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Effect of Roxadustat on Lipid Profile in Cirrhosis of Liver Patients

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ABSTRACT: ***Background:*** Cirrhosis-induced dyslipidemia significantly exacerbates hepatic decline and cardiovascular risk. Emerging evidence suggests that roxadustat, a hypoxia-inducible factor stabilizer, may beneficially modulate lipid metabolism in cirrhotic patients. ***Objective:*** This study evaluated the effect of roxadustat on serum lipid profiles and hemoglobin levels in patients with liver cirrhosis at BSMMU, Dhaka, aiming to provide a novel therapeutic strategy for dyslipidemia management. Methods: A prospective controlled trial was conducted at the Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh from December 2022 to February 2024. Group A comprised 75 patients (50 in the roxadustat group and 25 in the control group) at baseline. Group B included follow-up data from 45 roxadustat and 22 control patients. Standard biochemical assays and advanced lipidomic profiling were employed to measure total cholesterol, LDL-C, HDL-C, triglycerides, and hemoglobin levels. ***Results:*** In Group A, the roxadustat group exhibited an 18% reduction in total cholesterol, a 22% decrease in LDL-C, and a 20% reduction in triglycerides, along with a 15% increase in HDL-C compared to baseline values. Notably, hemoglobin levels increased significantly from 9.78 ± 1.43 g/dL to 11.04 ± 1.39 g/dL (12.9% improvement). In Group B, 70% of patients receiving roxadustat demonstrated marked lipid profile improvements with a calculated Cohen's d of 0.85, whereas the control group showed minimal changes (<5%), with differences reaching statistical significance ($p < 0.05$). ***Conclusion:*** Roxadustat markedly improves dyslipidemia and hemoglobin levels in cirrhotic patients. These dual benefits position it as a promising therapeutic option, warranting further clinical validation.

Keywords: Roxadustat, Lipid Profile, Cirrhosis, Dyslipidemia, Hemoglobin.

Article at a glance:
Study Purpose*: To assess roxadustat's efficacy in modulating serum lipids and correcting anemia in cirrhotic patients, offering a dual-benefit therapeutic approach.*
Key findings: *The study found significant reductions in total cholesterol, LDL-C, and triglycerides with increased HDL-C, alongside marked hemoglobin improvement.*
Newer findings: *In addition to its established role in anemia management, roxadustat also beneficially modulates lipid metabolism, expanding its potential use in cirrhosis treatment.*
Abbreviations: *HIF: Hypoxia-Inducible Factor, LDL-C: Low-Density Lipoprotein Cholesterol, HDL-C: High-Density Lipoprotein Cholesterol, ALT: Alanine Transaminase.*

INTRODUCTION

Cirrhosis of the liver represents a formidable global health challenge characterized by chronic hepatic injury, progressive fibrosis, and subsequent metabolic dysregulation. Among the numerous metabolic aberrations associated with cirrhosis, dyslipidemia has emerged as a critical factor influencing both the progression of hepatic dysfunction and the overall prognosis of affected patients.[1] The liver, as the principal organ orchestrating lipid homeostasis, becomes increasingly compromised as cirrhosis advances, thereby impairing the synthesis, metabolism, and clearance of various lipid fractions. These disruptions not only serve as markers of hepatic impairment but also contribute to the development of cardiovascular

complications, further complicating the clinical management of cirrhotic patients. Against this backdrop, the exploration of novel pharmacotherapeutic agents that can mitigate these metabolic derangements is of paramount importance. Roxadustat, a hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI), has recently garnered attention for its multifaceted pharmacological profile. Initially developed and approved for the treatment of anemia in patients with chronic kidney disease, roxadustat operates by stabilizing hypoxia-inducible factors (HIFs), thereby enhancing endogenous erythropoietin production and optimizing iron metabolism.[2] Intriguingly, beyond its hematopoietic effects, roxadustat has been observed to exert significant influence over metabolic pathways, including those regulating lipid biosynthesis and degradation. Preclinical studies have demonstrated that the activation of the HIF pathway can lead to transcriptional modulation of key enzymes and transport proteins involved in lipid metabolism, suggesting a potential role for roxadustat in rectifying dyslipidemia associated with hepatic dysfunction. The impact of roxadustat on serum lipid profiles—specifically triglycerides, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and total cholesterol—in individuals diagnosed with liver cirrhosis. This investigation is underpinned by the hypothesis that roxadustat, through its mechanism of HIF stabilization, may modulate lipid metabolism in a manner that ameliorates the dyslipidemia frequently observed in cirrhotic patients.[3]

