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Incidence of Human Cytomegalovirus Viremia among Egyptian Hepatitis C - Patients with Hepatocellular Carcinoma

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ABSTRACT

Background: Hepatocellular carcinoma (HCC) is the major hepatic complication that may arise after many years of hepatitis C virus (HCV) infection. In Egypt, HCV represents the major health problem, also human cytomegalovirus (HCMV) is known as one of the highest un-resolved latent infections among general population. HCMV viremia in the co-infection with HCV may cause life threatening in HCC patients. Our study aimed to detect HCMV viremia in HCV–patients experienced HCC, and to investigate its role in disease worsening. **Methods:** In HCC patients, HCV-RNA viral load was determined by real- time polymerase chain reaction. In HCV-HCC patients, HCMV-DNA was detected by amplification of gB gene region using nested-polymerase chain reaction. **Results:** HCMV-DNA was detected in 4/73 in control subjects with prevalence rate of 5.4%, whereas HCMV–DNA was recorded in 24/75 HCV-HCC patients with prevalence rate of 32 %. Data on the level of alpha feto protein (AFP) was available for 59 out of 75 HCV-HCC patients, this enabled us to differentiate between low risk HCC group of 40/59 patients with AFP < 500 ng/ml, from them HCMV- DNA was detected in 14/40 patients with prevalence rate 35%, and high risk HCC group of 19/59 patients with AFP > 500 ng /ml, from them HCMV-DNA was reported in 9/19 patients with prevalence rate 47.37%. High significant prevalence rate of HCMV-DNA ($P < 0.001$) among control and HCC subjects was reported. Significant change in HCMV – DNA prevalence between low and high risk HCC groups could not be achieved but tendency of higher prevalence rate in HCMV- DNA was observed towards HCC high risk group of patients. **Conclusion:** we illustrated information about HCMV/ HCV co-infection in HCC patients, which referred to the association of HCMV viremia with HCV-HCC patients, as well as the tendency of elevation in HCMV viremia from low to high risk HCC patients depending on AFP threshold of 500 ng/ml.

INTRODUCTION

Hepatocellular carcinoma (HCC) may develop and take its progressive nature after 20 to 40 years of chronic HCV infection. HCV is a major cause of chronic liver inflammation, hepatic fibrosis and initiation of neoplastic clones with irreversible genetic and epigenetic changes, then development and progression of the malignant clones into a carcinogenic tissue (Hoshida *et al.*, 2014; Goossens and Hoshida, 2015).

Unlike HBV which can incorporate into the host human genome leading to direct carcinogenic activity, HCV is RNA virus with limited incorporation of its genetic material into the host's genome (Mailly *et al.,* 2013; Billerbeck *et al.,* 2013). Therefore, the carcinogenic potential of HCV may involve indirect mechanisms, which may refer to interaction of HCV with cellular pathways causing field cancerization area which provide cirrhotic micro-environment that allows initiation and promotion of neoplastic clones by facilitating genetic alterations and cellular transformation (Aihara *et al.,* 1994). Additionally, the direct carcinogenic effects of HCV may be achieved by the mechanisms involving viral proteins interference with host cell metabolism (Koike, 2005). Human cyto-megalovirus (HCMV) is a beta - herpes virus that may affect 60-80% of the human population worldwide (Offermanns and Rosenthal, 2008; Bader El Din *et al.,* 2010), and approxi-mately 100 % seroprevalence in Africa (EL- Bassuoni et *al*., 2014). HCMV genomic DNA is a linear, double-stranded molecule, surrounded by a protein lining, called matrix, which contains highly immunogenic phosphoproteins that can interfere with cellular cycle of the host cell. This lining is surrounded by glycoproteins (gB, gN, gO, gH, gM, gL) essential for the virus to carry out its infectivity and entrance to the host cell. The chief cells that act as reservoirs of HCMV are the endothelial cells, fibroblasts and myeloid cells (Rowshani *et al.,* 2005). The HCMV infec-tion is characterized by alternating periods of latency and reactivation. The infection of endothelial cells and macrophages may experience an important role in virus latency, and this seems to be as a critical point in the maintenance of HCMV during host life (Jarvis *et al.,* 2002). Reactivation of the virus is usually observed during periods of down-regulation of the immunity, such as drug therapy and disease-related stress, or during activation of the immunity such as inflammatory diseases, or co-infection with other viruses (Prosch *et al.,* 2000; Gandhi *et al.,* 2004). HCMV viremia may act as a predictor of high mortality in patients with malignancy (Wang *et al.,* 2010). Despite the few published data regarding this issue, HCMV viremia may be referred to be as a risk factor during the course of chemotherapy (Han *et al.,* 2007; Kuo *et al.,* 2007). Alpha-fetoprotein (AFP) is the most famous and classical tumor marker used for HCC evaluation. AFP acts as a transporter molecule for many ligands, such as fatty acids, bilirubin, heavy metals, and other molecules in addition to different drugs (Mizejewski, 2001). Actually, significantly higher AFP serum levels may show an association with liver tumors (Marrero *et al.,* 2009). It has been proven that AFP serum concentration may peak in a parallel way with HCC tumor size **(**Kokudo *et al.,* 2009). In such regard, The current united- network for organ sharing (UNOS) criteria for transplantation of the liver had considered patients of elevated AFP level > 500 as high risk patients taking priority in liver translation (Kemmer *et al.,* 2006).

