coagulants	4
Hormones	8
Anti-fibrinolytics	5
Statins	10
Anti-haemorrhagic	3
Anti-convulsant	5
Anti-platelet	6
Antidiabetic	27
Opioids	4
Anti-anxiety	3
Nucleoside reverse transcriptase inhibitors (NRTI)	2
Anti-histamine	2
Electrolytes	6

with FDI included 15 patients between the ages of 20 and 40, 48 patients aged 41 to 60 and 24 patients who were 61 to 80 years old. On the other hand, the group without FDI had 26 patients aged 20 to 40, 57 patients in the 41 to 60 range and 30 patients who were 61 to 80. The differences we found weren't statistically significant ($p = 0.499$).

Polypharmacy and medication adherence

The majority of patients were categorised as having major polypharmacy ($n = 184$, 92.0 %). A smaller proportion demonstrated no polypharmacy ($n = 9$, 4.5 %), minor polypharmacy ($n = 2$, 1.0 %), or moderate polypharmacy ($n = 5$, 2.5 %) (Table 3).

Among the patients, 20 (10.0 %) had poor medication adherence (score 1–5), 96 (48.0 %) had moderate adherence (score 6–8) and 84 (42.0 %) demonstrated strong adherence (score 9–10) (Table 3). Table 3 highlights the relationship between demographic and behavioural factors and both polypharmacy and medication adherence. It turns out that polypharmacy is quite common across all groups, particularly among males and individuals aged 41 to 60. Interestingly, factors like education level and addiction status didn't show any significant link to polypharmacy ($p > 0.05$). Likewise, the patterns of adherence - whether poor, moderate, or strong—didn't vary much based on gender, age, education, or addiction ($p > 0.05$).

Association between DDIs, FDIs, polypharmacy and medication adherence/ various variables

Medication adherence was not significantly associated with polypharmacy ($p = 0.094$) or the presence of DDIs ($p = 0.522$). However, FDI was significantly associated with adherence ($p = 0.002$), with poor adherence being more common among patients with FDI (17 poorly adhered) compared to moderate (46) and strong adherence (50).

The study revealed a noteworthy connection (Table 4) between polypharmacy DDIs, highlighted by a correlation coefficient of $r = 0.390$ and a p -value of less than 0.001. This suggests a positive relationship, even though the r -value is negative. On the flip side, polypharmacy didn't show any significant link to medication adherence ($r = -0.124$, $p = 0.079$) and adherence itself also didn't correlate significantly with DDIs ($r = -0.035$, $p = 0.625$).

Table 3: Polypharmacy and medication adherence v/s patients demographics

Variable	N	Polypharmacy				Adherence			
		Minor	Moderate	Major	p-value	Poor	Moderate	Strong	p-value
Gender									
Male	8	36	67	47	0.596	15	74	69	0.843
Female	3	20	17	2		5	22	15	
Age									
20–40	1	10	19	11	0.736	18	55	45	0.426
41–60	7	30	43	25		11	33	22	
61–80	3	16	22	13		8	5	3	
Education									
Uneducated	2	19	20	10	0.417	10	29	12	0.128
Primary	0	1	1	2		1	3	0	
Middle/secondary	0	1	2	0		0	1	2	
High	7	20	32	24		4	39	40	
Graduated	2	15	29	13		5	24	30	
Addiction									
Alcohol	5	21	37	25	0.278	8	40	40	0.621
Smoking	0	1	4	1		1	3	2	
Both (alcohol and smoking)	3	5	19	16		4	26	13	
Tobacco chewing	0	1	0	1		0	1	1	
All three	0	0	0	1		0	1	0	
None	3	28	24	5		7	25	28	

Pearson's rank correlation coefficient (*r*) was used to assess association between variables.

Table 4: Correlation between different variables

Category	Variables	r-value	p-value	Correlation
DDIs	Polypharmacy	0.390	0.001	Positively correlated
Medication adherence	Polypharmacy	-0.124	0.079	Negatively correlated
Medication adherence	DDIs	-0.035	0.625	Negatively correlated

Pearson's rank correlation coefficient (*r*) was used to assess association between variables; DDI: drug-drug interaction;

Discussion

This study evaluated drug utilisation patterns and medication adherence among patients with CLD attending a tertiary care hospital, with the aim of examining relationships between prescribing practices, polypharmacy, DDIs, FDIs and patient adherence. Medication adherence was also assessed in relation to demographic characteristics and lifestyle factors, including substance use.