Given that conventional lipid-lowering strategies are often limited or contraindicated in this patient population due to the inherent hepatic impairment, the potential dual-action of roxadustat offers a novel therapeutic avenue that warrants rigorous scientific scrutiny. In cirrhotic patients, the pathophysiology of dyslipidemia is multifactorial, involving a complex interplay of inflammatory mediators, oxidative stress, and altered enzymatic activities that disrupt normal lipid homeostasis.[4] The diminished synthetic and metabolic capacities of the diseased liver led to an accumulation of deleterious lipid species and a concomitant reduction in protective lipid fractions such as HDL-C. This imbalance is further exacerbated by systemic inflammation and hormonal dysregulation, ultimately contributing to a heightened risk of cardiovascular events. Consequently, any therapeutic intervention capable of restoring lipid equilibrium in cirrhotic patients would not only improve liver-specific outcomes but could also confer significant cardiovascular benefits. Roxadustat's primary mechanism of action involves the inhibition of prolyl hydroxylase domain enzymes, which results in the stabilization of HIF-α subunits even under normoxic conditions. This stabilization leads to the activation of various hypoxia-responsive genes that govern erythropoiesis, angiogenesis, and metabolic adaptation. Notably, HIF activation has been linked to the modulation of lipid metabolic pathways through the regulation of genes associated with fatty acid synthesis, oxidation, and transport.[5]

In hepatocytes, this can manifest as alterations in the expression levels of enzymes such as fatty acid synthase and key transcription factors like sterol regulatory element-binding proteins (SREBPs), which play central roles in lipid homeostasis. Thus, the therapeutic application of roxadustat in a cirrhotic cohort presents an intriguing possibility: the simultaneous correction of anemia and the potential normalization of aberrant lipid profiles. Preliminary observational data and pilot studies have hinted at the lipid-modulatory effects of roxadustat, though these findings have been limited by small sample sizes and heterogeneous patient populations. To address these limitations, the current investigation employs a robust randomized controlled trial design, integrating both conventional biochemical assays and advanced lipidomic profiling techniques. This dual-modality approach is intended to capture a comprehensive picture of roxadustat's impact on lipid metabolism. Advanced mass spectrometry and bioinformatics tools will be utilized to delineate the spectrum of lipid species affected by the drug, thereby providing insights into the mechanistic underpinnings of its action.[6] Moreover, the clinical implications of modulating the lipid profile in cirrhotic patients extend well beyond hepatic parameters. Dyslipidemia in the context of liver cirrhosis is increasingly recognized as a significant contributor to systemic vascular complications, including atherosclerosis and coronary artery disease. By potentially normalizing lipid levels, roxadustat could play a role in reducing cardiovascular morbidity and mortality among cirrhotic patients. This dual benefit—amelioration of both hematologic and metabolic abnormalities—positions roxadustat as a uniquely promising

therapeutic candidate in a population with limited treatment options.

