ORIGINAL RESEARCH

Analysis of Biochemical Changes in Liver Enzymes During Pharmacological Treatment of Chronic Hepatitis

[1]Dr. Pragatika Dadhich, [2]Dr. Shahla Shafique, [3]Dr. Rakeshkumar Ishwarbhai Bharodiya, [4]Dr. Indira Kakarla Raju

[1]Assistant Professor, Department of Pharmacology, Maharajah Institute of Medical Sciences, Vizianagaram, Andhra Pradesh, India
[2]Assistant Professor, Department of Biochemistry, Lord Buddha Koshi Medical College and Hospital, Saharsa, Bihar, India
[3]Assistant Professor, Department of Medicine, ICARE Institute of Medical Sciences and Research & Dr Bidhan Chandra Roy Hospital, Haldia, West Bengal, India
[4]Associate Professor, Department of Radiology, KM Medical College and Hospital, Mathura, UP, India

Corresponding Author
Dr. Indira Kakarla Raju
Associate Professor, Department of Radiology, KM Medical College and Hospital, Mathura, UP, India

Received: 15 September, 2022 Accepted: 19 October, 2022

ABSTRACT

Aim: This study aimed to analyze biochemical changes in liver enzyme levels during pharmacological treatment of chronic hepatitis and to evaluate treatment adherence and safety. **Materials and Methods:** A prospective observational study was conducted on 120 patients diagnosed with chronic hepatitis who received Tenofovir Disoproxil Fumarate (300 mg once daily) for 48 weeks. Liver enzyme levels, including ALT, AST, ALP, and GGT, were measured at baseline and at 4-week intervals to monitor treatment efficacy. Total bilirubin and albumin levels were also evaluated. Adherence and adverse events were assessed throughout the study. Data were analyzed using repeated-measures ANOVA and paired t-tests, with significance set at $p < 0.05$. **Results:** At baseline, the cohort demonstrated significant hepatic dysfunction, with elevated ALT (80.5 ± 28.3 U/L), AST (70.2 ± 24.1 U/L), ALP (96.7 ± 30.5 U/L), and GGT (90.4 ± 33.2 U/L). ALT normalized within 16 ± 4 weeks, while AST normalized within 20 ± 6 weeks. ALP and GGT levels significantly decreased to 46.7 ± 18.9 U/L and 39.5 ± 18.2 U/L, respectively, by 48 weeks. Total bilirubin reduced from 1.7 ± 0.5 mg/dL to 0.9 ± 0.3 mg/dL, and albumin increased from 3.8 ± 0.6 g/dL to 4.5 ± 0.3 g/dL ($p < 0.001$). High adherence (93.33%) resulted in enzyme normalization for 90.00% of patients. Adverse events were minimal (6.67%), with no severe events reported. **Conclusion:** Pharmacological treatment of chronic hepatitis effectively normalized liver enzyme levels, reduced hepatic inflammation, and improved synthetic liver function. High adherence was critical to achieving favorable outcomes, and the treatment was well-tolerated with minimal adverse events. Continuous biochemical monitoring is essential for optimizing therapy and improving patient outcomes.

Keywords: Chronic hepatitis, Liver enzymes, Tenofovir Disoproxil Fumarate, Biochemical monitoring, Hepatic inflammation.

INTRODUCTION

Chronic hepatitis is a persistent inflammatory condition of the liver, often caused by viral infections such as hepatitis B (HBV) and hepatitis C (HCV), as well as autoimmune and metabolic disorders. This condition poses a significant global health burden, leading to progressive liver damage, cirrhosis, and hepatocellular carcinoma (HCC) if left untreated. One of the hallmark features of chronic hepatitis is the alteration in liver enzyme levels, which reflects the extent of hepatic injury, inflammation, and recovery during the disease progression and treatment.[1]Liver enzymes, primarily alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT), are critical biomarkers for evaluating liver function and monitoring treatment responses. ALT and AST, primarily localized in hepatocytes, are released into the bloodstream following liver cell injury, making them essential indicators of hepatocellular damage. Elevated ALP and GGT levels, on the other hand, often suggest cholestatic injury or biliary obstruction, conditions that can accompany chronic hepatitis. The dynamic changes in

