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ORIGINAL ARTICLE

Prevalence of SEN Virus and Torque Teno Virus in Hemodialysis Patients and Healthy Blood Donors in Menoufia University Hospitals

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ABSTRACT

Background: *Blood transfusion and hemodialysis are considered major sources for blood-borne infections by different ways as the equipment, surfaces, and personnel, not only for HCV and HBV but also for SENV and TTV.* ***Objectives:*** *To determine the prevalence of SENV-D/H and TTV among HD patients and blood Donors (control group) in relation to HBV and HCV infection in Menoufia University Hospitals.* ***Methodology:*** *Serum samples from all tested HD patients and blood donors were investigated for ALT, AST by automated chemistry analyzer, anti HBsAg. and HCV antibodies by immunoassay. Also, SENV-D/H and TTV were detected by nested PCR.* ***Results:*** *Total SENV prevalence was 67.5% & 9.6% for HD patients and controls respectively. TTV had a prevalence of 38.9% in HD group and 17.8% in controls. SENV& TTV coinfection was 12.1% and 3.8% for HD patients and controls respectively. Non-significant association between different SENV genotypes, TTV infections and HBV or HCV infections. The positivity of SENV and TTV infections were significantly related to increased duration of hemodialysis, history of blood transfusion and elevated AST and ALT.* ***Conclusions:*** *SENV and TTV are more prevalent in hemodialysis patients than controls. Duration of hemodialysis, history of blood transfusion, and elevated ALT and AST are significantly related to SENV and TTV infection. They have non-significant role in increasing the severity of HBV or HCV infection among hemodialysis patients.*

INTRODUCTION

Previously, several investigators have discovered the existence of hepatitis agents/viruses other than usual A to E ones. After noticing numerous patients with post-transfusion hepatitis that were negative for ordinary known hepatitis viruses A to E[1].

Genome analysis suggested non-A-E hepatitis and were designated hepatitis G virus (HGV) and TT virus, as the main agents of hepatitis of unknown origin[2].

The SEN virus is another novel virus detected by investigators group in Italy in 1999[2]. It is the latest viral agent that has been proposed as a cause of non-A-G hepatitis[3].

SEN virus (SENV), a member of the Circoviridae family is small, non-enveloped circular ss DNA virus. Its length is about 3800 nucleotides with 26 nm size. It has at least 3ORFs[4,5]. Today, SENV has a global incidence with variable prevalence geographically[6,7].

Genetic analysis detected nine SENV types (A to I) that differ in nucleotide sequence by about 25% [4,8]. SENV-D and SENV-H genotypes are the most prevalent[6].

The SENV genome is similar to Torque Teno virus (TTV) by about 55% in the nucleotide sequences. Since, TTV is one of Anelloviridae family[6], demonstrating the great association between SENV and TTV family[7].

TTV is negative stranded DNA virus that primarily detected in a Japanese patient with post-transfusional non-A-G hepatitis[9]. Molecular biology detected, seven genogroups of TTV with numerous genotypes[10], of which genotype 1 is the most frequently prevalent[11].

Although blood transfusion has a significant role in medical procedures worldwide. It can save a person's life during surgery, trauma, severe anemia, or pregnancy complications[12]. Also, the innumerable usefulness of hemodialysis for patients with renal failure. Those two procedures are considered major-sources for blood-borne infections, by different ways as the equipment, surfaces, and personnel, not only for HCV and HBV but also for SENV and TTV[3,9,13].

The purpose of this study is to determine the prevalence of SENV-D/H genotypes and TTV among hemodialysis patients and healthy blood donors and their relationship with the prevalence of HBV and HCV infection in Menoufia University Hospitals.

METHODOLOGY

Study design:

This study was done on hemodialysis patients (case group) attending to Hemodialysis Unit, Internal Medicine Department, and healthy blood donors (control group) attending to blood bank of Clinical Pathology Department, Menoufia University Hospitals during the period from April 2021 to March 2022. A full history was taken from all participants including age, history of DM, hypertension, previous surgery, blood transfusion, and duration of hemodialysis for patients' group. HIV positive individuals were excluded from the study. The study was conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent. The study design was approved by the ethical committee, Faculty of Medicine, Menoufia University **(IRB approval number and date: 11/22COM13)**.

