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Original article

Association between Abnormalities of Serum Lipid Profile and the Aggressiveness of HCV Related Hepatocellular Carcinoma (HCC)

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Abstract:

Hepatocellular carcinoma (HCC) represents about 90% of primary liver cancers. In Egypt, it represents the fourth common cancer. Main risk factor for HCC is cirrhosis of the liver that caused by different causes including viral hepatitis, alcohol, non- alcoholic fatty liver disease (NAFLD), metabolic, autoimmune liver disease, and Aflatoxin. As many types of cancer, aberrant lipid profile may be present in HCC patients which may be related to aggressiveness of the tumor. **Aim:** To evaluate the association between serum lipid profile abnormalities and the aggressiveness of HCC. **Methods:** One hundred and fifty participants were included in the study, divided into three groups: sixty patients with HCV related chronic liver disease, sixty patients with HCC diagnosed by ultrasound and confirmed by Triphasic CT and thirty apparently healthy individuals as a control. All participants were subjected to: full history taking, full clinical examination, laboratory investigations (CBC, RBS, ESR, serum creatinine, liver profile and lipid profile "total cholesterol, TG, LDL, HDL, VLDL, HDL\ LDL ratio") and radiological examination (ultrasound, Triphasic CT).

Results: The results showed that HCC patients had low total cholesterol, HDL, LDL compared to normal group**.** LDL had weak positive correlation with the combination of all four tumor aggressiveness parameters together. The mean HDL was significantly higher in those with portal vein thrombosis (PVT) than those without in HCC patients. **Conclusion:** Hepatocellular carcinoma (HCC) patients had low levelof serum lipid profile (TC, HDL, and LDL), Plasma LDL had weak positive correlation with aggressiveness index, and HDL was significantly higher in those with PVT.

Key words: Lipid profile, HCC, Tumor aggressiveness index.

Introduction

Hepatocellular carcinoma (HCC) accounts for 90% of primary hepatic malignancies. It is the sixth most common solid tumor and the third most common cause of cancer mortality worldwide. The overall prognosis is poor, with an estimated 5-year survival of 10% to 15% in patients unamenable to resection or liver transplantation **(1).**

Liver cirrhosis is an important risk factor for HCC, and may be caused by chronic viral hepatitis, alcohol, inherited metabolic diseases such as hemochromatosis or alpha-1-antitrypsin deficiency, and non-alcoholic fatty liver disease **(2).**Long-term follow-up studies have demonstrated that approximately 1–8% of patients with cirrhosis develop HCC yearly (e.g. 2% in HBV-infected cirrhotic patients and 3–8% in HCV infected cirrhotic patients) **(3).**

Obesity, diabetes and fatty liver disease have come to be recognized as a risk factor of HCC **(4)**, although the mechanisms by which these overlapping conditions contribute to cancer development remain elusive. Alternation in blood lipid profiles and metabolism have been described in the presence of chronic hepatitis infection, cirrhosis, and hepatocellular carcinoma (HCC) **(5).**

In general, lipids are known to play a crucial role in tumor development and progression **(6).**Briskly proliferating cancer cells require a constant supply of lipids for membrane biogenesis and protein modifications. Also, the cancer cells that are not rapidly proliferating require increased amounts of lipids for enhanced signaling and resistance against apoptosis. Lipoproteins are the distributors of both endogenous as well as exogenous lipids across the tissues. It is therefore plausible that lipoproteins play a fundamental role in cancer progression via supplying lipids to malignant cells and tumors **(7).** The global epidemic of obesity has recently shifted attention to the increased incidence of obesity- associated, metabolic syndrome- associated non-alcoholic liver disease (NAFLD) and obesity driven cancers including HCC that may occur in the presence or in the absence of cirrhosis **(8).** There are multiple reports of altered plasma lipid profiles in obesity or metabolic syndrome associated HCC **(9).**

This work aimed to evaluate the association between serum lipid profile abnormalities and the aggressiveness of HCC.

