SEN Virus Infection in Egyptian Chronic Hepatitis C and Haemodialysis Patients

Maisa Omar[1], Samah Saad El-Din[1], Nevine Fam[1], Manal Diab[1], Mohamed Shemis [2], Manar Raafat[3], Moataz Seyam[4], Moataz Hassan[4], Afkar Badawy[5], Maha Akl[5], Mohamed Saber[2].

Microbiology[1], Biochemistry[2],Nephrology[3], Tropical Medicine[4]and Pathology[5] Departments, Theodore Bilharz Research Institute (TBRI), Guiza, Egypt

ABSTRACT

SEN virus (SENV) has been tentatively linked to transfusion-associated non A-E hepatitis. The aim of the present study was to determine the prevalence of SENV among Egyptian patients with HCV-related chronic liver disease (CLD) and haemodialysis (HD) patients and to assess the clinical effect of SENV infection on co-existent hepatitis C either in the severity or the probability of developing hepatocellular carcinoma (HCC). Polymerase chain reaction (PCR) was used to detect SENV-D and SENV-H DNA in serum samples of 74 HCV-related CLD patients, 45 uraemic patients on maintenance HD and 28 healthy controls. SENV DNA was detected in 13.5%, 11.1%, and 7.1% of CLD, HD patients and healthy controls respectively with no significant differences between patients and control group. No statistically significant differences were demonstrated between SENV infected and non infected CLD or haemodialysis patients regarding the clinical and biochemical parameters. SENV infection was significantly higher in CLD patients with HCC (33.3%) than without (8.5%) ($p<0.05$). In conclusion, SENV does not seem to be a common infection in Egyptian patients. It has no apparent influence on the severity of co-existent HCV related CLD but it could be a risk factor for developing HCC in these patients. Further studies are needed to define the aetiopathogenic role of SENV infection in HCC development.

INTRODUCTION

SENV is identified as a putative non A to E hepatitis virus [(1)]. It was first isolated from the serum of an intravenous drug user infected with human immuno-deficiency virus [(2)]. By phylogenetic analysis, nine different strains (A–I) have been identified and provisionally classified as members of the *Circoviridae* family, a group of single stranded DNA viruses that includes the TT virus (TTV), TUS01, SANBAN and YONBAN [(3-5)]. SENV is transmitted by blood as demonstrated by comparing the sequence homology between donors and recipients. Moreover, transfused patients are at high risk of acquiring SENV than non-transfused ones [(6)].

Two SENV strains (SENV-D and SENV-H) were shown to be significantly associated with post transfusion non A-E hepatitis [(1, 7)]. SENV-D and SENV-H were also detected more frequently in patients with CLD and HCC than in healthy adults [(8, 9)]. However, the causal relation of these viruses to hepatic disease has not been proven yet.

Hepatitis C virus is a major cause of post transfusion hepatitis and CLD [(10)]. More than half of patients with acute HCV infection develop chronic hepatitis that leads to cirrhosis and HCC or both in at least 20% [(11)]. Among patients with acute or chronic HCV infection, 22% to 85% were reported to be coinfected with SENV [(7, 12-14)]. Although coinfection of HCV and SENV is common, the contribution of SENV infection to the course of HCV infection still needs clarification.

Patients on chronic HD are considered to be at risk of infection by blood-borne viruses because the therapeutic procedures are frequently associated with bleeding and blood transfusion [(15)]. Haemodialysis patients may also show hepatic dysfunctions consistent with viral hepatitis even in absence of documented hepatitis A to E infection [(16)].

The aim of the present study was to determine the prevalence of SENV infection among Egyptian patients with HCV-related CLD and uraemic patients on maintenance HD. Also to demonstrate the clinical effect of SENV infection on co-existent hepatitis C either in the severity or the probability of developing HCC.

PATIENTS AND METHODS:

Patients and Samples*:* The present study was conducted on a total of 119 patients who were consecutively examined and followed up at TBRI. They were classified as follows: 74 patients with HCV-related CLD and 45 uraemic patients on maintenance HD.