Blood sample collection:

Ten ml venous Blood samples were collected from all participants under complete aseptic technique. After serum separation in Medical Microbiology Department, Faculty of Medicine Menoufia University, samples were divided into 3 aliquots. The 1st aliquot was used for ALT and AST determination regarding manufacturer's guidelines (Au 680 automated chemistry analyzer, Beckman, USA). The 2nd aliquot was used for serum detection of anti HBsAg and anti HCV antibodies according to manufacturer's guidelines (Architect i2000, Abbott, immunoassay, USA). The 3rd aliquot was stored in -20˚C for SENV-D/H, and TTV DNA detection by PCR.

DNA extraction:

DNA was extracted from serum using KAPA Express Extract kits (KAPA BIOSYSTEMS, USA) regarding the manufacturer's guidelines and DNA was stored in -20˚C.

Detection of SENV DNA by nested PCR:

Partial ORF1 gene of SENV-D and SENV-H were amplified by nested PCR. For the 1st round, primers, and PCR conditions as mentioned in **table 1**, using a 25 µl total volume containing, 0.4 pmol/ µl of each primer, 12.5 µl of Taq Green Master Mix (Promega, USA) and 3µl of extracted DNA[14]. For the 2nd round PCR amplification, 1µl of the 1st round PCR product was used with specific forward and reverse primers for SENV-D or SENV-H and similar PCR cycle conditions[14] as mentioned in table 1

Detection of TTV by semi nested PCR:

The ORF1 gene of TTV was amplified by semi nested PCR using the same reverse primer in the 1st and 2nd PCR rounds.

PCR was performed in a 25 µl total volume containing 1 µl of template DNA, 1 µl of each primer and 12.5 µl of TaqGreen Master Mix (Promega, USA)[15,16]. For the 2nd round PCR, 2 µl from the first-round amplicon was used as a template in a 25 µl total volume DNA[15,16]. As demonstrated in **table 1**. The PCR products were analyzed by 1.5 % agarose gel electrophoresis in Tris- Borate EDTA buffer (TBE; Fermentas, USA) with ethidium bromide staining.

Table 1: Primers and PCR conditions for genes detected in the study

Gene	Primer Sequence (5′ –3′)	Amplicon size (bp)	PCR cycle conditions	Ref. No.
ORF1 for SENV-D/H	**F: AI-1F:** 5'-TWC YCM AAC GAC CAG CTA GAC CT-3'; W= A or T, Y= C or T, M= A or C **R: AI-1R:** 5'- GTT TGT GGT GAG CAG AAC GGA-3'		**1st round**: 44 cycles (94˚C for 20 seconds, 56˚C for 25 seconds and 72˚C for 30 seconds for each cycle) with final extension time for 5 minutes at 72˚C in the thermocycler (Eppendorf, Germany).	**14**
SENV-D	**D-1148F:** 5'- CTA AGC AGC CCT AAC ACT CAT CCA G-3' **D-1341R:** 5'- GCA GTT GAC CGC AAA GTT ACA AGA G-3'	**195 bp**	**2nd round:** 25 cycles (94˚C for 20 seconds, 65˚C for 30seconds and 72˚C for 30 seconds) for both SENV-D and SENV-H.	
SENV-H	**H-1020F:** 5'- TTT GGC TGC ACC TTC TGG TT-3' **H-1138R:** 5'-AGA AAT GAT GGG TGA GTG TTA GGG-3'	**119 bp**		
ORF1 for TTV	**TTV-F:** 5´- ACA GAC AGA GGA GAA GGC AAC ATG -3´ **TTV-R: 5**´CTG GCA TTT TA CCA TTT CCA AAG TT -3´	**271 bp**	**1st round:** initial denaturation at 95°C for 5 min, followed by 30 cycles of denaturation at 94°C for 1 min, annealing at 58°C for 1 min and extension at 72°C for 1 min. The program was followed by a final extension at 72°C for 6 min.	**15, 16**
TTV	**TTV-FF:** 5´- GGCAACATGTTATG GATAGACTGG -3´ **TTV-R: 5**´CTG GCA TTT TA CCA TTT CCA AAG TT -3´		**2nd round:** 25 cycles of the same conditions	

Statistical analysis:

The data were collected, tabulated, and analyzed using SPSS (statistical package for social science) version 20.0 (SPSS Inc., Chicago, IL, USA). Quantitative data were presented as mean, median, standard deviation and range and compared using student t test while, Categorical data were described as numbers and percent and compared using Chi-square test (χ^2) & Fisher's Exact test accordingly, binary logistic regression analysis was performed to estimate independent risk factors and adjusted odds ratio, p value of less than 0.05 was considered significant.

