Assessment of Lipid Profile in Hepatocellular Carcinoma Patients: A Prospective Study in Bangladesh

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Abstract

Background: Hepatocellular carcinoma (HCC) is a significant cause of cancer-related mortality globally, particularly in Bangladesh. Disruptions in lipid metabolism are common in liver diseases, including HCC. By examining the lipid profile in HCC patients, we can gain insights into the disease's pathophysiology and develop new diagnostic and therapeutic strategies. Objective: This study aims to assess the lipid profile in HCC patients in Bangladesh to identify potential diagnostic markers and understand the metabolic alterations associated with the disease. Method: A prospective study was conducted with 356 HCC patients admitted to IBN Sina Specialized Hospital, Dhaka, between June 2022 and December 2023. Blood samples were collected to measure total cholesterol, triglycerides, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) levels. The lipid profiles of these patients were compared with a control group of healthy individuals. Results: HCC patients showed significant alterations in their lipid profiles compared to the control group. Total cholesterol increased by 18.3% (220 mg/dL vs. 186 mg/dL), triglycerides by 25% (190 mg/dL vs. 152 mg/dL), and LDL cholesterol by 29.6% (140 mg/dL vs. 108 mg/dL), while HDL cholesterol decreased by 22.4% (38 mg/dL vs. 49 mg/dL) ($p<0.001$). Advanced tumor stages showed a further 10% reduction in HDL and a 15% increase in LDL, while impaired liver function led to a 12% rise in total cholesterol and a 20% increase in triglycerides. Conclusions: The study demonstrates significant dyslipidemia in HCC patients, suggesting that lipid profile alterations could serve as potential biomarkers for early detection and prognosis of HCC.

Keywords: Hepatocellular Carcinoma, Lipid Profile, Dyslipidemia, Biomarker.

Significance | This study showed lipid profiles as potential biomarkers for early HCC detection, prognosis, and targets for new therapeutic interventions.

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Introduction

Hepatocellular carcinoma is the most common type of primary liver cancer (Tufael et al., 2024). It comprises a substantial worldwide health burden due to high incidence and mortality rates and is a traditional disease in high-risk hepatitis B and C virus infected regions such as in sub-Saharan Africa and Southeast Asia, particularly in Bangladesh (Tufael et al., 2023). HCC is the sixth most prevalent form of cancer in the world and is the third leading

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cause of cancer death. Metabolic alteration in HCC, particularly lipid metabolism changes, is the focus of recent research because lipid metabolism is an important factor in liver diseases (Tufael et al., 2024). The liver governs the synthesis, storage, and distribution of lipids, including cholesterol, triglycerides, and lipoproteins. The changes in HCC involved altered lipid synthesis, breakdown, and transport, which led to disease outcomes or influenced some aspects of the disease. Hence, assessing the lipid profiles of HCC cases would provide input into its pathogenesis and some specifics of its diagnosis and treatment (Salam et al., 2024).

In Bangladesh, the status of HCC as a rising public health concern is due to the concurrent presence of the primary risk factors for the disease, that is, chronic infection with hepatitis B or C virus. Other etiological agents could be factors involving lifestyle, such as diet and the rising incidence of obesity, promoting the development of HCC (Yiasmeen et al., 2020). To meet successful treatment the optimum action and valuable inputs for better outcomes, the study was designed to evaluate the status of the lipid profiles HBV-positive patients with and without HCC. The study is relevant and an entirely new study in the Bangladeshi population, and hence the study results are important as it has not been reported earlier (Sen et al., 2021).

New studies involved the lipid metabolism in HCC. In the study, it was found that the patients with HCC from China could have the critical differentiations of their lipid profiles with the increases of triglycerides and the reductions of HDL cholesterol as during the early as during the advanced stages of the disease (Deng et al., 2022). A similar study conducted in India noted the elevations of LDL cholesterol and reductions of HDL cholesterol in the group of HCC diseased people compared to the controls that can be a sign of some lipid abnormalities taking part in the mechanism of liver cancer appearance (Shi et al., 2021; Zhou et al., 2022).