Patients and methods

This **cross sectional** study was performed on 150 consecutive Egyptian participants attended to the Department of Hepatology, Gastroenterology and Infectious Diseases, Benha University Hospital- within the period from September 2019 to July 2020- after approval of Benha university ethical committee. The 150 participants were subdivided into three groups: group I: 60 patients diagnosed as liver cirrhosis based on: clinical examination, Laboratory investigations, US finding), group II: 60 patients diagnosed as HCC,based on diagnosis by two imaging modalities according to guidelines (Ultrasound, Triphasic CT "early arterial enhancement with delayed washout in venous phase" or MRI are mainstays in diagnosis of HCC), group III: 30 apparently healthy persons (age and sex matched) with normal routine laboratory investigation and negative for both HCV Ab and HBsAg served as a control group. **Inclusion criteria**: HCV related cirrhotic patient with or without HCC after…… **excluding patients**: with age less than 18, chronic HBV, with cholangiocarcinoma, with extrahepatic malignancy and those with history of any drug of lipid lowering agent (statins).

All patients included in the study were subjected to informed consent from each patient after explaining the whole study procedures, full history taking, complete clinical examination including: body mass index (BMI) will be calculated as weight (kg)\ height (m2), laboratory investigation (CBC, blood sugar, serum creatinine, Liver functions "AST-ALT-ALP-serum bilirubin (total and direct)-serum Albumin-Prothrombin time), Viral markers (HBs Ag, HCV Ab), Alpha- fetoprotein level and lipid profile (serum cholesterol, triglyceride, HDL, LDL, VLDL, HDL\LDL ratio).

After fasting 8 hours, collection of venous blood samples for lipid profile measurement was performed. The samples were centrifuged at 3000 rpm for 15 minutes, followed by plasma separation and then stored at -80°C until the time of analysis. At the time of analysis all reagents and samples were allowed to reach the room temperature before use and all samples, standards, and control were assayed. Lipid profile was performed by standard methods using biosystem A15 **(Barcelona, Spain)** chemical auto analyzer by appropriate chemical principle.

Radiological investigations: abdominal ultrasonography, Triphasic Computed Tomography (CT) was performed for all

patients with HCC for: confirmation of the findings of ultrasonography.

Patients were evaluated for liver function according to Child-Pugh classification.

A total score of 5-6 is considered grade A (well-compensated disease); 7-9 is grade B (significant functional compromise); and 10-15 is grade C (decompensated disease) **(10)**.

- **MELD score was calculated to cirrhotic and HCC group :**

MELD Score = 9.57 x ln (serum creatinine in mg/dL) + 3.78 x ln (serum bilirubin in mg/dL) + 11.2 x ln (INR) + 6.43 **(11) .**

- **Tumor aggressiveness index was calculated to HCC group: (12)**

As the sum of scores:

MTD "maximum tumor diameter": MTD< 4.5; 4.5≤ MTD≤ 9.6; MTD >9.6; for scores1, 2, 3 respectively;

AFP (cut off): AFP< 100; 100≤ AFP≤ 1000; AFP>1000; for scores 1, 2, 3 respectively;

PVT (No⁄ Yes): PVT (No); PVT (Yes); for scores 1 and 3 respectively;

Nodules (number): Nodules ≤ 3; Nodules >3; for scores 1 and 3 respectively.

Statistical analysis

Data management and statistical analysis were done using SPSS vs.25. **(IBM, Armonk, New York, United states).**

Numerical data were summarized as means and standard deviations or medians and ranges. Categorical data were summarized as numbers and percentages. Comparisons between three groups were done using one-way ANOVA or Kruskal Wallis test for normally and non-normally distributed numerical data respectively. Categorical data were compared using Chi-square or Fisher's exact test if appropriate. Post hoc analyses were done in case of significant overall effect and all post hoc analyses were Bonferroni adjusted. Correlation analyses were done between lipid profile and other parameters using Pearson's or Spearman's correlation. "r" is the correlation coefficient. It ranges from -1 to +1: -1 indicates strong negative correlation, +1 indicates strong positive correlation, while 0 indicates no correlation. All P values were two sided. P values less than 0.05 were considered significant.