RESULTS

The current study that was performed on 157 hemodialysis patients (85 males and 72 females with mean age 47.62±10.71) and 157 age and sex matched healthy blood donors (90 males and 67 females with mean age 47.01±11.07). Sixty-five (41.4%) of hemodialysis patients were under hemodialysis for less than 12 months and 92 (58.6%) for more than 12 months. Hemodialysis patients showed significantly higher percentage of HBV, HCV, DM, hypertension, history of previous surgery, and increased liver enzymes (AST&ALT) (P value <0.001) and showed non-significant difference regarding history of blood transfusion, (P value >0.05) as documented in **table 2**.

Table 2: Demographic data and clinical history of hemodialysis patients in relation to healthy blood donors

	HD patients N = 157	**Healthy blood donors N = 157**	test	P value
Age (years)			t-test	
Mean ± SD	47.62±10.71	47.01±11.07	0.50	0.62
Median (Range)	48 (21 – 66)	47 (25 – 67)		
Sex [n (%)]			X^2	
Male	85 (54.1)	90 (57.3)	0.32	0.57
Female	72 (45.9)	67 (42.7)		
HBV				
Positive	47 (29.9)	0 (0.0)	55.27	<0.001
Negative	110 (70.1)	157 (100)		
HCV				
Positive	54 (34.4)	0 (0.0)	65.22	<0.001
Negative	103 (65.6)	157 (100)		
DM				
Positive	67 (42.7)	6 (3.8)	66.41	<0.001
Negative	90 (57.3)	151 (96.2)		
HTN				
Positive	56 (35.7)	5 (3.2)	52.92	<0.001
Negative	101 (64.3)	152 (96.8)		
Previous surgery				
Yes	42 (26.8)	13 (8.3)	18.54	<0.001
No	115 (73.2)	144 (91.7)		
H. of bl. transfusion				
Yes	18 (11.5)	9 (5.7)	3.28	0.07
No	139 (88.5)	148 (94.3)		
AST (U/L)			U	
Mean ± SD	75.76±26.36	63.97±20.73	4.01	<0.001
Median (Range)	75 (20 – 148)	64 (14 – 100)		
ALT (U/L)			t-test	
Mean ± SD	70.67±24.83	55.58±14.41	6.59	<0.001
Median (Range)	66 (23 -145)	58 (21 – 85)		

The prevalence of SEN- D was 22.9% & 4.5%, SEN-H was 52.2% & 6.4, moreover. SEN-D/H was 7.6% & 1.3%, and total SEN virus prevalence was 67.5% & 9.6% for hemodialysis patients and healthy blood donors respectively. Torque Teno virus (TTV) had a prevalence of 38.9% in HD group and 17.8% in healthy blood donors. Combined SENV& TTV was 12.1% and 3.8% for hemodialysis patients and healthy blood donors respectively. So SENV alone was 55.4%& 5.7%, TTV alone was 26.8% & 14%, combined infection was 12.1% & 3.8% and negative cases was 5.7% & 76.4% for hemodialysis patients and healthy blood donors respectively as shown in **table 3 and fig.1.**

Table 3: Prevalence of SENV and TTV among HD patients versus apparently healthy blood donors

		HD N =157	Bl, donors N = 157	Test	P value
SENV	SENV-D +ve -ve	 36 (22.9) 121 (77.1)	 7 (4.5) 150 (95.5)	39.63	<0.001
	SENV-H +e -ve	 82 (52.2) 75 (47.8)	 10 (6.4) 147 (93.6)	76.70	<0.001
	SENV-D/H +ve -ve	 12 (7.6) 145 (92.4)	 2 (1.3) 155 (98.)	7.48	0.006
	Total +ve -ve	 106 (67.5) 51 (32.5)	 15 (9.6) 142 (90.4)	111.34	<0.001
TTV Positive negative		 61 (38.9) 96 (61.1)	 28 (17.8) 129 (82.2)	17.08	<0.001
Combined SENV& TTV positive negative		 19 (12.1) 138 (٨٧.9)	 6 (3.8) 151 (96.2)	7.35	0.007
SEN& TTV infection SEN infection TTV infection Combined SEN&TTV Negative		 87 (55.4) 42 (26.8) 19 (12.1) 9 (5.7)	 9 (5.7) 22 (14.0) 6 (3.8) 120 (76.4)	171.90	<0.001