MATERIALS AND METHODS

Subjects of study:

Seventy five patients with proven HCV infection who diagnosed with HCC were enrolled in the current study. The 75 cases included 63/75 (84 %) males and 12/75 (16 %) females, age ranged from 38 to 69 years (mean age 57.8) years. Also, negative control of seventy three subjects (negative for HCV-Ab, HBs-Ag and HIV Ab) were included in this study. The 73 subjects included 48/73 (65.75 %) males, and 25/73 (34.24 %) females, age ranged from 22 to 55 years (mean age 37.3). They were all Egyptians. Informed consent was taken from each subject before collecting blood samples. HCV-HCC patients were positive for anti-HCV antibody and HCV-RNA. They were subjected to routine serum investigations

included liver function tests, alanine amino-transeferase (ALT), aspartate amino-transfrase (AST), bilirubin total (Bil T), bilirubin direct (BilD), Alkaline Phosphatase (Alk Ph), albumin (Alb) and, alpha feto protein (AFP) as a tumor marker.

Methods:

HCV-RNA determination: RNA extracted from 140 µl of serum or plasma using QIAamp viral -RNA min kit (Qiagen, Valencia, California**,**USA). Initially, the samples were lysed using the buffer and 100 % ethanol for inactivation of RNase and yield intact viral-RNA. Subsequently, the HCV-RNA was purified in 3-steps procedure according to the Qiagen protocol including centrifugation at 8000 rpm. The RNA was eluted into 60 µl of RNase free buffer, and then HCV-RNA was determined by real time PCR using atrus HCV RG RT-PCR kit (Qiagen) that utilizes reverse-transcription polymerase chain reaction (RT-PCR) with Rotor gene Q instrument (Qiagen). It contains master A, and B that contain enzymes and regents for reverse - transcription and amplification of 240 bp region of HCV genome. Fluorescent oligonucleotide probes specifically bind and detect the amplified product. Monitoring of fluorescent intensities during real time PCR run, allowing detection as well as quantification of the product without re-open the reaction tube after PCR run. This was done by generating standard curve using 4 supplied quantitation standard. In 50 µl PCR reaction tube contained 12 µl master A and 18 µl master B, unknown RNA sample of 20 µl was added then applied to real time PCR device according to the following thermal profile: Reverse - transcription of RNA at 50°C for 30 sec, starting activation of hot-start enzyme at 95°C for 15 min, amplification of cDNA (50 cycle) at 95°C for 30 sec, 50°C for 60 sec, and 72°C for 30 sec.

HCMV-DMA detection:

Extraction of DNA: Genomic DNA was extracted from EDITA blood samples by QIAamp DNA purification Kits (Qiagen) according to manufacturer protocol. After digestion with proteinase K, QIAamp Mini spin columns were used for subsequent salting out of cellular proteins by centrifugation steps at 8000 rpm, that allowed optimal binding of the DNA to the QIAamp membrane followed by DNA elution and final storage at -20°C until required.