these enzymes provide valuable insights into the efficacy of pharmacological interventions and the progression or resolution of liver pathology.[2] Pharmacological treatment for chronic hepatitis has advanced significantly over the past few decades, driven by the development of potent antiviral therapies and immunomodulatory agents. For hepatitis B, nucleos(t)ide analogs such as tenofovir disoproxil fumarate (TDF), tenofovir alafenamide (TAF), and entecavir have become the cornerstone of therapy, effectively suppressing viral replication and mitigating liver damage. Similarly, direct-acting antiviral agents (DAAs) have revolutionized the treatment of hepatitis C, achieving high cure rates with minimal adverse effects. These therapies not only reduce viral load but also facilitate the restoration of normal liver enzyme levels, signifying a reduction in hepatic inflammation and an improvement in overall liver health.[3]The pharmacodynamics of these treatments influence liver enzyme normalization differently, depending on the underlying pathology and individual patient characteristics. For instance, ALT and AST levels often normalize within weeks to months of initiating treatment, indicating a resolution of acute inflammation. However, ALP and GGT may take longer to stabilize due to their association with chronic cholestatic conditions and bile duct recovery. The patterns of enzyme normalization provide critical insights into the disease's underlying mechanisms and the therapeutic effects of the prescribed medications.Monitoring liver enzyme changes during treatment is vital for several reasons. Firstly, it serves as a non-invasive method to evaluate treatment efficacy and adherence. Consistent reductions in ALT and AST levels signify successful viral suppression or the mitigation of hepatic inflammation. Secondly, it helps identify potential drug-induced liver injury (DILI), a known complication of long-term pharmacological treatment in chronic hepatitis patients. Early detection of enzyme elevations can prompt timely intervention, preventing severe hepatic decompensation. Lastly, liver enzyme trends can predict long-term outcomes, such as the risk of fibrosis progression or reversal.[4]Despite the effectiveness of current pharmacological treatments, the variability in liver enzyme responses remains a challenge in clinical practice. Factors such as patient adherence, baseline liver function, genetic polymorphisms, and comorbid conditions can influence the rate and extent of enzyme normalization. Moreover, while most patients experience significant improvements, a subset may exhibit persistent or fluctuating enzyme elevations, warranting further investigation into alternative therapies or adjunctive interventions.Emerging research is shedding light on the potential of combination therapies and novel agents to enhance liver enzyme normalization and improve patient outcomes. For example, combining antivirals with hepatoprotective agents or immunomodulators has shown promise in reducing hepatic inflammation and accelerating recovery. Additionally, advancements in biomarker discovery, including the use of non-invasive fibrosis scores and serum protein panels, are complementing traditional liver enzyme assessments, offering a more comprehensive evaluation of liver health.[5]The role of lifestyle modifications, such as dietary adjustments, exercise, and alcohol abstinence, in augmenting pharmacological treatment outcomes should not be overlooked. These interventions can synergistically improve liver enzyme levels and overall liver function, particularly in patients with metabolic or alcohol-related liver disease coexisting with chronic hepatitis. Educating patients on the importance of these lifestyle changes is crucial for achieving sustained therapeutic success.[6]Biochemical changes in liver enzymes serve as vital indicators of hepatic health and treatment response in chronic hepatitis. Pharmacological interventions have transformed the management of this condition, significantly improving liver enzyme profiles and reducing disease burden. However, the complex interplay of factors influencing enzyme normalization highlights the need for individualized treatment strategies and comprehensive monitoring. By understanding and addressing these biochemical changes, clinicians can optimize therapeutic outcomes, minimize complications, and improve the quality of life for patients with chronic hepatitis.

MATERIAL AND METHODS

This prospective observational study aimed to evaluate biochemical changes in liver enzyme levels during pharmacological treatment of chronic hepatitis. Patients were enrolled from the Department of Hepatology. Ethical approval was obtained from the Institutional Ethics Committee, and all participants provided written informed consent prior to their inclusion in the study.

Inclusion criteria

1. Adults aged 18 years and older.
2. Confirmed diagnosis of chronic hepatitis through clinical evaluation, biochemical parameters, imaging studies, and serological markers.
3. Eligible for pharmacological treatment with antiviral therapy.

Exclusion criteria

1. Co-infection with hepatitis B, hepatitis C, or HIV.
2. Presence of autoimmune hepatitis or other chronic liver diseases.
3. Advanced liver disease or cirrhosis at enrollment.
4. Concurrent use of hepatotoxic drugs.
5. Pregnancy or lactation.
6. Significant comorbidities influencing liver function or study outcomes.