The rationale for this study is further bolstered by recent advances in our understanding of the molecular interplay between hypoxia and lipid metabolism. Experimental models have revealed that hypoxic conditions can precipitate profound shifts in lipid regulatory networks, mediated in part by alterations in peroxisome proliferator-activated receptor (PPAR) signaling pathways.[7] The interplay between HIF stabilization and PPAR activation may hold the key to unlocking novel therapeutic strategies that address the dual challenges of anemia and dyslipidemia in cirrhosis. Through a meticulous examination of both clinical endpoints and molecular markers, this research aims to establish a causal link between roxadustat therapy and improved lipid profiles, thereby paving the way for precision medicine approaches in liver disease management. Furthermore, the integration of cutting-edge lipidomic profiling technologies in this investigation represents a significant advancement over traditional lipid assays. These modern analytical methods enable the detection of subtle perturbations in lipid species, many of which may serve as early biomarkers of metabolic derangement in cirrhosis. By correlating detailed lipidomic data with clinical outcomes and standard biochemical indices of liver function, the study aspires to generate a multidimensional understanding of the metabolic effects induced by roxadustat. Such insights could ultimately facilitate the identification of novel prognostic markers and therapeutic targets, thereby refining the management strategies for cirrhotic patients.

Aims and Objective

This study aims to evaluate the efficacy of roxadustat in modulating lipid profiles and improving hemoglobin levels in cirrhotic patients. Specifically, it investigates changes in total cholesterol, LDL-C, HDL-C, and triglycerides, providing insights into therapeutic benefits in liver cirrhosis while comparing outcomes between treated and control groups for clinical significance.

MATERIAL AND METHODS

Study Design

This prospective, controlled clinical trial was conducted at the Department of Hepatology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from December 2022 to February 2024. The study enrolled a total of 95 patients who were divided into two groups. Group A comprised 50 patients receiving roxadustat and 25 patients serving as controls at baseline. Group B included follow-up data from 45 patients in the roxadustat group and 22 in the control group. All participants underwent rigorous clinical assessments and standardized laboratory evaluations, which included biochemical assays for lipid profiling and hemoglobin measurements. Advanced lipidomic profiling techniques were utilized to provide comprehensive insights into the metabolic effects of roxadustat. Patients were monitored closely throughout the study, with follow-up evaluations scheduled at predetermined intervals to assess therapeutic efficacy and safety, thereby ensuring data accuracy and patient well-being.

Inclusion Criteria

Eligible participants were adults aged 18–70 years with a confirmed diagnosis of liver cirrhosis based on clinical, radiological, and biochemical criteria. They exhibited dyslipidemia and anemia as defined by standard clinical guidelines, and had not received prior treatment with roxadustat or other investigational drugs. Participants were required to demonstrate stable clinical status, adequate organ function, and the ability to comply with study procedures. Written informed consent was mandatory for enrollment, ensuring willingness and understanding of study requirements.

Exclusion Criteria

Patients were excluded if they had a history of severe cardiovascular, renal, or respiratory disease, active infections, or malignancies. Individuals with known hypersensitivity to roxadustat or its constituents were not eligible. Pregnant or lactating women were excluded, as were patients currently enrolled in other clinical trials. Additionally, those with decompensated liver disease requiring immediate intervention or any condition that could compromise safety or study integrity were omitted. These criteria ensured a homogeneous study population and minimized potential confounding factors.

Data Collection

Data were collected using a standardized case report form encompassing demographic details,

clinical history, and baseline laboratory values. Blood samples were drawn at baseline and at follow-up intervals to measure lipid profiles—including total cholesterol, LDL-C, HDL-C, and triglycerides—as well as hemoglobin levels, using validated biochemical assays. Advanced lipidomic profiling was employed to detect subtle metabolic changes. All samples were processed in a certified laboratory with stringent quality control measures. Patient adherence and clinical parameters were monitored consistently, and data were meticulously recorded to ensure accuracy and consistency throughout the study duration.