HCMV-DMA detection by PCR: HCV DNA was amplified using primers derived from the gB region of HCMV genome. PCR protocols were followed as described previously by (Fox *et al.,* 1995; Jones *et al.,* 2000; Tabll *et al*., 2011) in two round PCR. First-round PCR**:** The master mix prepared by addition of 10 pmole of each primer HCMV1 and HCMV2 (Biolegio, Netherlands), 0.2 mmol/l from each dNTP (Promega, Madison, USA) 0.1 U Taq polymerase enzyme (Promega, Madison, USA), 1 x Taq buffer, 5 µl of DNA template, and completed with distilled H_2O to a final volume of 20 µl. One negative control (in which water replaced the DNA sample as a check for contamination) and one positive control were incorporated into each run. In the second – round PCR: One µl of first-round PCR product was added to the reaction mixture, which is the same as the first-round reaction mixture except for using HCMV3 and HCMV4 as nested primers (Biolegio, Netherlands). The thermal cycling protocol was as follows: 1 min at 94°C, 1 min at 55°C and 1 min at 72°C for 30 cycles using Biometra T1 thermal cycler (Biometra, Germany), then the nested PCR product was analyzed on agarose-gel electrophoresis. Results were positively documented with a visible 100-bp product on the gel. Primers used for the first- and second-round PCR were as follows: **CMV1**:5'GAGGACAACG AAATCCTGTTGGGCA3';**CMV2**:5'GTCG ACGGTGGAGATACTGCTGAGG3'; **CMV3**:5'ACCACCGCACTGAGGAATGT CAG3';**CMV4**:5TCAATCATGCGTTTGA AGAGGTA3'.

RESULTS

Incidence of HCMV-DNA among HCV-HCC patients versus controls:

The nested PCR product of HCMV gB gene in were reported in Table 1. In control subjects, HCMV-DNA positivity were detected in 4/73 (5.48%), and HCMV-DNA negativity were detected in 69/73 (94.52 %) whereas, in HCV-HCC patients, HCMV-DNA positivity were detected in 24/75 (32.00%), and HCMV-DNA negativity were detected in 51/75 (68 %) patients. Chi-square test applied to compare between two groups regarding prevalence of HCMV –DNA resulted in high significant correlation towards HCC patients with p value of <0.001*. Also, receiver operating characteristic (ROC) Analysis for both groups had referred to that HCMV might consider as a predictive factor by which non HCV subjects when get infected with HCV might develop HCC by 32 % (referring to sensitivity) depending on detection of HCMV-DNA with PPV of 85.71%. HCMV-DNA incidence was obviously illustrated in Figure 1.

Table 1: Statistical expressions and comparison between control and HCC groups of patients.

HCMV-DNA	Groups						Chi-Square		Sens.	Spec.	PPV	NPV	Accuracy
	Control		HCC		Total								
	N	%	N	%	N	%	X^2	P-value					
Pos.	4	5.48	24	32.00	28	18.92	15.277	<0.001*	32.00	94.52	85.71	57.50	62.84
Neg	69	94.52	51	68.00	120	81.08							
Total	73	100.00	75	100.00	148	100.00							

Where; Pos. = positive, Neg = negative N= number, HCC= hepatocellular carcinoma, Sens= sensitivity, Spec= specificity, PPV= positive - predictive value, NPV= negative - predictive value, and * = significant value.

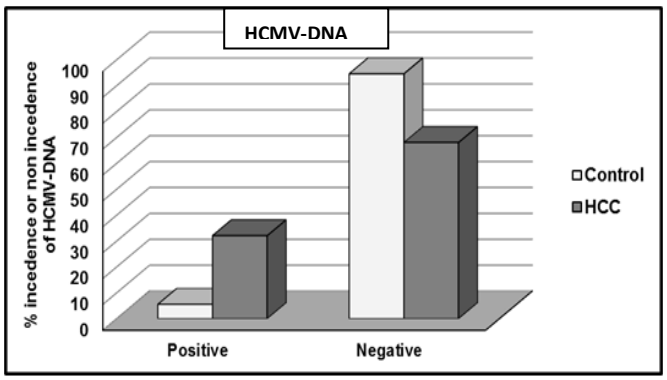

Figure 1: Incidence of HCMV viremia among subjects of control and HCC groups.

In Figure 1, the significant variation in positivity as well as negativity in HCMV-DNA incidence among patients of control and HCC groups is noticed. Regarding HCMV-DNA positivity area, lower positivity of HCMV-DNA is observed in control group subjects whereas, the higher positivity is observed in HCC group of patients. Contrastly, in HCMV-DNA negativity area, the higher negativity of HCMV-DNA is observed in subjects of control group and lower negativity is seen in HCC group of patients.