Chronic liver disease group included 49 males and 25 females with a mean age of 46±11 years (range 13-72years). Diagnosis of chronic HCV infection was based on the following criteria: (1) detection of HCV RNA and/or continuous positivity for antibody to HCV (anti-HCV) in serum for more than 6 months; (2) absence of detectable hepatitis B surface antigen; (3) exclusion of other causes of CLD. Diagnosis of CLD was based on prolonged elevation of serum ALT for more than 6 months. Liver cirrhosis was diagnosed by histopathological examination and/or characteristic clinical signs of advanced liver disease. Hepatocellular carcinoma was diagnosed by histopathological examination

of liver biopsy sample and/or imaging studies and serum alpha-fetoprotein levels above 400 ng/ml. Serum samples were collected from all patients at the time of their clinical evaluation and stored at -70°C until further tested. Eleven patients were receiving interferon alpha (IFNα)/ribavirin combination therapy for 24 weeks, their serum samples were available before and 12 weeks after they had received the treatment. Haemodialysis group comprised 38 males and 7 females, their age ranged from 34 to 72 years with a mean of 56±9 years. The length of HD ranged from 0.5 to 16 years. Past history of blood transfusion was recorded in 34 (66.7%) patients. Maintenance HD had been performed three times a week using disposable dialysers with standard acetate dialysate. Serum samples were collected from all patients before the dialysis session and stored at -70°C.

Sera from 28 healthy volunteers who had no clinical, virological or biochemical signs for liver disease served as a control group.

Methods: All patients were subjected to full clinical assessment with special emphasis on symptoms and signs of CLD. Abdominal ultrasonography and upper endoscopy were performed. Liver biopsy was taken from 48 patients for histopathological examination.

Laboratory tests: Liver biochemical tests (ALT, AST and total bilirubin) were done using autoanalyser. Commercially available ELISAs were used for measurement of serum α-fetoprotein, (DiaMetra, Italy), HBsAg, HBcAb (DiaSorin, Italy) and third generation HCV antibody (version 4) and for HCV serotyping (1-6) (Murex-Biotech Ltd, UK). HCV RNA and HGV RNA were detected by means of qualitative RT-PCR with primers in the 5' non-coding region as reported previously [17,18]. TTV DNA was detected by nested PCR using primers as designated by Takahashi et al.[19].

Detection of SENV DNA by PCR: Total DNA was extracted from 100 µl of serum as previously described by Boom et al [20]. The extracted DNA was resuspended in 60µl TE buffer. The oligonucleotide primers used were according to Tanaka et al. [4] . For the PCR, 50 µl of reaction mixture containing 10 µl of the DNA sample, 1X PCR buffer (10m*M* Tris-Hcl [pH 9.0],50 m*M* Kcl, 1.5m*M* Mgcl2, 0.01% gelatin and 0.1% TritonX-100), 200 µ*M* of each dNTP, 20 pmole of each primer (sense primer for SENV-D, 5'-GTAACTTTGCGGTCAACTGCC-3'; sense primer for SENV-H, 5'-GGTGCCCCTWGTYAGTTGGCGGTT-3' [W = A or T]; universal anti-sense primer, 5'-CCTCGGTTKSAAAKGTYTGATAGT-3' [K = G or T, S = C or G and Y= C or T], and 1.5U of Taq DNA polymerase was amplified in thermal cycler (MJ research PTc < 200) for 40 cycles. Each cycle consisted of denaturation at 95°C for 60s, primer annealing at 55°C for 30s and extension at 72°C for 60s with final extension step at 72°C for 10 min [8]. The amplified products (231 bp for SENV-D and 230 bp for SENV-H) were separated in 3% agarose gel electrophoresis, stained with 0.3µg/ml ethidium bromide and visualized using UV transilluminator.

Statistical analysis: Numerical data were compared using Mann Whitney U test while categorical data were compared using Chi square test. P value ≤ 0.05 is considered significant. Data analysis was performed using SPSS computer program (version 10).