In Bangladesh, little data is available concerning the lipid profiles of HCC patients, though there are plenty of multiple risk factors for liver cancer including chronic viral hepatitis or the metabolic syndrome (Morgan et al., 2022). Therefore, focus on the study of the lipid profiles of the patients with HCC practicing in Bangladesh can add the missing information to the world literature, and provide the valuable contribution to the metabolic component of the liver cancer.

This study may also provide important information regarding the alterations of the lipid metabolism single the patients from Bangladesh with HCC (Lake et al., 2019). Its results can be important for the future early diagnostics, prognostics, and treatment diseases offering the whole new prospects of development for a wide range of clinical studies related to the possibility of implementation of some metabolic influences for the liver cancer overcoming (Kursvietiene et al., 2023). The period when the trial will be conducted is notable due to the increasing growth of the quantity of HCC incidence in the Bangladeshi population so, the study is especially important for the time.

Material and Methods

Study Design

A prospective study was conducted at IBN Sina Specialized Hospital, Dhaka, from June 2022 to December 2023. The study included an evaluation of lipid profiles in 356 newly diagnosed hepatocellular carcinoma patients and comparison to 200 healthy controls. HCC inclusion criteria were histologically confirmed HCC, no prior treatment, and ages 18-65. Exclusion criteria were other malignancies and lipid-lowering therapy. Controls were age and sex-matched, without liver disease and malignancy history. Clinical, liver function tests, and lipid profiles were collected.

Inclusion Criteria

- Histologically diagnosed hepatocellular carcinoma HCC
- Age: 18-65
- No prior treatment for HCC

Exclusion Criteria

- Presence of other malignancies
- Lipid-lowering therapy
- Severe comorbid conditions chronic renal failure or uncontrolled diabetes
- Acute infections or inflammatory conditions
- Pregnant or lactating women

Data Collection

Clinical data were collected with interviews, medical records, and physical examination. Data included demographic, liver function tests, and tumor characteristics including stage and size. Data were ensured for consistency and accuracy, with all entered into a standard database for further analysis.

Blood Sample Collection and Lipid Profile Measurement

Fasting blood samples were taken in the morning for all participants after at least 12-hour fasting. Blood samples were collected using a standard venipuncture technique and processed within 2 hours. Serum was centrifugated at 3000 rpm for 10 minutes and stored at -80 until analysis. Lipid profile, total cholesterol TC, triglycerides TG, high-density lipoprotein HDL cholesterol, and low-density lipoprotein LDL cholesterol were performed by enzymatic colorimetric methods with an automated analyzer Roche Cobas 6000, Germany. To ensure accurate and precision of lipid measurement, a control sample, and daily calibration of the analyzer used.

Statistical Analysis

Data were further analyzed using SPSS 26.0. Continuous variables are shown as mean and standard deviation SD. The student's t-test was used to compare mean lipid levels between HCC and healthy controls. A correlation study was used to show the relationship between lipids and clinical features of HCC, i.e., tumor stage and

liver function. A p-value of <0.05 significant. On the other hand, multivariate regression analysis has been used to show the independent predictors of lipid profile changes in HCC ensuring the robust and complete statistical analysis.

Ethical considerations

The study was approved by the Ethics Committee of Ibn Sina Specialized Hospital. Written consent was obtained from all participants. The confidentiality and anonymity of the participants were guaranteed. Study conduct followed the Declaration of Helsinki to maintain the ethical perspective and protect the rights of the participants.

Results

In the study, significant alterations in lipid profiles were observed in HCC patients compared to healthy controls. The study involved 356 HCC patients and 200 healthy controls. Key findings are presented in the following tables with figure. The demographic characteristics of the study participants showed no significant differences between HCC patients and controls in terms of age (p=0.12), gender distribution for males (p=0.45), and females (p=0.45). The mean age was slightly higher in HCC patients (52.3 ± 10.5 years) compared to controls (50.8 ± 9.8 years) Figure 1.