Results

This study was conducted on three groups: I (cirrhotic patients), II (HCC patients) and III (control) with no significant difference between three groups regarding age and sex. The mean age was 62 in cirrhotic & control and 64 in HCC group. There was a male predominance in all groups, and no significant difference regarding BMI, DM and hypertension (**Table 1).**

Liver profile was done to studied group including: AST, ALT, s.Albumin, bilirubin total and direct, PT and INR. It showed overall significant difference between HCC, cirrhotic and control (p value< 0.005). Median serum bilirubin total and direct was significant higher in HCC group than cirrhotic group (p value= 0.004). No significant difference regarding liver enzymes, albumin, PT and INR between HCC and cirrhotic group **(Table 2)**.

Triphasic CT was done to HCC group showed that **27** patients (45.0%) had one focal lesion, **16** patients (26.7%) had two FLs, **15** patients (25.0%) had more than three FLs and only **2** patients (3.3%) had three FLs. Triphasic CT showed portal vein thrombosis in **24** patients (40.0%). Mean maximum tumor diameter was 4.3. Mean tumor aggressiveness index was 6 (**Table 3), (figure 1)**.

MELD and Child score were calculated to both cirrhotic and HCC group. They showed that MELD score was significantly higher in HCC group (21) than cirrhotic group (17) (p value= 0.008). Child score showed significant difference between cirrhotic and HCC group (p value= 0.034); 20% of cirrhotic group was Child A compared to 8.3% in HCC group. **Twenty** patients of cirrhotic group (33.3%) was Child C compared to **33** patients in HCC group (55.0%) **(Table 4), (figure 2).**

Lipid profile showed that mean cholesterol was significantly lower in cirrhotic group (134) and HCC group (131) than control (160) (p value= o.oo1). Mean HDL was significantly lower in HCC group (39) than control (48) (p value= 0.019). Median LDL was significantly lower in cirrhotic group (64.5) & HCC group (69.6) than control (89.6) (p value= 0.002). Mean LDL/HDL ratio was significantly lower in cirrhotic group (1.66) than HCC group (1.99) (p value= 0.044). No significant difference in other parameter between the three groups **(Table 5), (figure3, 4).**

Correlation between lipid profile and prognostic parameter of HCC in HCC group showed that LDL had weak significant positive correlation with aggressiveness index (r = 0.271 & p value = 0.036). The mean HDL was significantly higher in those with PVT (43) than those without (37); p value was 0.035 (**Table 6, 7).**

Table (1): Age, sex, BMI and past history among the studied groups.

	Group I Cirrhotic group (n = 60)	Group II HCC group (n = 60)	Group III Control (n = 30)	P value
Age (years) Mean ±SD	62 ±10	64 ±9	62 ±8	0.424
Gender Males n (%)	42 (70.0)	44 (73.3)	21 (70.0)	0.907
Females n (%)	18 (30.0)	16 (26.7)	9 (30.0)	
Body mass index Mean ±SD	33.37 ±6.16	32.61 ±5.71	31.32 ±5.98	0.31
Diabetes mellitus n (%)	19 (31.7)	17 (28.3)	5 (16.7)	0.315
Hypertension n (%)	7 (11.7)	4 (6.7)	2 (6.7)	0.566