RESULTS

The prevalence of SENV-D/H DNA among different studied groups is shown in table (1). SENV DNA was detected in 13.5%, 11.1% and 7.1% of CLD patients, HD patients and healthy controls respectively with no significant differences between patients and control group. SENV-D genotype was detected in 10 (59%) out of 17 SENV positive cases while SENV-H genotype was detected in 7 (41%) cases. There were no significant differences in the distribution of either SENV-D or SENV-H between patients and control group. Results of PCR assay are shown in fig. (1).

A subgroup analysis of 74 patients with CLD showed that of these patients, 15 had HCC and 59 did not. The positivity rate of SENV was significantly higher in CLD patients with HCC (33.3%) than in those without (8.5%) ($p< 0.05$).(Fig.2)

Based on clinical, ultrasonographic and histopathological findings, 39 (52.7%) of CLD patients were diagnosed as chronic hepatitis and 35 (47.3%) were cirrhotic. HCV serotyping was done for 29 serum samples of CLD patients. Serotype 4 was detected in 20 (69%) samples while other serotypes (1, 3, mixed) were detected in 9 (31%) samples. Although SENV coinfection was more associated with HCV serotype 4, no statistically significant differences were found in the distribution of different serotypes among SENV infected and non-infected patients. Demographic, virologic and clinical data of CLD patients were compared according to the status of SENV infection. There were no significant differences between SENV infected and non -infected patients regarding mean age, sex distribution, mean ALT serum levels, virological and clinical features. (Table 2)

Coinfection with SENV was detected in one out of 11 chronic HCV patients before receiving

IFNα/ribavirin combination therapy. Clearance of both HCV RNA and SENV DNA was observed 12 weeks after they had received the treatment.

Table (3) shows comparison of clinical and virological backgrounds of HD patients with and without SENV infection. No statistically significant differences were detected as regards duration of HD and history of blood transfusion between infected and non infected patients. Coinfection with either HCV (80%) or HBV (20%) was observed among SENV infected HD patients.

Table (1): Prevalence of SEN-V infection (genotype-D and H) among the different studied groups.

Group (N)	Genotype D		Genotype H		Total	
	N	%	N	%	N	%
CLD (74)	6	8.1	4	5.4	10	13.5
HD patients (45)	2	4.4	3	6.7	5	11.1
Healthy control (28)	2	7.1	0	0	2	7.1

CLD: Chronic liver disease
HD: Haemodialysis

Fig. (1): Agarose gel electrophoresis of PCR amplified 230 bp fragment of SENV-H (M: molecular size marker [Bio-Rad Amplisize], lane 1,3: positive samples, lane 2: negative sample, lane 4: positive control and lane 5: negative control)

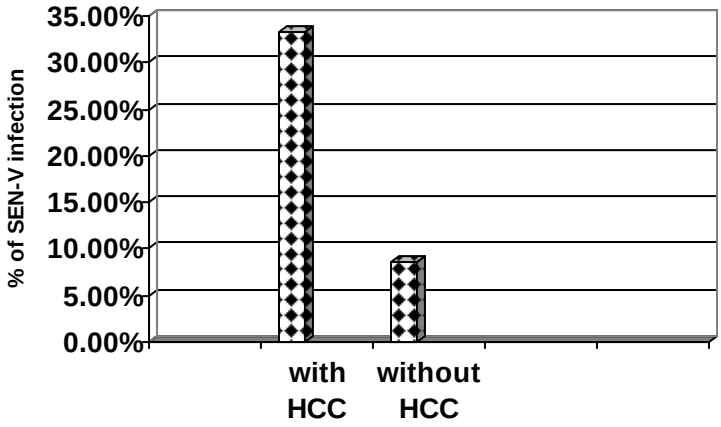

Fig. (2): Prevalence of SEN-V infection among CLD patients with and without hepatocellular carcinoma
CLD: Chronic liver disease
HCC: Hepatocellular carcinoma
pvalue <0.05

Table (2): Demographic, virological and clinical features of HCV-related CLD patients relative to SEN-V viraemia.