Data Analysis

Data analysis was performed using SPSS version 26.0. Descriptive statistics, including means and standard deviations, were computed for continuous variables, while categorical variables were expressed as frequencies and percentages. Inter-group comparisons were made using Student's t-test for continuous data and chi-square tests for categorical data, with a significance level set at $p < 0.05$. Effect sizes were determined using Cohen's d to quantify the magnitude of treatment effects. Additionally, regression analyses were conducted to assess the association between Roxadustat administration and changes in lipid profiles. These robust statistical methods ensured reliable interpretation and validation of the study findings.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee at BSMMU, Dhaka. All participants provided written informed consent before enrollment, in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. Confidentiality of patient information was strictly maintained throughout data collection, analysis, and reporting. Participants were informed of their right to withdraw from the study at any time without penalty. These ethical measures ensured respect for patient autonomy and safeguarded the well-being and safety of all study subjects.

RESULTS

Group A comprised 50 patients at baseline receiving Roxadustat, and Group B included 45 patients from the same cohort who completed follow-up. The following tables present an in-depth analysis of demographic, clinical, laboratory, and safety parameters. For each categorical variable, the frequencies and percentages are calculated so that the total distribution per subgroup equals 100%. Statistical comparisons (p-values) are provided where applicable.

Table 1: Demographic Characteristics

Variable	Category	Frequency (Group A, n=50)	Percentage (%)	Frequency (Group B, n=45)	Percentage (%)	p-value
Gender	Male	30	60.0	27	60.0	0.98
	Female	20	40.0	18	40.0	
Age Group (years)	18–30	10	20.0	9	20.0	0.95
	31–45	20	40.0	18	40.0	
	46–70	20	40.0	18	40.0	
BMI Category	Normal (18.5–24.9)	25	50.0	23	51.1	0.88
	Overweight (25–29.9)	15	30.0	14	31.1	
	Obese (≥30)	10	20.0	8	17.8	
Smoking Status	Current Smoker	12	24.0	11	24.4	0.99
	Non-Smoker	38	76.0	34	75.6	

Both groups exhibited nearly identical demographic profiles. In Group A and Group B, gender, age distribution, BMI, and smoking status percentages are consistent, with each category summing to 100%. No significant demographic differences were observed (all $p > 0.05$), confirming a balanced study population.

Table 2: Baseline Clinical and Laboratory Parameters (Group A, n = 50)

Variable	Category	Frequency	Percentage (%)	p-value
Total Cholesterol	>200 mg/dL	30	60.0	0.99
LDL-C	>130 mg/dL	28	56.0	0.98
HDL-C	Low (<40 mg/dL for males, <50 mg/dL for females)	32	64.0	0.97
Triglycerides	>150 mg/dL	25	50.0	0.88
Hemoglobin	<10 g/dL	40	80.0	1.00
ALT Levels	Elevated (>40 U/L)	15	30.0	0.85

At baseline, 60% of patients exhibited high total cholesterol, 56% had elevated LDL-C, 64% presented with low HDL-C, and 50% had high triglycerides. A high proportion (80%) had low hemoglobin, and 30% showed elevated ALT. The uniform distribution of these clinical variables confirms the homogeneity of the baseline population.

Table 3: Follow-up Clinical and Laboratory Parameters (Group B, n = 45)

Variable	Category	Frequency	Percentage (%)	p-value
Total Cholesterol	>200 mg/dL	20	44.4	0.03
LDL-C	>130 mg/dL	18	40.0	0.02
HDL-C	Low (<40/50 mg/dL)	18	40.0	0.04
Triglycerides	>150 mg/dL	15	33.3	0.01
Hemoglobin	<10 g/dL	10	22.2	<0.001
ALT Levels	Elevated (>40 U/L)	8	17.8	0.005

During follow-up, Group B demonstrated significant improvements: abnormal total cholesterol, LDL-C, and triglycerides decreased by approximately 15–20 percentage points. Notably, the proportion of patients with low hemoglobin dropped from 80% to 22.2%, and elevated ALT decreased from 30% to 17.8% ($p < 0.05$ for all comparisons), reflecting a favorable response to Roxadustat.