HCV. RNA titre and clinical biochemical parameters in HCV-HCC at positive and negative incidence of HCMV viremia:

HCV.RNA and clinical parameters (ALT, AST, Bil T, Bil D, Alk Ph, Alb, and AFP) regarding HCV-HCC mono-infection and HCMV/ HCV co-infected patients were recorded in Table 2. Significant change in

such parameters is not seen except in Alk Ph exhibits a significance change towards HCV-HCC mono-infection (p value = 0.048*).

Table 2: HCV.RNA titre and clinical biochemical parameters regarding incidence of HCMV viremia in HCV-HCC patients.

Parameters	HCMV-DNA						T-Test	
	Positive			Negative				
	Mean	±	SD	Mean	±	SD	T	P-value
HCV-RNA (IU/mL)	387111.111	±	222876.897	448583.333	±	354407.946	0.50	0.617
ALT (U/mL)	58.957	±	50.220	66.486	±	59.042	-0.610	0.545
AST(U/mL)	73.667	±	73.375	87.000	±	82.448	0.059	0.953
Bil T (mg/dL)	3.317	±	1.700	4.566	±	5.287	-0.974	0.335
Bil D (mg/dL)	1.625	±	0.998	7.320	±	6.972	-1.587	0.144
Alk Ph (U/mL)	101.000	±	22.554	338.125	±	204.579	-2.256	0.048*
Alb (g/dL)	2.794	±	1.170	2.838	±	0.572	-0.182	0.856
AFP (ng/mL)	793.458	±	1589.200	1116.356	±	2310.626	-0.956	0.346

Where; ALT= alanine amino- transferase, AST = aspartate amino- transferase, Bil T = Bilirubin total, Bil D = bilirubin direct, Alp Ph = alkaline phosphatase, Alb = albumin, AFP = alpha feto protein, positive = HCMV/HCV co-infection, Negative= HCV mono-infection, and * = significant value.

HCV. RNA titre and clinical biochemical parameters regarding HCC Sub-grouping according to AFP threshold of 500 ng/ml:

Level of AFP was determined in 59 out of 75 HCV-HCC patients. AFP threshold of 500 ng/ml was served in classification of HCC patients into 40/59 patients of low risk (HCC1) as well as 19/59 patients of high risk (HCC2). In Table 3, student-t test application result in significantly bad outcome in clinical parameters of AST, Alb, and AFP. Regarding HCC2 (AFP > 500 ng/ml), whereas non significant change is seen in HCV-RNA, ALT, Bil T, Bil D, and Alk Ph parameters.

Table 3: HCV.RNA titre and clinical biochemical parameters regarding low and high risk HCV-HCC patients.

Parameters	HCC patients						T-test	
	HCC1(AFP <500)			HCC2(AFP>500)				
	Mean	±	SD	Mean	±	SD	T	P-value
HCV-RNA (IU/mL)	365800.000	±	332127.815	563333.333	±	131856.993	-1.396	0.179
ALT (U/mL)	55.410	±	50.063	80.105	±	63.142	-1.616	0.112
AST(U/mL)	65.568	±	55.929	114.000	±	105.165	-2.259	0.028*
Bil T (mg/dL)	3.399	±	3.826	5.532	±	5.231	-1.715	0.092
Bil D (mg/dL)	7.287	±	9.290	4.800	±	5.514	0.578	0.576
Alk Ph (U/mL)	376.333	±	145.039	220.000	±	208.378	1.188	0.262
Alb (g/dL)	3.053	±	0.760	2.400	±	0.742	3.041	0.004*
AFP (ng/mL)	161.984	±	157.236	2734.684	±	2959.608	-5.535	<0.001*

Where; ALT= alanine amino- transferase, AST = aspartate amino- transferase, Bil T = bilirubin total, Bil D = bilirubin direct , and Alk Ph = alkaline phosphatase, Alb = albumin, AFP = alpha feto protein, HCC= hepatocellular carcinoma , HCC1 = low risk HCC, HCC2= high risk HCC, and * = significant value.