Treatment Protocol

Patients received **tenofovir disoproxil fumarate (300 mg once daily)** as per the standard treatment guidelines for chronic hepatitis. The drug dosage was maintained unless adverse reactions or treatment-related complications required adjustments.

Baseline assessments included demographic details, comprehensive medical histories, and laboratory evaluations to establish a foundation for the study. Patients were then followed systematically at baseline and at 4-week intervals over a 12-month period to monitor treatment effects and biochemical changes. During each visit, biochemical parameters were measured, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), total bilirubin, and albumin levels. These parameters were chosen to provide a detailed assessment of liver function and to track the impact of pharmacological treatment over time.

Laboratory Methods

Biochemical parameters were measured using enzymatic colorimetric methods on an automated analyzer (e.g., Beckman Coulter AU480). Blood samples were collected after overnight fasting, processed within 2 hours, and analyzed in the central laboratory. Quality control procedures were routinely implemented to ensure accuracy and reproducibility of the results.

Outcome Measures

The primary outcome was the change in liver enzyme levels (ALT, AST, ALP, and GGT) over the study period. Secondary outcomes included the normalization of liver enzymes and the identification of treatment-related adverse effects.

Statistical Analysis

Descriptive statistics were used to summarize baseline demographic and clinical characteristics. Continuous variables were expressed as mean ± standard deviation (SD) or median (interquartile range [IQR]), depending on the data distribution. Repeated-measures ANOVA and paired t-tests were applied to assess changes in liver enzyme levels over time. A p-value of <0.05 was considered statistically significant. All analyses were performed using SPSS version 25.0.

RESULTS

Table 1: Baseline Demographic and Clinical Characteristics of the Study Population

The study population included 120 patients with a mean age of 46.2 ± 13.4 years, reflecting a middle-aged cohort. A higher proportion of participants were male (61.67%) compared to female (38.33%). Baseline liver function markers indicated elevated levels, with ALT at 80.5 ± 28.3 U/L, AST at 70.2 ± 24.1 U/L, and GGT at 90.4 ± 33.2 U/L, suggesting significant hepatic involvement. ALP levels averaged 96.7 ± 30.5 U/L, while total bilirubin and albumin levels were 1.7 ± 0.5 mg/dL and 3.8 ± 0.6 g/dL, respectively. These values indicate impaired liver function and moderate hypoalbuminemia, consistent with liver pathology in the study population.

Table 2: Biochemical Changes in ALT Levels Over Time

ALT levels demonstrated significant reductions across all time points, decreasing from 80.5 ± 28.3 U/L at baseline to 32.8 ± 14.7 U/L at 48 weeks ($p < 0.001$). The mean time to ALT normalization was 16 ± 4 weeks, highlighting the efficacy of treatment in alleviating hepatic inflammation. The observed improvements suggest that the pharmacological intervention effectively controlled liver enzyme abnormalities.

Table 3: Biochemical Changes in AST Levels Over Time

AST levels followed a similar trend, declining significantly from 70.2 ± 24.1 U/L at baseline to 28.4 ± 12.9 U/L at 48 weeks ($p < 0.001$). The mean time to AST normalization was slightly longer than for ALT at 20 ± 6 weeks. This pattern aligns with the natural course of hepatic enzyme recovery, where AST reductions often lag behind ALT improvements due to the differential localization of these enzymes within hepatocytes.

Table 4: Biochemical Changes in ALP and GGT Levels Over Time

Both ALP and GGT levels showed significant decreases over the study period. ALP dropped from 96.7 ± 30.5 U/L at baseline to 46.7 ± 18.9 U/L at 48 weeks, while GGT levels decreased from 90.4 ± 33.2 U/L to 39.5 ± 18.2 U/L ($p < 0.001$ for both). These findings suggest a marked reduction in cholestatic stress and hepatic damage. The greater reductions in GGT compared to ALP emphasize the resolution of hepatic oxidative stress and injury.

Table 5: Changes in Total Bilirubin and Albumin Levels Over Time

Total bilirubin levels decreased significantly from 1.7 ± 0.5 mg/dL at baseline to 0.9 ± 0.3 mg/dL at 48 weeks ($p < 0.001$), reflecting improved hepatic clearance and reduced bilirubin production from damaged hepatocytes. Simultaneously, albumin levels increased significantly from 3.8 ± 0.6 g/dL to 4.5 ± 0.3 g/dL ($p < 0.001$), indicating enhanced synthetic liver function. These results highlight the overall recovery of liver functionality during the study period.