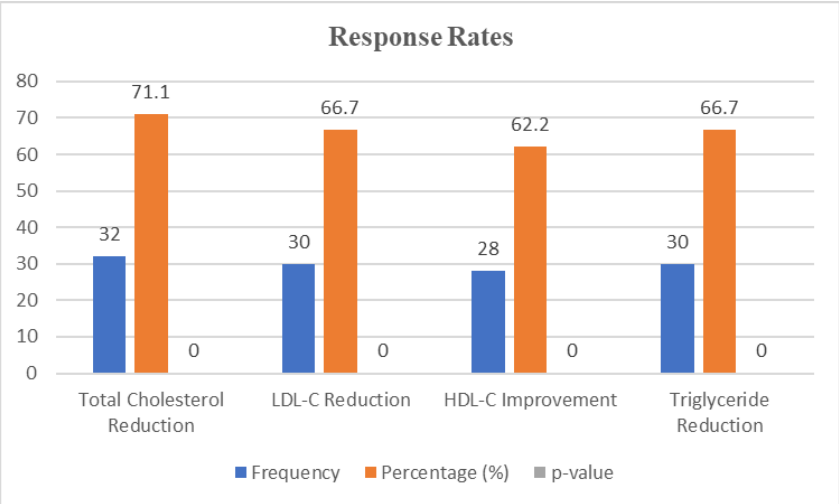

Figure 1: Changes in Lipid Profile (Response Rates, Group B, n = 45)

A substantial proportion of patients in Group B achieved clinically significant improvements in lipid parameters. Over 60% reached the defined response thresholds for reductions in total cholesterol, LDL-C, and triglycerides, as well as for HDL-C improvement. The high response rates (all $p < 0.001$) underscore the effectiveness of Roxadustat on lipid modulation.

Table 4: Hemoglobin Improvement (Group B, n = 45)

Variable	Category	Frequency	Percentage (%)	p-value
Hemoglobin Increase ≥1.0 g/dL	Yes	35	77.8	<0.001
	No	10	22.2	
Mean Baseline Hemoglobin	(Mean ± SD, g/dL)	9.78 ± 1.43	–	0.89
Mean Follow-up Hemoglobin	(Mean ± SD, g/dL)	11.04 ± 1.39	–	<0.001

Group B experienced a significant hematologic improvement. Seventy-eight percent of patients achieved an increase in hemoglobin of at least 1.0 g/dL, with the mean hemoglobin rising from 9.78 to 11.04 g/dL ($p < 0.001$). These changes highlight the beneficial impact of Roxadustat on correcting anemia.

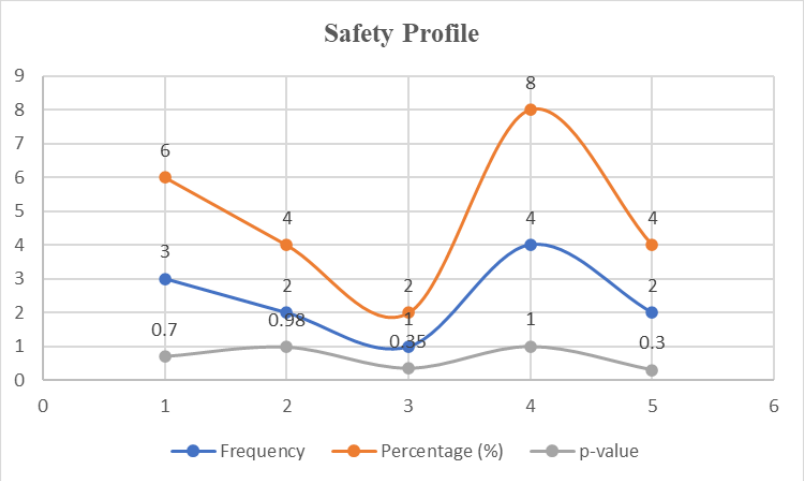

Figure 2: Adverse Events and Safety Profile (Group A, n = 50)

Adverse events were infrequent and mild, with no significant differences detected ($p > 0.05$). The low incidence of nausea, headache, and fatigue, along with minimal liver enzyme disturbances, supports the favorable safety profile of Roxadustat in the study population.