Characteristics	CLD patients (n=74)			Patients with HCC (n=15)			Patients without HCC (n=59)		
	SEN-V positive (n=10)	SEN-V negative (n=64)	pvalue	SEN-V positive (n=5)	SEN-V negative (n=10)	pvalue	SEN-V positive (n=5)	SEN-V negative (n=54)	pvalue
Age	45±10	46±12	NS	46±14	58±8	NS	43±4	44±11	NS
Gender (M/F)	5/5	44/20	NS	1/4	6/4	NS	4/1	38/16	NS
Mean ALT (IU/L)	58±22	61±23	NS	54±19	52±18	NS	53±12	62±31	NS
Virological features:									
- HCV:									
Anti HCV +ve	10 (100)	64 (100)	NS	5 (100)	10 (100)	NS	5 (100)	54 (100)	NS
HCV RNA +ve	5 (50)	39 (61)	NS	3 (60)	5 (50)	NS	2 (40)	34 (63)	NS
* Serotype 4	3/3(100)	17/26(65)	NS	2/2 (100)	4/4(100)	NS	1/1(100)	13/22 (59)	NS
*Other serotypes: (1, 3, mixed)	0/3 (0)	9/26(34.6)	NS	0/2 (0)	0/4 (0)	NS	0/1 (0)	9/22 (41)	NS
- HBc Ab +ve	3 (30)	23 (36)	NS	1 (20)	5 (50)	NS	2 (40)	18 (33.3)	NS
- TTV DNA +ve	3 (30)	18 (28.1)	NS	3 (60)	3 (30)	NS	0 (0)	15 (27.7)	NS
- HGV RNA +ve	1 (10)	11 (17.1)	NS	0 (0)	0 (0)	NS	1 (20)	11 (20.4)	NS
Clinical features:									
-Chronic hepatitis:	3 (30)	36 (56.3)	NS	1 (20)	3 (30)	NS	2 (40)	33 (61)	NS
-Cirrhosis:	7 (70)	28 (43.8)	NS	4 (80)	7 (70)	NS	3 (60)	21(38.9)	NS

*The data represent the number of samples positive/number of samples tested (percent)
NS: Not significant

Table (3): Demographic, clinical and virological data of haemodialysis patients with and without SEN-V infection.

Characteristics	SEN-D/H Positive (n=5) N	%	SEN-D/H Negative (n=40) N	%	P value
- Age	59±9		56±10		NS
- Gender (male/female)	4/1		34/6		NS
- Mean ALT (IU/L)	16±12		15±8		NS
- Duration of haemodialysis	4.4±3.05		7.12±4.37		NS
- Transfusion history	4	80	26	65	NS
- Virological features:					
HBVs Ag	1	20	3	7.5	NS
HCV Ab	4	80	31	77.5	NS

NS: Not significant

DISCUSSION

The clinical relevance of SENV infection alone or in combination with HCV infection remains controversial. By taking the advantage of high incidence of HCV in Egypt [21], we investigated the prevalence and clinical impact of SENV on coexistent HCV infection. Also we determined the prevalence of SENV among HD patients, a group at high risk of being infected with parenterally transmitted viruses.

Infection with SENV has been frequently observed in 22% to 85% of patients with chronic hepatitis C [7,12-14] and in 27% to 61% of uraemic patients on maintenance HD [16, 22-24]. The results of the present study showed that the prevalence rates of SENV-D/H infection in chronic HCV and HD patients were 13.5% and 11.1% respectively which were comparable to that in healthy controls. The observed differences in the prevalence of SENV DNA between our patients and previous studies may be attributed to routes of transmission which are favored by the way of life in one or other population or to the use of slightly different primers [25].