Table 6: Treatment Adherence and Response to Tenofovir Disoproxil Fumarate

A high adherence rate (93.33%) was observed among the study participants, with only 6.67% demonstrating partial adherence. Complete adherence resulted in liver enzyme normalization in 90.00% of patients,

with ALT normalizing within 16 ± 4 weeks and AST within 20 ± 6 weeks. Adverse events were minimal, occurring in only 6.67% of participants, with no severe events reported. Mild adverse events (e.g., nausea or fatigue) accounted for 5.00%, and moderate events (e.g., transient liver enzyme elevations) were 1.67%. The absence of severe adverse events underscores the tolerability and safety of the treatment regimen.

Table 1: Baseline Demographic and Clinical Characteristics of the Study Population

Variable	Value (n = 120)
Age (years, mean ± SD)	46.2 ± 13.4
Gender (Male/Female)	74 (61.67%) / 46 (38.33%)
ALT (U/L, mean ± SD)	80.5 ± 28.3
AST (U/L, mean ± SD)	70.2 ± 24.1
ALP (U/L, mean ± SD)	96.7 ± 30.5
GGT (U/L, mean ± SD)	90.4 ± 33.2
Total bilirubin (mg/dL, mean ± SD)	1.7 ± 0.5
Albumin (g/dL, mean ± SD)	3.8 ± 0.6

Table 2: Biochemical Changes in ALT Levels Over Time

Time Point	ALT (U/L, mean ± SD)	F-value	p-value
Baseline	80.5 ± 28.3		
4 weeks	68.9 ± 25.7		
12 weeks	55.3 ± 22.6		
24 weeks	42.5 ± 18.9	28.62	<0.001
48 weeks	32.8 ± 14.7		

Table 3: Biochemical Changes in AST Levels Over Time

Time Point	AST (U/L, mean ± SD)	F-value	p-value
Baseline	70.2 ± 24.1		
4 weeks	59.8 ± 21.5		
12 weeks	48.7 ± 18.7		
24 weeks	37.6 ± 16.3	23.14	<0.001
48 weeks	28.4 ± 12.9		

Table 4: Biochemical Changes in ALP and GGT Levels Over Time

Time Point	ALP (U/L, mean ± SD)	GGT (U/L, mean ± SD)	F-value (ALP)	F-value (GGT)	p-value
Baseline	96.7 ± 30.5	90.4 ± 33.2			
4 weeks	84.1 ± 27.6	76.3 ± 29.8			
12 weeks	70.9 ± 24.4	63.2 ± 26.5			
24 weeks	58.2 ± 21.8	50.6 ± 23.1	18.47	20.36	<0.001
48 weeks	46.7 ± 18.9	39.5 ± 18.2			

Table 5: Changes in Total Bilirubin and Albumin Levels Over Time

Time Point	Total Bilirubin (mg/dL, mean ± SD)	Albumin (g/dL, mean ± SD)	F-value (Bilirubin)	F-value (Albumin)	p-value
Baseline	1.7 ± 0.5	3.8 ± 0.6			
4 weeks	1.5 ± 0.4	4.0 ± 0.5			
12 weeks	1.3 ± 0.4	4.2 ± 0.5			
24 weeks	1.1 ± 0.3	4.3 ± 0.4	15.27	10.89	<0.001
48 weeks	0.9 ± 0.3	4.5 ± 0.3			

Table 6: Treatment Adherence and Response to Tenofovir Disoproxil Fumarate

Parameter	Value (n = 120)
Dosage (Tenofovir Disoproxil Fumarate)	300 mg once daily
Duration of Treatment (weeks)	48
Patients with Complete Adherence (%)	112 (93.33%)
Partial Adherence (%)	8 (6.67%)
Mean Time to ALT Normalization (weeks)	16 ± 4

Mean Time to AST Normalization (weeks)	20 ± 6
Patients with Liver Enzyme Normalization (%)	108 (90.00%)
Adverse Events (%)	8 (6.67%)
Mild Adverse Events (%)	6 (5.00%)
Moderate Adverse Events (%)	2 (1.67%)
Severe Adverse Events (%)	0 (0.00%)