Incidence of HCMV- DNA in high and low risk HCV-HCC subgroups of patients: In forty patients of subgroup HCC1, HCMV-DNA positivity was detected in 14/40 (35%) patients, and HCMV-DNA negativity were detected in 26/40 (65 %) patients. On the

other hand, HCMV-DNA positivity in subgroup HCC2 was reported as 9/19 (47.37 %) and HCMV- DNA negativity was reported as 10/19 (53 %). Correlations among HCV-HCC patients in the two subgroups were done depending on HCMV-DNA prevalence by application of chi-Square test. The results in Table (4) refer to non-significance change in HCMV incidence between the two subgroups. Also, ROC analysis in HCC1 and HCC2 subgroups refer to the consideration that HCMV may act as a predictive factor by which HCV –HCC1 may develop to HCV-HCC2 by 47.37%, (referring to sensitivity) depending on HCMV verimia, with PPV of 39.13 %. Incidence of HCMV - DNA viremia is obviously illustrated in Figure 2.

Table 4: Statistical expressions and comparison between HCC1 and HCC2 subgroups of patients.

HCMV-DNA	HCV- HCC patients						Chi-Square		Sens.	Spec.	PPV	NPV	Accuracy
	HCC1		HCC2		Total								
	N	%	N	%	N	%	X^2	P-value					
Pos	14	35	9	47.37	23	32.00	0.390	0.532	47.37	65	39.13	72.22	59.32
Neg	26	65	10	52.63	36	68.00							
Total	40	100.00	19	100.00	59	100.00							

Where; Pos = positive, Neg = negative, HCC= hepatocellular carcinoma, HCC1 = low risk HCC, HCC2= high risk HCC, Sens= sensitivity, Spec= specificity, PPV= positive -predictive value, NPV= negative -predictive value.

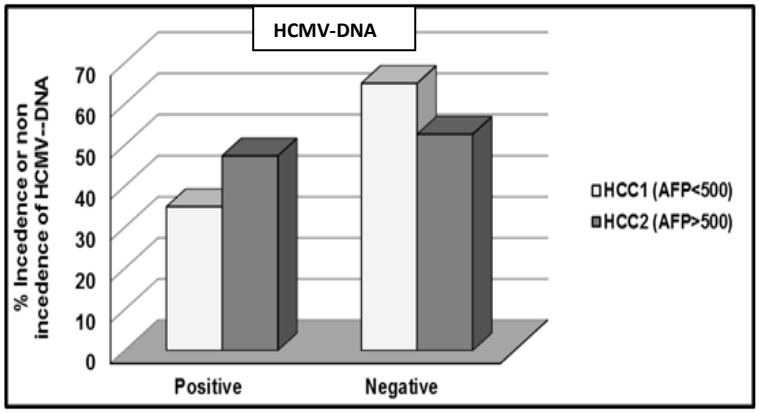

Figure 2: Incidence of HCMV viremia among patients of HCC1and HCC2 subgroups.

In Figure (2) an observable variation in positivity as well as negativity concerning incidence of HCMV viremia is seen among patients of HCC1 and HCC2 subgroups. Regarding HCMV-DNA positivity area, lower positivity of HCMV-DNA is observed in HCC1 subgroup whereas, the higher positivity is observed in HCC2 subgroup. contrastly, in HCMV-DNA Negativity area, the higher HCMV negativity is observed in HCC1 subgroup and lower negativity is observed in HCC2 subgroup.

DISCUSSION

Hepatocellular carcinoma (HCC) was proved to be one of the major complications of HCV infection. Experimentally, HCV proteins interact with cellular proliferation and functional pathways leading to an elevated risk of HCC. Over-expression of