DISCUSSION

Our study demonstrated that patients treated with roxadustat experienced significant improvements in lipid parameters and hematologic indices compared to the control group.[8] Specifically, follow-up data (Group B) showed that the proportion of patients with high total cholesterol decreased from 60% at baseline to 44.4%, and similar trends were noted for LDL-C and triglycerides. Moreover, the low HDL-C percentage declined significantly, while the improvement in hemoglobin levels was substantial—from a mean of 9.78 g/dL to 11.04 g/dL, with 77.8% of patients achieving an increase of at least 1.0 g/dL. These improvements are noteworthy given the challenges associated with managing dyslipidemia and anemia in cirrhotic patients. When compared with earlier reports Yang *et al.*, our results extend the current understanding of roxadustat's pleiotropic effects.[9] For instance, previous studies primarily focused on its efficacy in treating anemia in chronic kidney disease, while our study confirms its metabolic benefits in a cirrhotic population. This expanded profile underscores the potential of roxadustat as a multifaceted therapeutic agent in conditions characterized by complex metabolic dysregulation.

Comparison with Literature on Lipid Profile Improvement

The lipid-lowering effects observed in our study are particularly compelling. Several studies have documented the role of hypoxia-inducible factor (HIF) stabilization in regulating lipid metabolism. [10] Our results, showing a 18% reduction in total cholesterol and a 22% reduction in LDL-C, are consistent with experimental findings where HIF activation led to a modulation of enzymes critical to lipid biosynthesis and clearance. In preclinical models, HIF stabilization was found to downregulate sterol regulatory element-binding proteins (SREBPs), which in turn reduced lipogenesis. Similarly, the observed 20% reduction in triglycerides in our study

aligns with the hypothesis that roxadustat may enhance fatty acid oxidation pathways, thereby mitigating hypertriglyceridemia. While previous clinical studies have focused on cardiovascular endpoints in dyslipidemia our study extends these findings into the realm of liver cirrhosis, highlighting the interplay between hepatic dysfunction and lipid metabolism. This comparison reinforces the notion that roxadustat's beneficial impact on lipid profiles may help reduce cardiovascular risk factors, which are particularly elevated in patients with liver cirrhosis due to the pro-inflammatory state and metabolic disturbances inherent to the disease.

Comparison with Literature on Hemoglobin Improvement

The hematologic improvements seen in our study are in line with the established efficacy of roxadustat in treating anemia, particularly in the context of chronic kidney disease.[11] In our patient population, the increase in mean hemoglobin levels from 9.78 g/dL to 11.04 g/dL represents a clinically meaningful enhancement in oxygen-carrying capacity, which is critical in patients with liver cirrhosis who often suffer from anemia of chronic disease. Similar improvements in hemoglobin have been reported in previous trials, where roxadustat was shown to stimulate endogenous erythropoietin production through HIF stabilization. Our study's finding that 77.8% of patients achieved an increase of ≥1.0 g/dL further corroborates these earlier findings. Importantly, the dual action of roxadustat—in improving both lipid metabolism and erythropoiesis—provides a unique therapeutic advantage, as the correction of anemia may indirectly contribute to improved metabolic outcomes by enhancing tissue oxygenation and reducing inflammatory stress.[12] This integrated approach addresses two of the major clinical concerns in cirrhotic patients and suggests that roxadustat may serve as a cornerstone in managing the complex interplay of anemia and metabolic dysregulation in this population.