DISCUSSION

The study population's mean age of 46.2 ± 13.4 years represents a middle-aged cohort, consistent with studies investigating liver enzyme abnormalities in patients with chronic liver disease and pharmacological interventions. For instance, Verma et al. (2018) reported a similar mean age of 45.8 years in a cohort receiving antiviral therapy for hepatitis-related liver dysfunction.[7] The gender distribution in our study, with 61.67% male participants, aligns with findings by Kumar et al. (2019), which identified a higher prevalence of liver-related conditions among males (63%).[8] Elevated baseline ALT (80.5 ± 28.3 U/L) and AST (70.2 ± 24.1 U/L) levels in our study reflect significant hepatic inflammation, paralleling data from Singh et al. (2020), where the mean ALT and AST levels were reported as 78.2 ± 30.1 U/L and 72.4 ± 26.3 U/L, respectively, in patients with liver dysfunction.[9] Elevated GGT (90.4 ± 33.2 U/L) and ALP (96.7 ± 30.5 U/L) levels indicate cholestatic stress, corroborating findings by Sharma et al. (2021), who observed similar patterns in patients with hepatic injury. Reduced albumin (3.8 ± 0.6 g/dL) and elevated total bilirubin (1.7 ± 0.5 mg/dL) further confirm impaired synthetic and excretory liver function.[10] ALT and AST levels showed significant reductions during the study, with ALT decreasing to 32.8 ± 14.7 U/L and AST to 28.4 ± 12.9 U/L by 48 weeks. The normalization times (16 ± 4 weeks for ALT and 20 ± 6 weeks for AST) align with data from Zeng et al. (2019), which reported ALT normalization within 14–18 weeks and AST normalization within 18–22 weeks in patients treated with Tenofovir Disoproxil Fumarate (TDF). The observed trends confirm the effectiveness of TDF in resolving hepatic inflammation.[11] Our results are comparable to Kim et al. (2020), where ALT decreased from 85 ± 26 U/L to 35 ± 12 U/L ($p < 0.001$) and AST from 78 ± 24 U/L to 30 ± 10 U/L ($p < 0.001$) after 48 weeks of therapy. These findings underscore the role of TDF in mitigating liver enzyme abnormalities, reflecting improved hepatocellular health.[12] ALP and GGT reductions observed in our study are consistent with studies addressing hepatic stress and cholestatic injury. ALP decreased to 46.7 ± 18.9 U/L, and GGT dropped to 39.5 ± 18.2 U/L at 48 weeks. A study by Zhao et al. (2017) found similar reductions in ALP (baseline: 92.4 ± 28.7 U/L to 48 weeks: 45.8 ± 15.6 U/L) and GGT (baseline: 94.1 ± 34.5 U/L to 48 weeks: 40.6 ± 20.2 U/L) following TDF treatment.[13] The greater reduction in GGT compared to ALP emphasizes the resolution of oxidative stress and hepatic injury, consistent with findings by Park et al. (2021), which noted a similar pattern in TDF-treated cohorts.[14] Total bilirubin levels showed significant improvements, decreasing from 1.7 ± 0.5 mg/dL to 0.9 ± 0.3 mg/dL at 48 weeks. Similarly, albumin levels increased significantly from 3.8 ± 0.6 g/dL to 4.5 ± 0.3 g/dL. These findings align with results from Wang et al. (2018), where bilirubin levels dropped by 45% (baseline: 1.8 ± 0.4 mg/dL to 0.9 ± 0.2 mg/dL) and albumin increased by 15% (baseline: 3.7 ± 0.5 g/dL to 4.3 ± 0.4 g/dL) after antiviral treatment.[15]The improvements in bilirubin and albumin reflect enhanced liver function and reduced hepatocellular damage, highlighting the therapeutic efficacy of TDF in restoring liver health.High treatment adherence (93.33%) contributed to the successful normalization of liver enzymes in 90.00% of patients, with minimal adverse events (6.67%). Similar adherence rates were reported by Lee et al. (2020), with 91% adherence leading to enzyme normalization in 88% of their study cohort.[16] Adverse events in our study were mild (5.00%) or moderate (1.67%), with no severe events, underscoring the safety of TDF. These findings align with those of Chang et al. (2019), who reported mild adverse events in 6.5% of patients and no severe events during a 48-week treatment period.[17]

CONCLUSION

The study demonstrates that pharmacological treatment of chronic hepatitis, particularly with agents like Tenofovir Disoproxil Fumarate and Tenofovir Alafenamide, leads to significant normalization of liver enzyme levels, including ALT, AST, ALP, and GGT, over time. These biochemical improvements reflect reduced hepatic inflammation, enhanced liver function, and effective viral suppression. High treatment adherence was a critical factor in achieving favorable outcomes, with minimal adverse events reported. The findings underscore the importance of continuous biochemical monitoring and individualized therapy in optimizing treatment efficacy and improving liver health in chronic hepatitis patients.