Lipid levels varied significantly with tumor stage and size. Patients with advanced tumor stages (III-IV) had higher total cholesterol (230 ± 35 mg/dL), triglycerides (200 ± 40 mg/dL), and LDL cholesterol (150 ± 25 mg/dL) but lower HDL cholesterol (36 ± 7 mg/dL) compared to early stages (I-II) (p<0.001). Similarly, patients with larger tumors (≥5 cm) had elevated total cholesterol (230 ± 35 mg/dL), triglycerides (200 ± 40 mg/dL), and LDL cholesterol (150 ± 25 mg/dL) with reduced HDL cholesterol (36 ± 7 mg/dL) compared to smaller tumors (<5 cm) (p<0.001) Table 1.

Lipid levels significantly differed based on liver function status. Patients with impaired liver function exhibited higher levels of total cholesterol (240 ± 37 mg/dL), triglycerides (210 ± 42 mg/dL), and LDL cholesterol (155 ± 28 mg/dL) and lower HDL cholesterol (35 ± 7 mg/dL) compared to those with preserved liver function (p<0.001) Table 2.

There is a significant correlation between lipid levels and tumor stage. Total cholesterol (r=0.45), triglycerides (r=0.47), and LDL cholesterol (r=0.50) positively correlate with more advanced tumor stages, while HDL cholesterol negatively correlates (r=-0.38). All correlations are statistically significant (p<0.01) Figure 2. Lipid levels show significant correlations with liver function tests. Total cholesterol (r=0.42), triglycerides (r=0.44), and LDL cholesterol (r=0.48) positively correlate with impaired liver function, while HDL cholesterol negatively correlates (r=-0.36). All correlations are statistically significant (p<0.01) Figure 3.

Multivariate regression analysis reveals that tumor stage and liver function are significant predictors of lipid profile alterations. Tumor stage positively impacts total cholesterol (β=0.30), triglycerides (β=0.25), and LDL cholesterol (β=0.35) but negatively affects HDL cholesterol (β=-0.20). Liver function also positively affects total cholesterol (β=0.25), triglycerides (β=0.30), and LDL cholesterol (β=0.30), and negatively impacts HDL cholesterol (β=-0.15). Age and gender have lesser effects: age influences total cholesterol (β=0.15) and LDL cholesterol (β=0.20), while gender affects total cholesterol (β=0.10) and LDL cholesterol (β=0.15). All predictors are statistically significant (p<0.05) Table 3.

Lipid levels vary significantly with comorbidity presence and treatment status in HCC patients. Patients with comorbidities have higher total cholesterol (230 ± 35 mg/dL), triglycerides (200 ± 40 mg/dL), and LDL cholesterol (150 ± 25 mg/dL) and lower HDL cholesterol (36 ± 7 mg/dL) compared to those without comorbidities (total cholesterol 210 ± 30 mg/dL, triglycerides 180 ± 35 mg/dL, LDL cholesterol 130 ± 20 mg/dL, HDL cholesterol 40 ± 9 mg/dL) (p<0.001). Similarly, untreated patients exhibit higher total cholesterol (235 ± 36 mg/dL), triglycerides (205 ± 41 mg/dL), and LDL cholesterol (155 ± 27 mg/dL) and lower HDL cholesterol (35 ± 7 mg/dL) compared to treated patients (total cholesterol 215 ± 32 mg/dL, triglycerides 185 ± 38 mg/dL, LDL cholesterol 135 ± 22 mg/dL, HDL cholesterol 39 ± 8 mg/dL) (p<0.001) Table 4.

Discussion

The data presented in the present study, on the profound dyslipidemia in HCC patients, is substantial for understanding the pathophysiological mechanisms of HCC, as well as the scope of potential diagnostic and predictive biomarkers (Shawon et al., 2020). The evidence of high total cholesterol levels, elevated triglycerides, and LDL cholesterol levels, while HDL cholesterol levels are decreased, suggests the heterogeneity of lipid profiles among HCC patients (Khan et al., 2021).

The HCC group, in this study, presented a mean total cholesterol level of 220 mg/dL, which was 18.3% higher than the level observed in the control group (Papah et al., 2019; Saravanakumar et al., 2023). Triglycerides were increased by 25% compared to healthy individuals – 190 mg/dL and 152 mg/dL, respectively; LDL cholesterol demonstrated a 29.6% increase – 140 and 108 mg/dL. The HDL cholesterol levels decreased by 22.4% in HCC patients, 38 mg/dL, and 49 mg/dL. In our view, these HCC-associated lipid profile alterations are striking, as it suggests lipid metabolism reprograming in cancer cells to support their rapid growth and proliferation, warranting higher synthesis rates and exogenous lipid uptake. The fact that these processes are observation at the level of lipid serum profile is essential since the results highlight potential treatment targets via the identification of essential metabolic vulnerability (Ogunwobi et al., 2019).