Dual infection with HCV and either hepatitis A virus or hepatitis B virus has been associated with a more and rapidly progressive disease [26]. In contrast, in this study, clinical and biochemical evaluations of patients with CLD as well as HD patients did not significantly differ between those infected with HCV alone and those coinfected with HCV and SENV. In this and previous studies [13,27-29], there is no evidence to suggest that SENV causes hepatitis, when it is the sole agent detected, or worsens the severity or persistence of coexistent chronic HCV. Some authors have suggested that there is a specific link between HCV genotypes 2a and 1b and coinfection with SENV among chronic HCV patients [14, 30]. In the present study, the association of SENV with HCV serotype 4 may be attributed to high prevalence of this serotype in Egypt (>90%) [31].

The influence of coinfection with SENV on HCV response to combination therapy was investigated with contradictory results. Rigas et al.[32] reported that coinfection with SENV might adversely affect the outcome of treatment with combination therapy. However, other studies found that HCV response is not affected by the presence of SENV and recorded a significantly higher response rate of SENV to combination therapy than that of HCV [14, 28, 30]. This influence could not be judged in our study as SENV DNA was detected in only one patient before receiving combination therapy. However, clearance of both HCV RNA and SENV DNA was observed after treatment for 12 weeks. Additional studies using a large number of patients are required to confirm this finding and to document the duration of response and rate of spontaneous clearance of this virus over time.

Most cases of HCC are associated with chronic infection with either hepatitis B or hepatitis C virus [33]. In the present study, a significantly higher prevalence rate of SENV infection was detected in CLD patients with HCC than without, which may suggest a possible role of SENV as a cofactor in the development of HCC. However, no significant differences were observed between SENV infected and non-infected HCC patients concerning clinical or virological features. High prevalence of SENV infection among HCC patients may be attributed to increased risk of exposure as a result of multiple medical or radiological intervention plus decreased rate of spontaneous clearance due to immunosuppression [34, 35]. Whether coexistent SENV infection has a role in the aetiology of HCV-related HCC or it is just an innocent bystander needs further investigation .

Our results showed that SENV DNA was detected in 7.1% of healthy volunteers, a rate which is comparable to that previously reported in Thailand, Turkey and Japan (5% – 10%) [9,12,29], but higher than that in the United States and Italy (2% - 3%) [36,37] and lower than that detected among Chinese population (31%) [7]. These data suggest that SENV has a global distribution with

marked geographic differences in its prevalence. The explanations for these differences are unknown, but they may result from interactions among behavioral, social and biological factors [38].

Geographic distribution of different SENV variants was also noted. Previous studies have shown that SENV-D is the predominant genotype in Japan and Greece [39,40], whereas SENV-H genotype is predominant in the United States and Taiwan [1,8]. Our results indicated that SENV-D is more prevalent than SENV-H among Egyptian patients and healthy controls. This variability in the prevalence of different genotypes may be attributed to different exposure rate or routes of infection or different rates of spontaneous clearance between these two strain [30]. Whether differences in SENV variants affect the heterogeneity in clinical outcome or response to antiviral therapy in patients with chronic SENV infection needs further study.

Previous studies strongly suggest that SENV is transmitted through blood transfusion [1,14,41]. However, our results showed that SENV was not associated with blood transfusion history or duration of HD. In addition, no statistically significant differences were observed regarding the distribution of either HCV or HBV, which are well-known blood-borne viruses, between SENV infected and non-infected HD patients. A possible explanation is that SENV can be transmitted through not only parenteral but also non-parenteral routes. This possibility is supported by the finding that TTV, which is distantly related to SENV, can be transmitted also via faecal-oral route [42]. Recent data have suggested that vertical transmission of SENV does occur, presumably, at delivery but it may not induce persistent viraemia [43].

In conclusion, SENV does not seem to be a common infection in Egyptian patients. It has no apparent influence on the severity of coexistent HCV-related CLD but it may have a role in HCC development in these patients. SENV is most likely transmitted via parenteral and non parenteral routes. Further studies are needed to define the pathogenic and clinical importance of SENV infection.

Acknowledgement: This work was funded by Hepatitis Research Project number 74D of Microbiology Department, TBRI.