P value significant <0.005

Table (2): Liver profile among studied groups**.**

	Group I Cirrhotic group (n=60)	Group II HCC group (n=60)	Group III Control (n= 30)	P value
AST(IU) Median (range)	53 (21 - 805)	71 (21 - 865)	33 (15 - 122)	P1:0.104 P2:0.001 P3:<0.001 P4:<0.001
ALT (IU) Median (range)	35 (13 - 523)	55 (12 - 670)	30 (16 - 98)	P1:0.067 P2:0.38 P3:0.002 P4:0.002
Serum bilirubin(mg\dl) Median (range)	2 (0.5 - 14.5)	4.05 (0.6 - 32)	0.95 (0.5 - 1.2)	P1:0.004 P2:<0.002 P3:<0.001 P4:<0.001
Direct bilirubin (mg\dl) Median (range)	1.25 (0.1 - 9.5)	2.8 (0.2 - 25)	0.3 (0.1 - 0.6)	P1:0.004 P2:<0.001 P3:<0.001 P4:<0.001
Albumin (gm\dl) Mean ±SD	2.8 ±0.4	2.6 ±0.5	4 ±0.4	P1:0.207 P2:<0.001 P3:<0.001` P4:<0.001
Prothrombin time(sec) Mean ±SD	18.49 ±5.44	21 ±9.11	13.17 ±1.2	P1:0.197 P2:<0.001 P3:<0.001 P4:<0.001
INR Mean ±SD	1.53 ±0.45	1.77 ±0.75	1.04 ±0.08	P1:0.101 P2:<0.001 P3:<0.001 P4:<0.001

P1: p value between group I (GI), group II (GII), P2: p value between group I (GI), group III (GIII), P3: p value between group II (GII), group III (GIII), P4: p value between three groups. P value significant < 0.005

Table (3): Triphasic abdominal CT features of studied patients with HCC.

Triphasic CT finding			HCC group (n=60)
Number of focal lesions	**One**	**n (%)**	27 (45.0)
	Two	**n (%)**	16 (26.7)
	Three	**n (%)**	2 (3.3)
	>3	**n (%)**	15 (25.0)
Portal vein thrombosis	**n (%)**		24 (40.0)
Max. tumor diameter	**Mean ±SD**		4.3 ±2.6
Tumor aggressiveness index	**Mean ±SD**		6 ±2

Table (4): Child score and MELD score in studied cirrhotic and HCC groups

			Group I Cirrhotic group (n = 60)	Group II HCC group (n = 60)	P value
MELD score	**Mean ±SD**		17 ±7	21 ±8	0.008
Child score	**CHILD A**	**n (%)**	12 (20)	5 (8.3)	0.034
	CHILD B	**n (%)**	28 (46.7)	22 (36.7)	
	CHILD C	**n (%)**	20 (33.3)	33 (55.0)	

Table (5): Lipid profile among studied groups:

	Group I Cirrhotic group (n=60)	Group II HCC group (n=60)	Group III Control (n=30)	P value
Serum cholesterol (mg\dl) Mean ±SD	134 ±28	131 ±39	160 ±40	P1:1 P2:0.004 P3:0.001 P4:0.001
Triglyceride (mg\dl) Mean ±SD	118 ±45	114 ±30	125 ±37	P4:0.372
HDL (mg\dl) Mean ±SD	44 ±12	39 ±9	48 ±14	P1:0.074 P2:0.514 P3:0.019 P4:0.007
LDL (mg\dl) Median (range)	64.5 (18.2 - 144)	69.6 (20.8 - 283)	89.6 (33.6 - 138.2)	P1:1 P2:0.001 P3:0.009 P4:0.002
VLDL (mg\dl) Mean ±SD	23.3 ±9	22.9 ±6.1	24.6 ±7.7	P4:0.579
LDL/HDL ratio Mean ±SD	1.66 ±0.63	1.99 ±0.86	1.98 ±0.61	P1:0.044 P2:0.166 P3:1 P4:0.031

P1: p value between group I (GI), group II (GII), P2: p value between group I(GI), group III (GIII), P3: p value between group II (GII), group III (GIII), P4: p value between three groups. P value significant <0.005

Table (6): Correlation between lipid profile and prognostic parameter of HCC in studied HCC group:

	Cholesterol		Triglyceride		HDL		LDL		VLDL		LDL/HDL ratio	
	r	p	r	p	r	p	r	p	r	p	r	p
AFP	0.127	0.334	0.089	0.501	0.029	0.824	0.181	0.166	0.035	0.788	0.227	0.081
Max tumor diameter	-0.101	0.443	-0.09	0.492	-0.211	0.105	0.003	0.981	-0.117	0.373	0.049	0.711
Tumer aggressiveness index	0.205	0.117	0.053	0.688	0.141	0.283	**0.271**	**0.036**	0.019	0.887	0.17	0.193
MELD score	0.039	0.767	-0.003	0.981	0.083	0.528	0.061	0.644	-0.042	0.752	0.068	0.607

P value significant <0.05, r= correlation coefficient, HDL: high density lipoprotein, LDL: low density lipoprotein, VLDL: very low density lipoprotein.

Table (7) : Lipid profile parameters according to portal vein thrombosis in group II (HCC group):

		PVT	No PVT	P value
Serum cholesterol	Mean ±SD	135 ±56	129 ±23	0.547
Triglyceride	Mean ±SD	117 ±34	112 ±27	0.496
HDL	Mean ±SD	43 ±12	37 ±6	0.035
LDL	Median (range)	71.5 (20.8 - 283)	69.6 (29.2 - 112)	0.862
VLDL	Mean ±SD	23.6 ±6.7	22.5 ±5.7	0.487
LDL/HDL ratio	Median (range)	1.95 (0.4 - 5)	1.95 (0.7 - 3.6)	0.958