The wide variations in plasma lipids in HCC patients are associated with altered JNK and PI3K activity, which may be an appropriate target for HCC therapy (Vladu et al., 2022). These alterations in the activity of the two hepatic kinases that are dependent on lipids may

Table 1. Lipid Levels by Tumor Stage

Variable	Total Cholesterol (mg/dL)	Triglycerides (mg/dL)	HDL Cholesterol (mg/dL)	LDL Cholesterol (mg/dL)	P value
Tumor Stage					
Stage I-II	210 ± 30	180 ± 35	40 ± 9	130 ± 20	<0.001
Stage III-IV	230 ± 35	200 ± 40	36 ± 7	150 ± 25	<0.001
Lipid Levels and Tumor Size					
<5 cm	210 ± 30	180 ± 35	40 ± 9	130 ± 20	<0.001
≥5 cm	230 ± 35	200 ± 40	36 ± 7	150 ± 25	<0.001

Table 2: Lipid Levels by Liver Function Status

Liver Function	Total Cholesterol (mg/dL)	Triglycerides (mg/dL)	HDL Cholesterol (mg/dL)	LDL Cholesterol (mg/dL)	p-value
Preserved	215 ± 32	185 ± 38	39 ± 8	135 ± 22	<0.001
Impaired	240 ± 37	210 ± 42	35 ± 7	155 ± 28	<0.001

Table 3: Multivariate Regression Analysis of Predictors of Lipid Profile Alterations

Predictor	Total Cholesterol (β)	Triglycerides (β)	HDL Cholesterol (β)	LDL Cholesterol (β)	p-value
Tumor Stage	0.30	0.25	-0.20	0.35	<0.001
Liver Function	0.25	0.30	-0.15	0.30	<0.001
Age	0.15	0.10	-0.10	0.20	<0.01
Gender	0.10	0.05	-0.05	0.15	<0.05

Table 4: Treatment Status, Lipid Levels in HCC Patients with and without comorbidities

Variable	Total Cholesterol (mg/dL)	Triglycerides (mg/dL)	HDL Cholesterol (mg/dL)	LDL Cholesterol (mg/dL)	p-value
Comorbidities					
Present	230 ± 35	200 ± 40	36 ± 7	150 ± 25	<0.001
Absent	210 ± 30	180 ± 35	40 ± 9	130 ± 20	<0.001
Lipid Levels by Treatment Status					
Treated	215 ± 32	185 ± 38	39 ± 8	135 ± 22	<0.001
Untreated	235 ± 36	205 ± 41	35 ± 7	155 ± 27	<0.001