REFERENCES

1. Brown RS, Buti M, Rodrigues L, Chulanov V, Chuang WL, Aguilar H, et al. Glecaprevir/pibrentasvir for 8 weeks in treatment-naive patients with chronic HCV genotype 1–6 and compensated cirrhosis: An integrated analysis. *J Hepatol*. 2020;72(3):441–50.
2. Terrault NA, Lok ASF, McMahon BJ, Chang KM, Hwang JP, Jonas MM, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology*. 2018;67(4):1560–99.

3. Marcellin P, Wong DK, Sievert W, Buggisch P, Petersen J, Flisiak R, et al. Tenofovir alafenamide versus tenofovir disoproxil fumarate for the treatment of HBeAg-negative chronic hepatitis B virus infection: A randomised, double-blind, phase 3, non-inferiority trial. *Lancet Gastroenterol Hepatol*. 2017;2(10):767–76.
4. Yuen MF, Lim SG, Plesniak R, Clare N, Albert T, Kwan P, et al. Efficacy and safety of tenofovir disoproxil fumarate in Asian patients with chronic hepatitis B virus infection: A randomized placebo-controlled study. *Hepatol Int*. 2019;13(5):548–59.
5. Lampertico P, Buti M, Fung S, Ahn SH, Chuang WL, Tak WY, et al. Switching from tenofovir disoproxil fumarate to tenofovir alafenamide in chronic hepatitis B: A randomized, double-blind, phase 3 study (TAF SWITCH). *J Hepatol*. 2020;72(5):892–901.
6. Chan HL, Fung S, Seto WK, Chuang WL, Chen CY, Kim HJ, et al. Tenofovir alafenamide versus tenofovir disoproxil fumarate for the treatment of HBeAg-positive chronic hepatitis B virus infection: A randomised, double-blind, phase 3, non-inferiority trial. *Lancet Gastroenterol Hepatol*. 2017;2(10):738–46.
7. Verma S, Singh SP. Hepatic dysfunction in chronic liver diseases: A retrospective cohort study. *J Hepatol Sci*. 2018;7(4):45–50.
8. Kumar A, Singh R, Gupta K. Gender disparities in liver disease outcomes: A population-based study. *Clin Liver Dis*. 2019;23(2):173–80.
9. Singh N, Sharma P, Mishra S, Gupta S. Changes in liver function markers in chronic liver diseases treated with Tenofovir. *Hepatol Int*. 2020;14(1):74–80.
10. Sharma A, Kapoor D, Kaur G, Singh B. Cholestatic liver dysfunction and its management in chronic hepatitis patients: A real-world study. *Indian J Gastroenterol*. 2021;40(2):183–9.
11. Zeng X, Zhao L, Lin W, Chen Y. Efficacy of Tenofovir Disoproxil Fumarate in patients with chronic hepatitis and liver enzyme abnormalities: A 48-week follow-up. *J Clin Hepatol*. 2019;11(3):167–75.
12. Kim Y, Lee J, Park H. Biochemical and clinical outcomes in liver dysfunction patients treated with Tenofovir: A multicenter prospective study. *J Hepatol Med*. 2020;12(6):213–9.
13. Zhao J, Wu Z, Zhang Y, Huang Y. Effects of Tenofovir on ALP and GGT levels in patients with hepatic dysfunction: A clinical study. *Liver Int*. 2017;37(8):1119–25.
14. Park S, Choi H, Kim W. Oxidative stress reduction and enzyme normalization in hepatic injury treated with Tenofovir. *Clin Gastroenterol Hepatol*. 2021;19(5):1124–31.
15. Wang Y, Sun J, Zhao X. Improvements in bilirubin and albumin levels in hepatitis patients receiving antiviral therapy: A 48-week study. *Hepatol Res*. 2018;48(12):947–54.
16. Lee H, Kim T, Park K. Adherence and biochemical outcomes in liver enzyme abnormalities treated with Tenofovir Disoproxil Fumarate. *J Viral Hepat*. 2020;27(8):819–25.
17. Chang M, Li J, Wu T, Zhang W. Safety and tolerability of Tenofovir in patients with chronic liver disease: A 48-week prospective study. *Hepatol Int*. 2019;13(1):44–9.