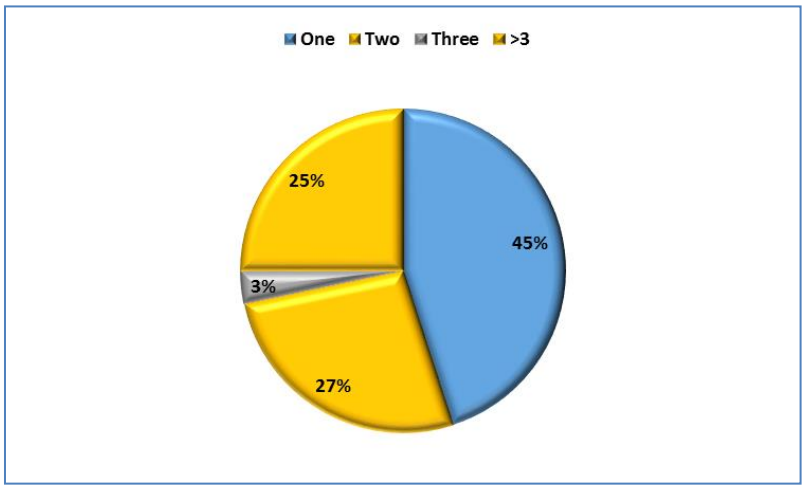

Figure (1): Number of focal lesions by triphasic CT in patient with HCC

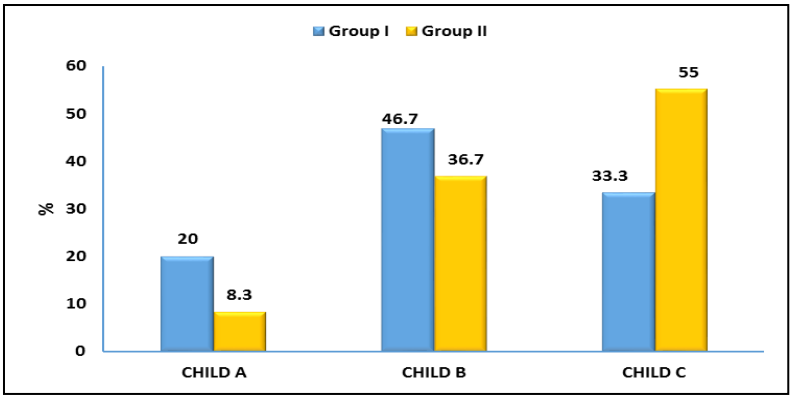

Figure (2): CHILD score in cirrhotic and HCC groups

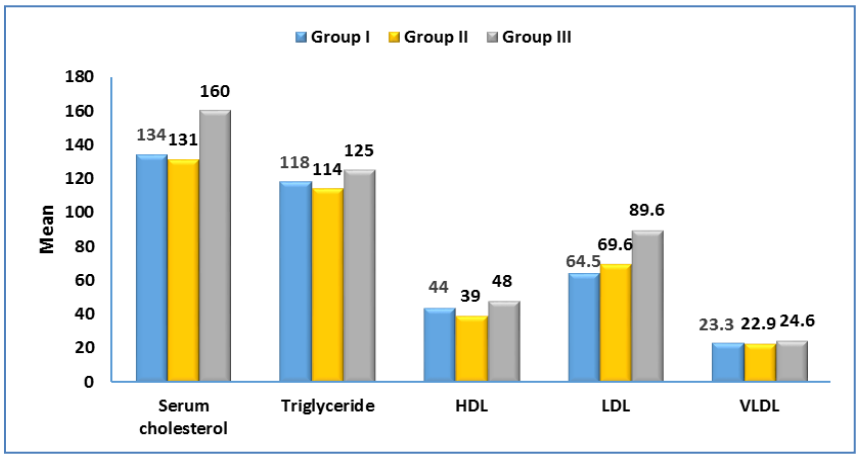

Figure (3): Lipid profile in the studied groups

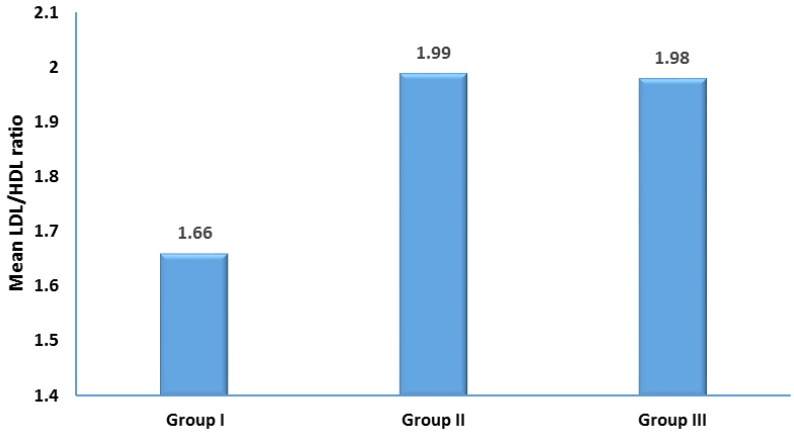

Figure (4): LDL/HDL ratio in the studied groups

Discussion

Hepatocellular carcinoma (HCC) represents the sixth most common cancer worldwide. In Egypt, it represents the fourth common cancer. Many hospital- based studies reported increasing the incidence of HCC. The reason for increased incidence could be attributed to (1) improvement in screening programs and diagnostic tools, (2) increasing the survival rate of cirrhotic patients that increases the chance of developing HCC, and (3) increasing the incidence and complications of hepatitis C virus (HCV) which is the most important risk factor in developing liver cancer including HCC in Egypt **(13)** . Alterations in blood lipid profiles and metabolism have been described in association with hepatocellular carcinoma (HCC). Furthermore, lipid abnormalities have been described during the processes of hepato-carcinogenesis **(14).**

In the current study, the mean age of patients with HCC was 64 ±9 years, ranging from 47 to 90 years. This result agreed with other investigators who reported in a study including 165 HCC patients that the mean age of HCC patients was 62± 9 years **(15)** and other authors who documented that the mean age was 60.60 ± 7.35 years for the HCC patients **(16).**

In contrast, other authors reported younger age with average 59 years **(17)** and so the other authors showed the same result **(18).**

This study was carried out on sixty patients with hepatocellular carcinoma; including (73.3%) males and (26.7%) females with male to female ratio 2.75:1.