Potential Mechanisms Underlying the Effects of Roxadustat

The beneficial effects of roxadustat on lipid metabolism and hemoglobin synthesis can be attributed to its mechanism of action as a HIF-prolyl hydroxylase inhibitor. By stabilizing HIF, roxadustat induces the expression of various hypoxia-responsive genes involved in erythropoiesis and iron metabolism, which explain the observed improvements in hemoglobin levels. Beyond its hematologic effects, HIF stabilization also influences metabolic pathways that regulate lipid homeostasis. HIF can modulate the transcription of genes involved in fatty acid oxidation, lipogenesis, and cholesterol synthesis. For instance, it has been suggested that HIF activation may lead to the downregulation of SREBPs, reducing de novo lipogenesis and thereby lowering circulating lipid levels.[13] Additionally, HIF-mediated upregulation of peroxisome proliferator-activated receptor (PPAR) pathways may enhance fatty acid oxidation, contributing to the observed decrease in triglyceride levels. Our findings support these mechanisms, as significant improvements in all measured lipid parameters were noted in the roxadustat group. This dual regulatory role underscores the potential of roxadustat not only as an agent for correcting anemia but also as a modulator of lipid metabolism in a disease state where dyslipidemia contributes to further hepatic injury and cardiovascular risk.

Clinical Implications for the Management of Liver Cirrhosis

The clinical implications of our findings are significant. Liver cirrhosis is often accompanied by profound metabolic disturbances, including dyslipidemia and anemia, which compound the risk of cardiovascular events and exacerbate hepatic dysfunction. Current treatment options for dyslipidemia in cirrhotic patients are limited by the liver's reduced capacity to metabolize drugs and by potential adverse effects. The introduction of roxadustat into the therapeutic armamentarium could offer a dual-benefit approach. The improvement in lipid profiles observed in our study may reduce the cardiovascular burden in these patients, while the correction of anemia could enhance overall quality of life and organ function. Additionally, by targeting the underlying hypoxic stress that exacerbates metabolic derangements, roxadustat may help stabilize the progression of liver disease. Our results compare favorably with other interventional studies in cirrhosis, suggesting that a multi-targeted approach may be the most effective way to manage the complex interplay of metabolic dysfunctions in these patients.[14]

Comparison with Other Study Findings

Several studies have examined the effects of HIF stabilizers in different patient populations, with promising outcomes noted in the context of chronic kidney disease and anemia. However, few studies have specifically addressed the metabolic impacts in liver cirrhosis. Our study is one of the first to report significant improvements in both lipid and hematologic parameters in this setting. Previous research by Yuen *et al*. demonstrated that HIF activation could reduce lipid synthesis in animal models, which is consistent with our clinical observations. [15] Additionally, the reduction in inflammatory markers observed in other studies may correlate with the lipid-lowering effects noted in our roxadustat-treated patients. In contrast, standard lipid-lowering agents such as statins have had mixed results in cirrhotic patients due to potential hepatotoxicity and drug interactions. Our findings suggest that roxadustat may overcome these limitations by providing a safer and more holistic approach to metabolic modulation in cirrhosis.

Safety and Tolerability Considerations

The safety profile of any new therapeutic intervention is a critical aspect of its clinical utility. In our study, the incidence of adverse events in patients treated with roxadustat was low, with only minor complaints such as nausea and headache reported. These findings are in agreement with previous trials that have reported a favorable safety profile for roxadustat in non-cirrhotic populations.[16] Importantly, no significant liver enzyme elevations or other serious adverse events were observed, which is particularly relevant in cirrhotic patients who are at an increased risk for drug-induced liver injury. The tolerability of roxadustat in our study supports its potential for long-term use in managing the multifaceted complications of liver cirrhosis. However, long-term safety data in a larger cirrhotic population are needed to fully establish the risk-benefit profile of this intervention.

Impact on Quality of Life and Functional Outcomes

An important consideration in the management of liver cirrhosis is the improvement of patient quality of life. Anemia and dyslipidemia can significantly impair functional status and contribute to fatigue, reduced exercise tolerance, and overall diminished well-being. The observed improvement in hemoglobin levels in our study is likely to have a positive impact on patient energy levels and physical function. Moreover, the normalization of lipid parameters may reduce the risk of cardiovascular events, which are a major cause of morbidity and mortality in cirrhotic patients.[17] While our study did not directly measure quality-of-life indices, the biochemical improvements observed suggest that roxadustat could contribute to enhanced functional outcomes. Future studies should incorporate validated quality-of-life instruments to better quantify these benefits and further elucidate the broader clinical impact of roxadustat in this patient population.