HCV proteins promotes cellular proliferation, transformation, and tumor formation in mice, referring to the direct effect of viral proteins to activate oncogenic pathways (Moriya *et al*., 1998; Fukutomi *et al*., 2005). The viral core protein inhibits tumor suppressor genes [TSG] (Kao *et al*., 2004; Machida *et al*., 2009). HCV protein core induces mitochondrial dysfunction, oxidative bad outcome, and elevates cell growth signals (Koike, 2009), this activates somatic mutations regarding telomerase reverse-transcriptase in early neoplastic process of HCC with HCV and other etiologies (Nault *et al*., 2013). Generally, hepatocyte proliferation is declined at the cirrhosis stage after several rounds of regeneration with telomere shortening that promotes cellular senescence to prevent carcinogenesis (Herbig *et al*., 2004; Goossens *et al*., 2015). HCMV infection was appeared to be a dangerous issue in patients with malegnancies (Wang *et al*., 2011). The association of HCMV infection with HCC is not completely defined till now (EL-Bassuoni *et al*., 2014). The diagnosis of HCMV active infection was depended on the detection of HCMV replication in the blood (HCMV-DNA) that referred to as HCMV viremia and virus reactivation in absence of effective immunity leading to serious disease (Gandehi and Khanna, 2004). In the current study, the incidence of HCMV viremia was reported with significantly higher percentage 32 % of entire HCV-HCC patients, compared with 5.4 % in control subjects with p-value of (<0.001). This result may refer to the higher association of HCMV viremia with HCV-HCC patients compared with control subjects. In such regard, ROC curve analysis referred to predictive value of HCMV virema may be a predictor of HCC in HCV patients by 32%. Incidence of HCMV viremia in control subjects may be slightly similar to that reported in control group in a previous report (Taherkhani *et al*., 2015) who reported prevalence rate of (0%) in their work to study prevalence of HCMV in patients with ulcerative colitis (Taherkhani *et al*., 2015). On the other hand, the present data on the incidence of HCMV viremia in entire HCV-HCC patients agree with those reported in a recent study regarding the association of HCMV with HCC patients, El-Bassiuoni *et al*., (2014), reported HCMV prevalence rate with as 26.7 % in HCC patients (El-Bassiuoni *et al*., 2014). Among the 75 HCC patients, AFP results are available for 59 which were divided into low [< 500 ng/ml] and high risk [> 500 ng/ml] according to Kemer *et at*., (2006). Burnett *et al.,* (2013) concluded that HCC staging according to AFP level might be a predictor of prognosis in non-cirrhotic HCC patients. In the current study, the prevalence of HCMV viremia was observed in 14/40 [35%] of the low risk HCC1 patients group and in 9/19 [47.37%] of the high risk HCC2 patients group. Despite the markedly higher difference in HCMV prevalence in HCC1 than HCC2, the difference was not statistically significant. El- Bassiuoni *et al*, (2014) reported a 26.7% prevalence of HCMV in HCC patients regardless of the risk score of the patients. The present results regarding HCMV incidence in HCC patients agree with those of Lepiller *et al.,* (2011), who reported significantly higher prevalence rate of HCMV in HCC patient than in non HCC subjects. During the determination of HCMV prevalence among patients from different departments in a university hospital in France. Lepiller *et al.,* (2011) detected HCMV-DNA in tissues of liver tumor areas, whereas it could not be detected in adjacent non tumor healthy tissues, indicating the unique role of HCMV in hepatocellular carcinoma. Lepiller *et al*., (2011) reported that elimination of HCMV infection by antiviral drugs or vaccination may reduce HCC related mortality (Lepiller *et al.,* 2011). One of the evidences that support HCMV contribution in HCC and tumor progression from low to high risk disease was the suggestion emerged by in vitro study which proved that HCMV could transform embryonic fibroblast cells in cell culture and could promote chromosomal damage and

exerted mutations, however HCMV could not be categorized as an oncogenic virus (Michells *et al*., 2009; Lepiller *et al*., 2011). Oncomodulation was the accepted mechanism by which HCMV could contribute in tumor progression (Clnat *et al*., 1996; Lepiller *et al*., 2011), in such mechanism, HCMV could infect tumor tissues and acted as a cofactor in amplifying processes of carcino-genesis without the necessity of the tumor to be initiated firstly. This was supported by experiments which revealed that HCMV proteins could enhance and influence tumor growth by interference with cell cycle (Lepiller *et al*., 2011). Elevation of interlukin 6 (IL-6) was found to be accompanied with HCMV replication and its reactivation. It is widely accepted that IL-6 level would act as a critical factor especially in liver inflammation as well as liver cancer (Park *et al*., 2010). Moreover, IL-6 mRNA expression could be up-regulated by HCMV infection, hence IL-6 production might depend on transcriptional factors (Dondorfer *et al*., 1994: Lepiller *et al*., 2011), that might be stimulated by HCMV and HCV, when IL-6 is secreted from activated monocytes. It could systematically act on hepatocyte and bind to non-signaling receptor IL-6R on hepatocyte surface, causing Janus kinase (JAK) activation that could in turn activates signal transducer and activator of transcription 3 (STAT3) as a major trans-criptional oncogenic factor initiating trans-criptional program of cell growth and differentiation (Heinrich *et al*., 2003). The above findings might explain the role of HCMV in HCC development beside HCV, in addition to its role in tumor worsening from low to high risk HCC patients that reported 35% HCMV viremia prevalence compared with 47.37 % HCMV viremia prevalence reported in high risk HCC patients. **Conclusion:** In the current study we demonstrated information regarding HCMV/ HCV co-infection in HCC patients, which referred to the association of HCMV viremia with HCV-HCC patients, as well as tendency of elevated HCMV viremia in high risk HCC patients, thus suggesting that HCMV viremia contributes in disease worsening. Further studies are still required to assess the significant role of HCMV viremia in HCC progression in HCV patients.