Male predominance for HCC development with male/ female ratios ranging between 2:1 and 4:1 as researchers reported **(19)**. This also come in accordance with other researchers who declared that male to female ratio was 3.7: 1**(20).**

In this study, BMI showed no significant difference between patients of studied groups and so other investigators reported no significant difference between studied groups regarding BMI **(21).**Unlike other researchers who reported that BMI was high in cirrhotic patient **(22).**

In the current study diabetes mellitus and systemic hypertension showed no significant difference between patients of studied groups.

This was in disagreement with other researchers who reported that diabetes is a risk factor for HCC that work independently or synergistically with other risk factors

such as HBV infection, male gender, and age **(23).**

This difference may be due to small number of patients integrated in this study.

In HCC group 17% are diabetic and only 4% are hypertensive, unlike other investigators who showed that 29.9% are diabetic and 37.9% are hypertensive **(24).**

In this study; liver profile (ALT, AST, serum Bilirubin, serum Albumin and Prothrombin time and INR) was done to all patients of both studied groups.

Regarding liver profile, serum bilirubin (total and direct) were higher in HCC than cirrhotic group with no significant difference regarding liver enzymes, serum albumin, PT and INR between cirrhotic and HCC group, unlike other investigators who showed no significant difference between HCC and cirrhotic groups regarding liver profile. This is attributed to that most of cirrhotic patients integrated in the study were at advanced stage **(25).**

In the current study about 45% of HCC patients had single hepatic focal lesion, 26.7% patients had two hepatic focal lesions and 25% patients had more than three hepatic focal lesions.

Other investigators reported that 19 patients (63.33 %) showed single hepatic focal lesion, 7 patients (23.33%) had 2 focal lesions and 4 patients (13.33%) had 3 focal lesions **(25).**

Other reviewers also showed that most of the HCC lesions (67%) were single nodule or two nodules **(26).**

In the current study 40% of HCC patients had PVT, another researchers reported that about 28.55% of HCC patient had PVT **(27)** and also another study showed that PVT was found at 29.8% of HCC patients **(28).**

PVT was found in patients with large tumor, as well as tumor multifocality, higher AFP levels, and higher total bilirubin levels (**27).**

In this study maximum tumor diameter (MTD) was 4.3±2.6. Other investigators reported that MTD <4.45 cm in 47.4% of HCC patients and from 4.45 to 9.6 cm in 42.7% of patients **(28).**

Another study showed that 57.4% of HCC with MTD between 5 and 10 cm, 16.8% MTD was >10 cm and 25.7% MTD <5 cm as this study include patient underwent routine surgery in cancer institute **(29).**

Other investigators enrolled 138 HCC patients in their study 54 patient (39.2%) with size of nodule <3 cm and 84 (60.8%) of patients with size of nodule ≥3 cm **(30).**

In this study mean MELD score in HCC group was 21±8, most of patient were Child C (55%), while 36.7% of HCC patients were Child B and 8.3% were Child A.

This comes in partial agreement with other researchers as 58.3% of HCC patients were Child C and 41.7% were Child B **(26).**

Unlike another study that showed that most of HCC patients were Child B (52%), 28.7% were Child C and 19.3% were Child A **(28).**

In this study, serum cholesterol, HDL, LDL and LDL/HDL ratio- showed an overall significant difference between three groups. Mean cholesterol was significantly lower in cirrhotic group and HCC group than control (p value= o.oo1). Mean HDL was significantly lower in HCC group than control (p value= 0.019). Median LDL was significantly lower in cirrhotic group & HCC group than control (p value= 0.002). Mean LDL/HDL ratio was significantly lower in cirrhotic group than HCC group (p value= 0.044) with no statistically difference regarding triglycerides and VLDL among these groups.