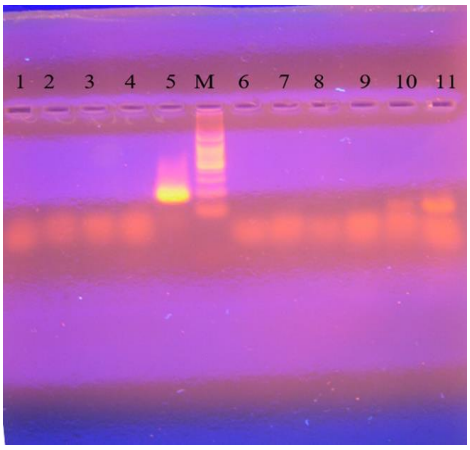

Fig. 1a: Column 5: positive SENV-D (195 bp).

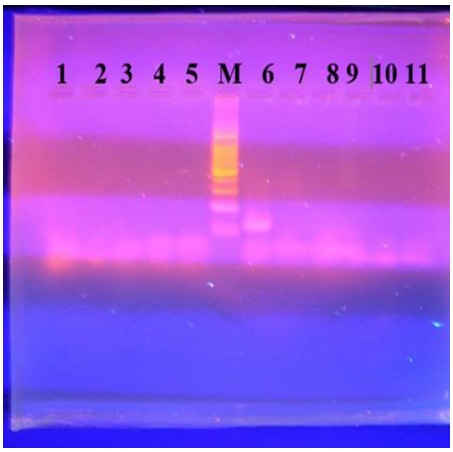

Fig. 1b: Column 6: positive SENV-H positive (119 bp).

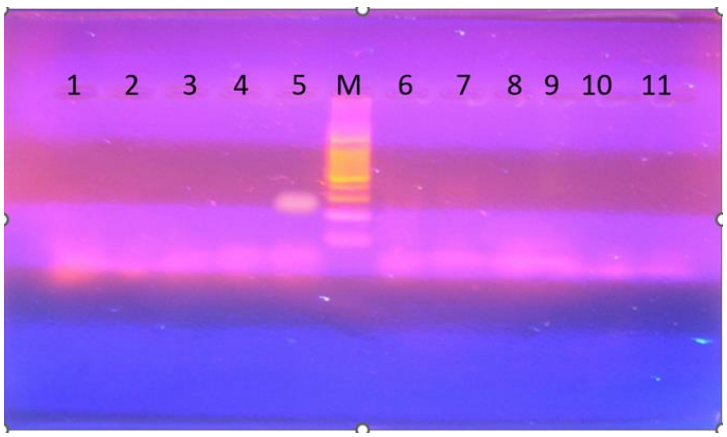

Fig. 1c: Column 5: positive TTV (271 bp).

Fig. 1: Agarose gel electrophoresis of PCR products M: Marker 100 bp DNA (Fermentas, EU).

Coincident SENV-D and TTV infections were 16.7% & 42.9%, SENV-H and TTV coinfection was 18.3% & 40%, SENV-D/H and TTV infection was 16.7% &50% in hemodialysis patients and healthy blood donors respectively as shown in **table 4 and fig.2**.

Table 4: Prevalence of TTV in relation to SENV genotypes in the studied groups

	SEN -D/H		**SEN-D**		**SEN-H**		Test	P value
HD group	**Positive N = 12**	**Negative N = 145**	**Positive N = 36**	**Negative N = 121**	**Positive N = 82**	**Negative N = 75**		
TTV							2.69	0.13[1]
Positive	2 (16.7)	59 (40.7)	6 (16.7)	55 (45.5)	15 (18.3)	46 (61.3)	9.68	0.002[2]
Negative	10 (83.3)	86 (59.3)	30 (83.3)	66 (54.5)	67 (81.7)	29 (38.7)	30.54	<0.001[3]
	SEN -D/H		**SEN-D**		**SEN-H**			
Healthy BD	**Positive N = 2**	**Negative N = 155**	**Positive N = 7**	**Negative N = 150**	**Positive N = 10**	**Negative N = 147**		
TTV							1.43	0.33[1]
Positive	1 (50.0)	27 (17.4)	3 (42.9)	25 (16.7)	4 (40.0)	21 (14.3)	3.13	0.11[2]
Negative	1 (50.0)	128 (82.6)	4 (57.1)	125 (83.3)	6 (60.0)	126 (85.7)	3.58	0.08[3]
Test	0.94		2.43		2.56			
P value*	0.32		0.12		0.12			