REFERENCES

1. **Umemura T, Yeo AE, Sottini A, et al (2001):** SEN virus infection and its relation to transfusion-associated hepatitis. *Hepatology; 33: 1303-1311.*
2. **Primi D, Fiordalisi G, Mattioli S, et al (2000):** Identification of SEN V genotypes. International patent number WO00280 39. *(http://ep.espacenet.com/).*
3. **Takahashi K, Iwasa Y, Hijikata M, et al (2000):** Identification of a new human DNA virus (TTV-like mini virus, TLMV) intermediately related to TT virus and chicken anaemia virus. *Arch Virol; 145: 979-993.*
4. **Tanaka Y, Primi D, Wang RYH, et al (2001):** Genomic and molecular evolutionary analysis of a newly identified infectious agent (SEN virus) and its relationship to the TT virus family. *J Infect Dis; 138: 359-367.*
5. **Kojima H, Kaita KD, Zhang M, et al (2003):** Genomic analysis of a recently identified virus (SEN virus) and genotypes D and H by polymerase chain reaction. *Antiviral Res; 60: 27-33.*
6. **Akiba J, Umemura T, Alter HJ, et al (2005):** SEN virus: Epidemiology and characteristics of a transfusion transmitted virus. *Transfusion; 45: 1084-1088.*
7. **Mu SJ, Du J, Zhan LS, et al (2004):** Prevalence of a newly identified SEN virus in China. *WJ Gastroenterol; 10: 2402-2405.*
8. **Kao JH, Chen W, Chen PJ, et al (2002):** Prevalence and implication of a newly identified infectious agent (SEN virus) in Taiwan. *J Infect Dis; 185: 389-392.*
9. **Tangkijvanich P, Theamboonlers A, Sriponthong M, et al (2003):** SEN virus infection in patients with chronic liver disease and hepatocellular carcinoma in Thailand. *J Gastroenterol; 38: 142-148.*
10. **Alter HJ and Seeff LB (2000):** Recovery, persistence and sequelae in hepatitis C virus infection: A perspective on long-term outcome. *Semin Liver Dis; 20: 17-35.*
11. **Lauer GM and Walker BD (2001):** Hepatitis C virus infection. *N Engl J Med; 345: 41-45.*
12. **Shibata M, Wang RY, Yoshida M, et al (2001):** The presence of a newly identified agent (SEN virus) in patients with liver diseases and in blood donors in Japan. *J Infect Dis; 184: 400-404.*
13. **Schréter I, Kristian P, Jarčušaka P, et al (2006):** Detection of SEN virus in the general population and different risk groups in Slovakia. *Folia Microbiol; 51: 223-228.*
14. **Kao JH, Chen W, Chen PJ, et al (2003):** SEN virus infection in patients with chronic hepatitis C: Preferential coinfection with hepatitis C genotype 2a and no effect on response to therapy with interferon plus ribavirin. *J Infect Dis; 187: 307-310.*
15. **Wreghitt TG (1999):** Blood-borne virus infections in dialysis units-a review. *Rev Med Virol; 9: 101-109.*
16. **Pirovano S, Gregorini G, Malacarne F, et al (2005):** High prevalence of SEN virus infection in patients on maintenance haemodialysis: Frequent mixed infections with different variants and evidence for nosocomial transmission of the virus. *Intervirology; 48: 216-222.*
17. **Van Doorn LJ (1994):** Molecular biology of the hepatitis C virus. *J Med Virol; 43: 345-356.*
18. **Schauder GG, Dawson GJ, Simons JN, et al (1995):** Molecular and serological analysis in the transmission of the GB hepatitis agents. *J Med Virol; 46: 81-90.*
19. **Takahashi K, Hoshino H, Ohta Y, et al (1998):** Very high prevalence of TT virus (TTV) infection in general population in Japan revealed by a new set of PCR primers. *Hepatol Res; 12: 233-239.*
20. **Boom R, Sol CJA, Salimans MM, et al (1990):** Rapid and simple method for purification of nucleic acid. *J Clin Microbiol; 28: 495-503.*
21. **Mohamed MK (2004):** Epidemiology of HCV in Egypt. *Afro-Arab Liver J; 3: 41-52.*
22. **Kobayashi N, Tanaka E, Umemura T, et al (2003):** Clinical significance of SEN virus infection in patients on maintenance haemodialysis. *Nephrol Dial Transplant; 18: 348-352.*
23. **Dai CY, Chuang WL, Chang WY, et al (2005):** SEN virus infection among patients on maintenance