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ARABIC SUMMERY

معدل انتشار الفيروس المضخم للخلايا فى مرضى الالتهاب الكبدى الفيروسى "سى" المصريين المصابين بسرطان الكبد

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الخلفية العلمية: يعتبر مرض سرطان الكبد من المضاعفات الخطيرة التى تنشأ بعد عدة سنوات من الاصابة بالفيروس الكبدى"سى"، و تمثل الاصابة بهذا الفيروس مشكلة طبية كبيرة فى مصر ، و ايضا الاصابة بالفيروس المضخم للخلايا حيث يعتبر واحد من اكثر الامراض المعدية التى تظل كامنة فى المرضى, فالفيروس المضخم للخلايا النشط فى وجودة كعدوى مزدوجة مع الفيروس الكبدى"سى" قد يهدد حياة مرضى سرطان الكبد الناشىء عن الفيروس الكبدى "سى"، و قد هدفت دراستنا الى رصد معدل الاصابة النشطة بالفيروس المضخم للخلايا كعدوى مزدوجة مع الفيروس الكبدى "سى" فى مرضى سرطان الكبد.

المنهجية: تم فحص وجود الفيروس المضخم للخلايا فى ٧٥ من مرضى السرطان الكبدى بتقنية تفاعل البلمرة المتسلسل (بى سى ار) و الذين قد تم تحديد وجود الفيروس الكبدى "سى" لهم بتقنية (ريال تيم بى سى ار) بعد الكشف المسبق لوجود الاجسام المضادة للفيروس، بالأضافة لفحص وجود الفيروس المضخم للخلايا فى ٧٣ من الاشخاص الغير مصابيين بالفيروس "سى" (مجموعة الكنترول) بنفس التقنية.

النتائج: وجد ان معدل انتشار الفيروس المضخم للخلايا كان بنسبة ٥،٤ % فى مجموعة الكنترول بينما وصلت النسبة الى ٣٢% فى مرضى سرطان الكبد المصابيين بالفيروس "سى" و ظهرت قيمة عالية لمعامل الارتباط الاحصائى (قيمة بى) بمعدل اقل من ٠،٠٠١، و بعد تقسيم هولاء المرضى الى مجموعتين اعتمادا على ما توفر ل ٥٩ مريض منهم لقياسات دلائل الاورام الفا فيتو بروتين، فقد سجلت المجموعة الاقل خطورة لسرطان الكبد معدل انتشار ٣٥% للفيروس المضخم للخلايا و الذى زاد الى ٤٧،٣٧% فى المجموعة الاكثر خطورة لسرطان الكبد و لكن بدون الوصول الى لارتباط احصائى لقيمة ال بى ، حيث ان التقسيم اعتمد على المعدل ٥٠٠ نانوجرام/ملليتر للألفا فيتوبروتين.

الخلاصة: اظهرت الدراسة الارتباط الاحصائى العالى لمعدل الاصابة النشطة بالفيروس المضخم للخلايا فى مرضى سرطان الكبد المصابين بالالتهاب الكبدى الفيروسى"سى" مع الاصابة النشطة للفيرس المضخم للخلايا مقارنة بالاشخاص الكنترول ، بينما ظهرت القابلية فى زيادة معدل الاصابة فى المجموعة الاكثر خطورة لسرطان الكبد اعتمادا على المعدل ٥٠٠ نانوجرام/ ملليتر لدلائل الاورام الفا فيتو بروتين ولكن بدون الحصول على معامل ارتباط احصائى، و الذى يحتاج دراسات مستقبلية فى هذا الصدد.