P1 = significance of SEN-D/H and TTV coinfection
P2 = significance of SEN-D and TTV coinfection
P3 = significance of SEN-H and TTV coinfection
P* = comparing coinfection between HD and healthy BD groups

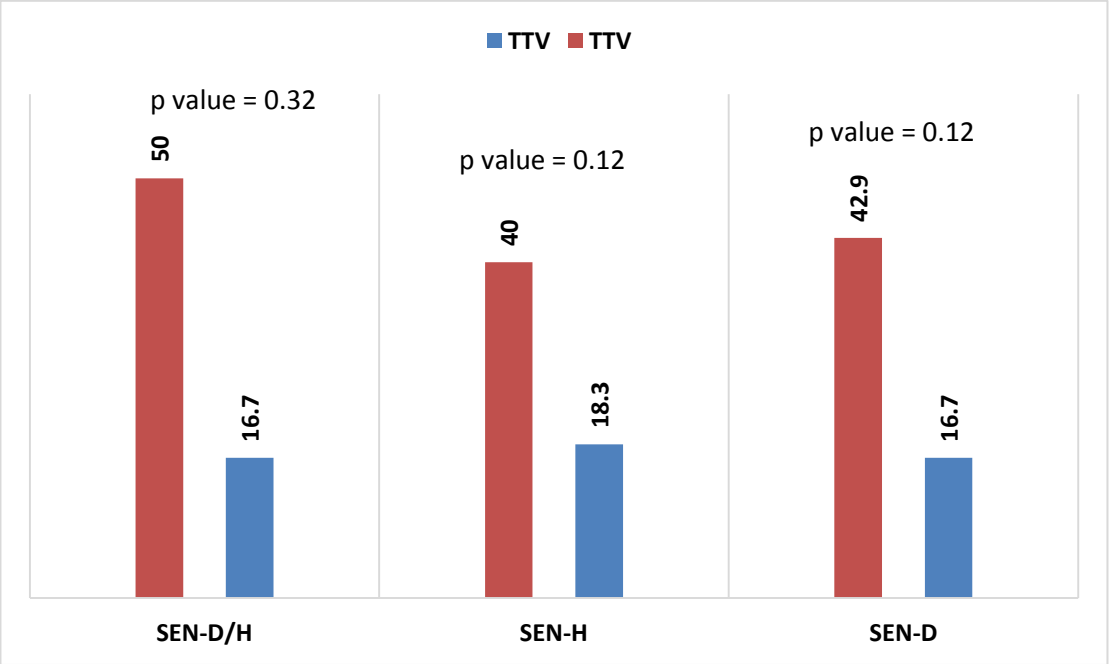

Fig. 2: Prevalence of TTV in relation to SENV genotypes in the studied groups

There was non-significant association between different SENV genotypes, TTV infections and HBV or HCV infections as documented in **table 5.**

Table 5: SENV genotypes and TTV in relation to HBV & HCV among hemodialysis patients

	HBV		**Test**	**P value**	**HCV**		Test	P value
	Positive N = 47	**Negative N = 110**			**Positive**	**Negative**		
SENV-D +ve (15) -ve (85)	 10 (27.8) 37 (30.6)	 26 (72.2) 84 (69.4)	0.10	0.75	 11 (30.6) 43 (35.5)	 25 (69.4) 78 (64.5)	0.31	0.58
SENV-H +ve (45) -ve (55)	 22 (26.8) 25 (33.3)	 60 (73.2) 50 (66.7)	0.79	0.37	 24 (29.3) 30 (40.0)	 58 (70.7) 45 (60.0)	2.0	0.16
SENV-D/H coinfection +ve (7) -ve (93)	 2 (16.7) 45 (31.0)	 10 (83.3) 100 (69.0)	1.09	0.51	 3 (25.0) 51 (35.2)	 9 (75.0) 94 (64.8)	0.51	0.55
SEN virus total Positive Negative	 30 (28.3) 17 (33.3)	 76 (71.7) 34 (66.7)	0.42	0.52	 32 (30.2) 22 (43.1)	 74 (69.8) 29 (56.9)	2.56	0.11
TTV +ve (27) -ve (73)	 19 (31.1) 28 (29.2)	 42 (68.9) 68 (70.8)	0.07	0.79	 26 (42.6) 28 (29.2)	 35 (57.4) 68 (70.8)	2.99	0.08
SENV & TTV coinfections SEN infection TTV infection Combined SEN & TTV Negative	 24 (27.6) 13 (31.0) 6 (31.6) 4 (44.4)	 63 (72.4) 29 (69.0) 13 (68.4) 5 (55.6)	1.17	0.76	 26 (29.9) 20 (47.6) 6 (31.6) 2 (22.2)	 61 (70.1) 22 (52.4) 13 (68.4) 7 (77.8)	4.69	0.20