haemodialysis in southern Taiwan. *J Infect; 51: 110-115.*

24. **Hsu BG,Wang LY, Hu CT, et al (2007):** SEN virus infection in patients on peritoneal dialysis. *Perit Dial; 27: 74-78.*
25. **Schroter M, Laufs R, Zollner B, et al (2002):** Prevalence of SEN-H viraemia among healthy subjects and individuals at risk for parenterally transmitted diseases in Germany. *J Viral Hepat; 9: 455-459.*
26. **Chen YD, Liu MY, Yu WL, et al (2003):** Mix-infections with different genotypes of HCV and with HCV plus other hepatitis viruses in patients with hepatitis C in China. *WJ Gastroenterol; 9: 984-992.*
27. **Yoshida H, Kato N, Shiratori Y (2001):** Weak association between SEN virus viraemia and liver disease. *J Clin Microbiol; 40: 3140-3145.*
28. **Sagir A, Adams O, Kirschberg O, et al (2004):** SEN virus does not affect treatment response in hepatitis C virus coinfected patients but SEN virus response depends on SEN virus DNA concentration. *WJ Gastroenterol; 10: 1893-1897.*
29. **Serin MS, Koksal F, Oksuz M, et al (2005):** SEN virus prevalence among non-B and non-C hepatitis patients with high liver function tests in south of Turkey. *Jpn J Infect Dis; 58: 349-352.*
30. **Dai CY, Chuang WL, Chang WY (2005):** Co-infection of SENV-D among hepatitis C patients treated with combination therapy with high dose interferon-alfa and ribavirin. *WJ Gastroenterol; 11: 4241-4245.*
31. **Mezban ZD, El Wakil A (2006):** Hepatitis C in Egypt. Medical Writer's Circle. *(http://www.hcvadvocate.org/).*
32. **Rigas B, Hasan I, Rehman R, et al (2001):** Effect on treatment outcome of coinfection with SEN viruses in patients with hepatitis C. *Lancet; 358: 1961-1962.*
33. **Tabor K (2001):** Hepatocellular carcinoma: Global epidemiology. *Digest Liver Dis; 33: 115-117.*
34. **Tangkijvanich P, Theamboonlers A, Sriponthong M, et al (2003):** SEN virus infection and the risk of hepatocellular carcinoma: A case-control study. *Am J Gastroenterol; 28: 2500-2504.*
35. **Momosaki S, Umemura T, Scudamore CH, et al (2005):** SEN virus infection in patients with hepatocellular carcinoma. *J Viral Hepat; 12: 435-438.*
36. **Mushahwar IK (2000):** Recently discovered blood-borne viruses: Are they hepatitis viruses or merely endosymbionts? *J Med Virol; 62: 399-404.*
37. **Bowden S (2001):** New hepatitis viruses: Contenders and pretenders. *J Gastroenterol Hepatol; 16: 124-131.*
38. **Pfeiffer RM, Tanaka Y, Yeo AET, et al (2003):** Prevalence of SEN viruses among injection drug users in the San Francisco Bay area. *J Infect Dis; 188: 13-18.*
39. **Umemura T, Alter HJ, Tanaka E, et al (2002):** SEN virus: Response to interferon alfa and influence on the severity and treatment response of coexistent hepatitis C. *Hepatology; 35: 953-959.*
40. **Umemura T, Tanaka E, Ostapowicz G, et al (2003):** Investigation of SEN virus infection in patients with cryptogenic acute liver failure, hepatitis-associated aplastic anaemia, or acute and chronic non-A-E hepatitis. *J Infect Dis; 188: 1545-1552.*
41. **Spataro P, Di-Pietro A, Scoglio ME, et al (2006):** Prevalence of SENV-H and SENV-D virus: Epidemiological study in blood donors and dialysis patients. *Ren Fail; 28: 441-448.*
42. **Okamoto H, Nishizaw T, Kate N, et al (1998):** Molecular cloning and characterization of a novel DNA virus (TTV) associated with post-transfusion hepatitis of unknown etiology. *Hepatol Res; 10: 1-6.*
43. **Moriondo M, Resti M, Betti L, et al (2007):** SEN virus co-infection among HCV-RNA-positive mothers, risk and outcome of child infection during a 1-year follow-up. *J Viral Hepat; 14: 355-359.*