Among the 200 patients included, 79 % were male and 21 % were female. Most patients were aged 41–60 years and resided predominantly in urban areas. A substantial proportion had com-

pleted secondary education, followed a non-vegetarian diet and reported substance use, particularly alcohol, either alone or in combination with smoking or tobacco chewing (Table 1).

Prescription analysis indicated frequent use of antibiotics, vitamins, tonics and digestive enzymes. Injectable formulations were also commonly prescribed (Figure 2), reflecting the complexity of CLD management. More than half of the patients received between 11 and 20 medications, while smaller proportions were prescribed fewer than 10 or more than 20 medications.

DDIs were identified in 84.5 % of patients and food–drug interactions were present in 43.5 %. These interactions were more frequently observed among males and patients aged 41–60 years. Polypharmacy was most common in the same age group and was more prevalent among male patients. Medication adherence assessment showed that 48 % of patients had moderate adherence. Younger patients tended to demonstrate better adherence, whereas lower adherence was more commonly observed among patients with substance use.

In a cross-sectional study conducted over six months at a tertiary care hospital in Mangalore, Karnataka, researchers looked at 118 patients with CLD and found a moderate level of polypharmacy, reporting a total of 991 drug interactions.¹⁴ Similarly, Abdel-Naser Elzouki and his team studied 333 patients diagnosed with cirrhosis and discovered a strikingly high rate of polypharmacy at 83 %, with a staggering 808 prescribed medications in total.¹⁵ Another hospital-based cross-sectional study involving 416 patients highlighted that the complexity of medication regimens for those with multiple health issues was notably high, which negatively impacted their ability to stick to their medication plans.¹⁶ Additionally, a survey was conducted with fifty patients at a hospital hepatology outpatient clinic, using a mix of short-response and multiple-choice questions to gather insights.

Most of the studies reviewed to date have focused on individual aspects such as polypharmacy, prescription analysis, medication adherence, or drug interactions. Only a limited number have examined the relationship between two of these parameters simultaneously. In contrast, the present study sought to address this gap by evaluating the interrelationships among prescription patterns, polypharmacy, DDIs, FDIs and medication adherence within a population exclusively affected by CLD, irrespective of disease cause or stage.

Correlation analysis demonstrated a significant positive relationship between polypharmacy and DDIs, as well as between polypharmacy and the number of medications prescribed. A similar positive association was observed between DDIs and the number of medications prescribed. In contrast, medication adherence showed weak negative correlations with polypharmacy, DDIs and the number of medications prescribed, although these associations did not reach statistical sig-

nificance (Table 4). These findings suggest that increasing medication burden is associated with higher levels of polypharmacy and interaction risk, while adherence tends to decline as regimen complexity increases, highlighting the need for careful medication review and patient-centred management strategies.^{17, 18}

Limitations of the study

The study has several limitations that could affect the reliability and broader applicability of its findings. The use of convenience sampling poses a challenge to generalisability, as the selected sample may not accurately reflect the larger population. Additionally, self-reported adherence introduces potential biases, including recall bias and social desirability bias, which may lead to inaccurate or skewed responses from participants. Moreover, the absence of long-term follow-up restricts the ability to assess adherence behavior and clinical outcomes over an extended period, limiting insights into sustained effects and changes over time.

Conclusion

This study identified a high prevalence of polypharmacy and DDIs among patients with CLD, reflecting the complexity of pharmacotherapy in this population. An increasing number of prescribed medications was associated with higher levels of polypharmacy and a greater occurrence of DDIs and FDIs. These findings highlight the substantial medication burden commonly encountered in routine clinical practice.

Medication adherence was predominantly moderate to strong. Although variations in adherence were observed across demographic and behavioural subgroups, these differences should be interpreted with caution given the observational nature of the study. Prescription analysis showed frequent use of antibiotics, vitamins, digestive enzymes and injectable formulations, which is consistent with supportive and complication-oriented management strategies in CLD.

Overall, the findings are consistent with existing literature reporting extensive medication

use and interaction risk in patients with CLD. While polypharmacy and drug interactions were common, their relationship with medication adherence appeared limited. These observations underscore the importance of ongoing medication review, appropriate prescribing practices and patient education to support safe and effective pharmacotherapy. Further longitudinal studies are needed to clarify the clinical implications of medication complexity and its impact on adherence and outcomes in this population.

Ethics

This study was approved by Institutional Ethics Committee of MM College of Pharmacy, Maharishi Markandeshwar Deemed to be University, Mullana, Ambala, Haryana, India (Decision No: IEC-3074), dated 20 December 2024.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

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