The positivity of SENV and TTV infections were significantly related to increased duration of hemodialysis, history of blood transfusion and elevated liver enzymes AST and ALT while they weren't related to other parameters (age, sex, HBV, HCV, DM, HTN, and previous surgery). Binary logistic regression analysis revealed that duration of hemodialysis and blood transfusion were independent risk factors for SEN virus infection with odds ratio 3.79 (1.23 – 6.21) & 2.47 (1.02–7.14) respectively. While duration of hemodialysis was an independent risk factor for TTV infection with odds ratio 2.84 (1.39 – 5.78) as demonstrated in **table 6**.

Table 6: Univariate analysis for suspected risk factors SENV & TTV infections among HD patients and Binary logistic regression analysis for independent risk factors for SENV and TTV infection

	SENV		Test	P value	TTV		Test	P value
	Positive N = 106	**Negative N = 51**			**Positive N=61**	**Negative N= 96**		
Age (years) Mean ± SD (Range)	47.30±10.61 21 – 66	48.29±10.99 21 – 66	0.54	0.59	46.7±11.30 21 – 66	48.20±10.33 21 – 66	0.66	0.39
Sex [n (%)] Male Female	57 (53.8) 49 (46.2)	28 (54.9) 23 (45.1)	0.02	0.89	31 (36.5) 30 (41.7)	54 (63.5) 42 (58.3)		
HBV Positive Negative	30 (63.8) 76 (69.1)	17 (36.2) 34 (30.9)	0.42	0.52	19 (40.4) 42 (38.2)	28 (59.6) 68 (61.8)	0.07	0.79
HCV Positive Negative	32 (59.3) 74 (71.8)	22 (40.7) 29 (28.2)	2.56	0.11	26 (48.1) 35 (34.0)	28 (51.9) 68 (66.0)	2.99	0.08
Duration of HD <12 mo > 12 mo	36 (55.4) 70 (76.1)	29 (44.6) 22 (23.9)	7.44	0.006	33 (50.8) 28 (30.4)	32 (49.2) 64 (69.6)	6.63	0.01
DM Yes No	47 (70.1) 59 (65.6)	20 (29.9) 31 (34.6)	0.37	0.54	22 (32.8) 39 (43.3)	45 (67.2) 51 (56.7)	1.78	0.18
HTN Yes No	37 (66.1) 69 (68.3)	19 (33.9) 32 (31.7)	0.08	0.77	25 (44.6) 36 (35.6)	31 (55.4) 65 (64.4)	1.23	0.27
Previous surgery Yes No	28 (66.7) 78 (67.8)	14 (33.3) 37 (32.2)	0.02	0.89	17 (40.5) 44 (38.3)	25 (59.5) 71 (61.7)	0.06	0.80
H. of bl. transfusion Yes No	17 (94.4) 89 (64.0)	1 (5.6) 50 (36.0)	6.72	0.01	12 (66.7) 49 (35.3)	6 (33.3) 90 (64.7)	6.62	0.01
AST (U/L) Mean ± SD Range	80.10±25.23 20 – 148	66.75±26.61 20 – 145	2.92	0.004	82.46±29.33 32 - 148	71.51±23.47 20 – 130	2.20	0.028
ALT (U/L) Mean ± SD Range	74.81±25.22 28 – 145	562.08±21.84 23 – 115	2.73	0.006	76.97±27.01 23 – 138	66.68±22.59 23 – 145	2.39	0.017