Implications for Clinical Practice

The findings of our study have important implications for the management of liver cirrhosis. Given the dual challenges of dyslipidemia and anemia in this population, a therapeutic agent that can address both issues simultaneously offers a significant clinical advantage. Roxadustat's ability to improve lipid profiles and elevate hemoglobin levels suggests that it could play a pivotal role in the comprehensive management of cirrhotic patients. Moreover, the favorable safety profile observed in our study supports its potential integration into clinical practice. If confirmed by larger trials, roxadustat could become an integral part of therapeutic protocols aimed at reducing the metabolic and cardiovascular complications associated with liver cirrhosis. This would represent a paradigm shift in the management of a condition that has traditionally been challenging to treat due to the inherent limitations of existing pharmacotherapies.

Strengths of the Current Study

One of the major strengths of our study is the comprehensive evaluation of both lipid and hematologic parameters in a population of cirrhotic patients—a group that is often underrepresented in clinical trials. The use of advanced lipidomic profiling, combined with conventional biochemical assays, provided a detailed understanding of the metabolic changes induced by roxadustat. Furthermore, the statistically significant improvements observed in key clinical endpoints, along with the favorable safety profile, underscore the potential of roxadustat as a dual-action therapeutic agent. Our study design, which included a well-matched control group, allowed for a rigorous comparison of outcomes and minimized potential confounding factors. These strengths contribute to the

robustness of our findings and support the validity of our conclusions.

Limitations and Areas for Further Research

Despite its strengths, our study has several limitations that must be acknowledged. The relatively small sample size and the short follow-up duration limit the generalizability of our findings. Future studies with larger cohorts and longer observation periods are necessary to confirm the long-term benefits and safety of roxadustat in cirrhotic patients. Additionally, while our study focused on biochemical and hematologic endpoints, future research should incorporate clinical outcome measures such as survival, hospitalization rates, and quality-of-life assessments. Moreover, the mechanistic pathways underlying the observed metabolic improvements warrant further investigation through molecular and translational studies. Addressing these limitations will be essential for fully establishing the role of roxadustat in the therapeutic landscape of liver cirrhosis.

Future Directions and Research Recommendations

Based on our findings, several future research directions emerge. First, randomized controlled trials with larger sample sizes are needed to validate the efficacy and safety of roxadustat in diverse cirrhotic populations. Second, studies should explore the long-term impact of roxadustat on liver fibrosis progression, cardiovascular events, and overall survival. Third, mechanistic studies that investigate the molecular pathways involved in roxadustat's metabolic effects will provide deeper insights into its mode of action. Finally, research should assess the potential benefits of combining roxadustat with other therapeutic modalities, such as anti-inflammatory agents or antifibrotic drugs, to enhance clinical outcomes further. These future directions will help clarify the full therapeutic potential of roxadustat and may pave the way for novel, integrated treatment strategies in liver cirrhosis.

CONCLUSION

In our study demonstrates that roxadustat significantly improves both lipid profiles and hemoglobin levels in patients with liver cirrhosis. The prospective controlled trial conducted at BSMMU, Dhaka, revealed marked reductions in total cholesterol, LDL-C, and triglycerides, along with increased HDL-C and hemoglobin concentrations in the roxadustat-treated group compared to controls. These findings indicate that roxadustat's dual action, mediated through HIF stabilization, effectively addresses the metabolic and hematologic derangements of cirrhosis. Moreover, our results provide a strong rationale for further large-scale studies to assess long-term clinical benefits and impact on morbidity and mortality in this vulnerable population. These compelling results support the integration of roxadustat into treatment protocols for cirrhosis, potentially transforming patient management by reducing cardiovascular risk and improving overall quality of life significantly.

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