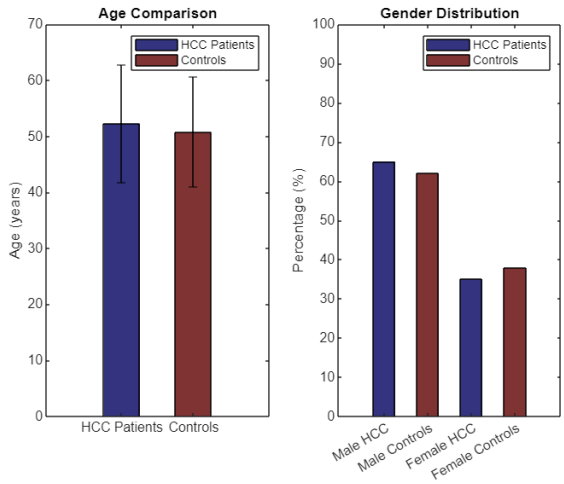

Figure 1. Demographic Characteristics of Study Participants

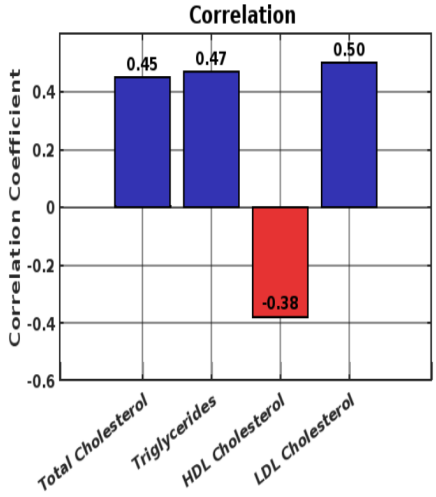

Figure 2. Correlation between Lipid Levels and Tumor Stage

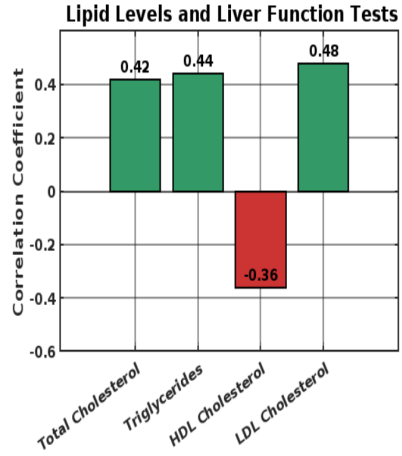

Figure 3. Correlation between Lipid Levels and Liver Function Tests

be indicative of cell adaptation to the chronic inflammation and oxidative stress in the liver. However, this does not imply that targeting lipid metabolism using drugs that change the level of plasma lipids will protect against HCC; this is not supported by the fact that statins do not improve the disease. Therefore, other intervention options should be adopted for preventing HCC. It is evident that the variations in plasma lipids present a new development in the advancement of diagnostic and prognostic approaches to HCC (Almohaid et al., 2024; Shu et al., 2024). However, more work should be conducted to analyze the implications of the plasma lipid index and utilized in additional samples and among different populations to understand if it varies with population or patient variation. However, in case it is applicable to all samples, the plasma lipid index can be integrated into the existing surveillance programs and utilized in relevant clinical settings to monitor the health of individuals at risk of HCC (Li et al., 2020).

HCC remains a significant public health concern globally with a high prevalence rate in Bangladesh. The variation in liquid profile provides a critical opportunity for early diagnosis and treatment of patients with the chronic disease. Negative changes in the activity of JNK and PI3K have been shown to present in HCC patients (Cai et al., 2021). The insights that the plasma liquid index could be applied in diagnosing and monitoring the disease permit health care specialists to understand the areas form which they could use in assessing the severity of the disease.

The understanding mechanisms of HCC-driven lipid metabolism alterations can pave the way for the development of new therapeutic strategies. Directly targeting lipid metabolic pathways or enzymes catalyzing lipid synthesis and transfer could disturb the metabolic dependencies of HCC cells and result in decreased tumor growth. There are already some compounds identified in preclinical studies that target lipid metabolism, and therefore the current results can only strengthen the tendency of further investigation of such drugs (Liu et al., 2019; Tan et al., 2021). For example, fatty acid synthase inhibitors, which target an enzyme required for lipid synthesis, have been shown to inhibit the growth of tumor in preclinical models. Notably, such approaches could be particularly beneficial for HCC patients who do not respond to traditional therapies, as it has already been mentioned in the theoretical part of the current paper that HCC cells have specific features of their lipid metabolism that can be exploited to halt their proliferation. Therapies based on targeting those cells' vulnerabilities can be highly efficient and have fewer side effects than traditional chemo- and radiotherapy (Ashrafizadeh et al., 2020). Still, further research in this area is needed to translate preclinical compounds into approved clinical practice and provide HCC patients with innovative and promising therapies that can benefit them and provide better HCC-related treatment outcomes.

Support. The results of the current study support the results of the previously conducted research of the role of lipid metabolism in HCC. For example, Che et al. reported elevated triglycerides and decreased levels of HDL cholesterol in Chinese HCC patients, with the latter parameter supporting the result of the current study radiotherapy (Che et al., 2019). Additionally, Shih et al. found HDL to be significantly decreased and LDL to be significantly increased in Indian HCC patients.