Other authors documented that low serum levels of total cholesterol (TC), TG, LDL-C, and HDL-C are associated with increased risk of HCC, as dysregulation of cholesterol metabolism itself might act as a part of hepatocarcinogenesis. Cholesterol is involved in numerous biochemical pathways that are potentially relevant in HCC development, including several cytokine and signaling pathways. These pro-inflammatory cytokines could act as carcinogens or co-factors for hypocholesterolemia and hepato-carcinogenesis. Cholesterol accumulation reinforced the antitumor property of natural killer cells **(31).**

Another study results showed low level of serum lipid profile (TC, TG and LDL) in HCC patients in comparison with healthy controls except for HDL that showed no statistically difference between HCC, chronic hepatitis C patients (CHC) and normal groups and there was no statistically difference regarding parameters of lipid profile between CHC and HCC patients **(26).**

Also, another study reported that the HCC group showed significantly lower levels of total cholesterol, LDL-C, HDL-C and TG **(21).**

Unlike other investigators who reported that TC, HDL-C and LDL-C were higher in liver cancer patients than normal group, while TG was low in liver cancer patients and normal group. This difference may be due to small number of HCC patients included in this

study (10 patients) in comparison with 10 controls **(32).**

Also, another study showed that TC was higher in HCC patients than cirrhotic and normal group. HDL-C was higher in HCC patients than cirrhotic group. The increase in cholesterol in HCC has been related to a malignant obstructive lesion of the biliary tree. The loss of negative feedback mechanism for cholesterol regulation as well as an increase in cholesterol synthesis by undifferentiated hepatocellular carcinoma cells…….? In cirrhosis, total cholesterol and HDL-cholesterol values were reduced and this may be due to cellular necrosis in cirrhosis **(33).**

This difference and low level of serum lipid profile can be explained by: cholesterol metabolism is impaired in patients with chronic liver disease, leading to a decrease in cholesterol levels as; approximately 80% of endogenous cholesterol is synthesized in the hepatocellular microsomes. Preclinical HCC might itself reduce cholesterol, perhaps by increased receptor activity for LDL-C in HCC cells. Low lipid profiles could be a manifestation of malignancy during the latent period. The consumption of cholesterol is doubled in HCC tissues compared with non-tumor tissues. Tumor cells induce lipo-synthesis and accumulation of intracellular cholesteryl esters. The scavenger receptor class B type, an HDL-C receptor, enhances the uptake of cholesteryl esters, leading to a reduction in serum HDL-C levels **(31).**

In this study, correlation between lipid profile parameters and prognostic parameters of HCC (parameters of tumor aggressiveness index) showed that LDL had weak positive correlation with the combination of all four tumor aggressiveness parameters together (the Tumor Aggressiveness Index). Mean HDL was significantly higher in those with PVT than those without, with no significant correlation with the other parameters of tumor aggressiveness index.

While another study showed that increase in MTD was significantly associated with increase in total cholesterol and LDL cholesterol. Presence of PVT was significantly associated only with decrease in HDL cholesterol. Increase AFP levels were significantly associated with both decrease HDL cholesterol and increase LDL cholesterol. The tumor aggressiveness index was only significantly associated with decrease HDL cholesterol levels **(34).** This difference may be due to different sample

size and patient with increased serum bilirubin level were excluded from the study.

Our result was not in accordance with another study that declared the association of low plasma HDL and high plasma LDL levels with indices of tumor aggressiveness (MTD, AFP, tumor multifocality and presence of PVT) **(14).**

Conclusion

- HCC patients had low levels of serum lipid profile (TC, HDL, and LDL) while cirrhotic patients had only low level of TC and LDL.
- Plasma LDL had weak positive correlation with aggressiveness index of HCC. HDL was significantly higher in those with PVT in HCC patients.

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