عدوى فيروس السن (SEN Virus) في المرضي المصريين المصابين بالالتهاب الكبدي المزمن لفيروس C ومرضي الإستصفاء الدموي

مايسة عمر[١]، سماح سعد الدين[١]، نيفين فام[١]، منال دياب[١]، محمد شميس[٢]، منار رأفت[٣]، معتز صيام[٤]، معتز حسن[٤]، أفكار بدوي[٥]، مها عقل[٥]، محمد صابر[٢]

أقسام الميكروبيولوجي[١]، الكيمياء الحيوية[٢]، أمراض الكلي[٣]، طب المناطق الحارة[٤]، الباثولوجي

معهد تيودور بلهارس للأبحاث- الجيزة

الملخص العربي:

يعتبر فيروس السن له علاقة مبدئية بالالتهاب الكبدي الناتج عن الفيروسات A-E والتي تنتقل عن طريق نقل الدم. وكان الهدف من البحث هو تحديد مدى انتشار فيروس السن بين المرضي المصريين المصابين بمرض الكباد المزمن الناتج عن الفيروس الكبدي C ومرضي الإستصفاء الدموي وتقييم التأثير الإكلينيكي للعدوى بالفيروس من حيث زيادة حدة المرض أو احتمال تطوره إلي السرطان الكبدي في مرضي الكباد المزمن لفيروس C.

وقد تم استخدام تفاعل البلمرة المتسلسل (PCR) للكشف عن الحامض النووي (DNA) لفيروسات السن (D, H) في عينات الدم والتي تم جمعها من ٧٤ مريضا بالالتهاب الكبدي المزمن لفيروس C، ٤٥ مريضا بالفشل الكلوي المزمن الخاضعين للإستصفاء الدموي و٢٨ من الأصحاء كمجموعة ضابطة.

أظهرت نتائج البحث وجود الحامض النووي للفيروس في ١٣،٥ %، ١١،١ %، ٧،١ % من مرضي الكباد المزمن للفيروس C ومرضي الإستصفاء الدموي والأصحاء علي التوالي مع عدم وجود فرق ذو دلالة إحصائية بين المرضي والأصحاء. كما أنه لم يتبين وجود أي فرق ذو دلالة إحصائية من حيث النواحي الإكلينيكية أو القياسات البيوكيميائية بين مرضي الكباد المزمن و الإستصفاء الدموي المصابين والغير مصابين بعدوي فيروس السن.

. وقد أظهرت النتائج وجود ارتفاع ذو دلالة إحصائية في مرضي الالتهاب الكبدي المزمن C المصاحب لسرطان الكبد (٣٣،٣%) عن غير المصاحب (٨،٥%)

ونستخلص من هذا البحث أن عدوي فيروس السن غير شائعة بين المرضي المصريين وليس لها تأثير واضح علي زيادة حدة المرض في مرضي الكباد المزمن الناتج عن فيروسC الا أنه قد يكون عامل مساعد في ظهور سرطان الكبد في هؤلاء المرضي. نحن بحاجة إلي دراسات مستقبلية لتحديد دور فيروس السن (SEN) فى حدوث سرطان الكبد.