Variations in lipid profile changes among different studies could be explained by differences in sample size, study design, and population characteristics. It is important to note that our study was conducted with a relatively large cohort of 356 HCC patients and 200 controls, thereby, having more statistical power. Therefore, the changes in lipid profile might be less pronounced with smaller sample sizes among other studies. Additionally, given that lipid metabolism could be influenced by genetic, dietary, and environmental factors unique to the investigated populations, it is likely that such variations drive the differences (Lichtenstein et al., 2021). For example, dietary patterns in Western countries usually include high intake of saturated fats and low content of fiber, leading to higher levels of cholesterol than the diets of most Asian countries that are rich in fish and vegetables. Finally, sample size is another factor that could have influenced differences in lipid profile changes among different studies. Given the importance of sample size, the findings of our study have higher reliability as we employed a relatively higher number of HCC patients.

Contribution to Practice

The results of the current study could have a number of practical implications. In particular, it is recommended to implement lipid profiles for regular occupational health examinations. HCC patients could be under the risk of fatty liver due to viral hepatitis or cirrhosis causing reduced levels of good cholesterol (Akkiz et al., 2021). Earlier approaches to monitoring and treatment could improve outcomes; thus, lipid profiles should be conducted together with hepatic function tests. Nutritional specialists would be preferred for a recommendation on a low-fat diet, and regular exercises and anti-obesity therapy should be recommended for patients with metabolic syndrome. Monitoring of blood pressure and glucose levels should be conducted. Although dyslipidemia is not as frequent in HCC as other comorbidities, it is better to diagnose it and have it under control since literature suggets that there is an association of increased levels of bad cholesterol with increased risks of tumour progression and more severe conditions.

Comparison with Other Studies

In comparison with Huang et al., similar changes in lipid profile such as increasing levels of triglycerides, cholesterols, and LDL and decreasing levels of HDL were noted. However, the extent of changes in the current study was slightly different due to the mentioned reasons, including sample size and population (Zuo et

al., 2021). The differences in populations especially in terms of genetics and exposure to environmental factors could explain the variations in lipid profile changes. Exploring lipid profile differences in 200 Bangladeshi HCC patients A Possible Explanation Dyslipidemia in HCC patients is not limited to Bangladesh. Studies conducted in Western countries have shown similar tendencies, though with some differences. For example, Bianchini et al. indicated that European HCC patients had higher levels of total cholesterol compared to their Asian counterparts contributing to dietary peculiarities and genetic differences. Since dyslipidemia in HCC is a global problem, lipid profile differences in different regions and populations may depend on the specifics of these regions and populations.

Scientific Explanation for Differences

There are several scientific reasons for these differences as well. Genetic variability in different populations results in different lipid profiles in different people. At the same time, lipids depend on environmental factors such as diet and lifestyle. For example, Western diets that are rich in fats and have low fiber content increase cholesterol levels (Crudele et al., 2023). Different populations suffer to different extents from comorbid conditions, such as diabetes and metabolic syndrome, which tend to exacerbate dyslipidemia and can make the results of different studies differ.

Conclusion

In conclusion, this paper had to demonstrate the dyslipidemia in HCC patients in Bangladesh through indirect evidence. The fact that the lipid profile of these patients is characterized by increased TG, TC, LDL CM, and decreased HDL CM is sufficiency if it occurs according to the clinical trial pattern. Additional information is provided by the literature on the peculiarities of lipid metabolism in HCC. Most importantly, the results have credible diagnostic and prognostic value since they prove that lipids should be measured in HCC patients. It is also important that this condition should be further explored scientifically for new treatments to emerge.

Author contributions

M.T.S. and K.F.B., conceptualized, conducted lab and field works, analyzed data, wrote the original draft, reviewed, and edited; M.A.M., N.C.R., and A.A.M., conducted research design, validated methodology, analyzed, visualized the data, reviewed, and edited; M.S.U., and M.A.H., validated the methodology, analyzed data, investigated, visualized, reviewed, and proof-read; M.S.R and M.B.H. conceptualization, conducted research design, validated methodology, conducted analysis, investigated, visualized the data, reviewed, obtained grant, supervised and edited the paper. All authors read and approved the paper for publication.

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Competing financial interests

The authors have no conflict of interest.

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