	Binary logistic regression analysis							
	SEN infection				**TTV infection**			
	SE	**P value**	**Odds ratio**	**95%CI**	**SE**	**P value**	**Odds ratio**	**95%CI**
Duration of HD	0.38	0.01	3.79	1.23 – 6.21	0.36	0.004	2.84	1.39 – 5.78
Blood transfusion	0.01	0.04	2.47	1.02 – 7.14	0.60	0.07	1.66	0.90 – 9.43
AST	1.07	0.14	0.14	0.05 – 1.25	0.007	0.26	0.99	0.98 – 1.06
ALT	0.01	0.09	0.09	0.12 – 2.35	0.008	0.10	1.01	0.97 – 1.13

DISCUSSION

This study was conducted on 314 participants divided equally into 157 hemodialysis patients (85 males and 72 females with mean age 47.62±10.71) and 157 healthy blood donors as control group (90 males and 67 females with mean age 47.01±11.07). The two groups are matched in age and sex with non-significant difference ($p < 0.05$).

The hemodialysis group showed significantly higher percentage ($p < 0.001$) of HBV (29.9%), and HCV (34.4%) than the control group that was negative for both viruses. This is in accordance with Abd El-Hady et al.[3] results that documented the prevalence of HCV and HBV by 27.3% and 29.1% in hemodialysis patients and negative control group. It also matched with Dai et al[17] results who reported the prevalence of HCV and HBV in hemodialysis patients as 24.2% and 7.1% respectively and negative blood donors. While Abdel Hady et al[18] findings stated that, the HCV was detected in 25.3% of hemodialysis group with negative controls and HBV was detected in 35% and 30.6% of hemodialysis patients and blood donors respectively with non-significant difference This may be due to the difference in control group characteristics. Other studies documented high prevalence of HCV among hemodialysis group[19, 20].

Diabetes is considered as the commonest etiology of renal failure that ends in dialysis. Also, patients who developed chronic kidney disease are usually suffering from hypertension[21].

In our study, 42.7% and 35.7% of hemodialysis patients were significantly ($p<0.001$) complaining of diabetes and hypertension than control group (3.8% and 3.2) and most of them were males. That is nearly matched with Lea et al.[22] who found that 50.1% and 27% of the end stage renal disease patients were diabetic and hypertensive. Elfaki et al.[21] reported that 75% and 19% of hemodialysis patients were hypertensive and diabetic respectively and were mainly males. Gorsane, et at.[23] reported higher prevalence of hypertension among haemodialysis patients by 90%.

The current work results revealed significantly higher increase ($p < 0.001$) of liver enzymes, AST&ALT, in hemodialysis patients than control group. This goes in line with Abd El-Hady et al.,[3] where the difference between the tested groups was highly significant for AST ($P < 0.01$) and statistically significant for ALT ($P < 0.05$). This can be interpreted as heamodialysis patients showed more affection by HBV, HCV in addition to higher affection rate by SENV and TTV.

Our study showed that the prevalence of SENV alone was 55.4% & 5.7%, TTV alone was 26.8% & 14% and SENV/TTV coinfection was 12.1% & 3.8% and negative cases was 5.7% & 76.4% for hemodialysis patients and healthy blood donors respectively. So, in our study the total prevalence of SEN virus either alone with different genotypes D/H or coinfected with TTV was 67.5% & 9.6% and the total prevalence of TTV was 38.9% and 18.5% in hemodialysis and control groups respectively with highly significant difference ($P<0.001$). That is in accordance with previous study[3] that detected SEN virus in 89.1% & 16% in hemodialysis group and control group respectively. Kobayashi et al[19] and Kao et al[24] detected SENV by 68% and 38% in hemodialysis patients and control. For TTV, Wahid & Saadoon[9] and Ali ae al[25]. detected it by 40.9% and 38.7% among hemodialysis patients and control respectively.

In the present study, the prevalence of SENV-H (52.2%, 6.4%) was higher than SENV-D genotype (22.9%, 4.5%) and combined SENV-D/H (7.6%, 1.3%) of hemodialysis patients and healthy blood donors respectively with highly significant difference between both groups. This is in accordance with Abd El-Hady et al.[3] who detected SENV-H and SENV-D in (65.5%, 12%) and (23.6%, 4%) of hemodialysis patients and controls respectively. In contrast to Dai et al.[17] who documented the total prevalence of SENV with its two genotypes by (27.3%, 5.8%), (46.5%, 18.3%) and (61.6%, 23.3%) in hemodialysis patients and controls respectively with highly significant difference. Schroter et al.[26] reported non-significant difference between hemodialysis patients (12.8%) and controls (16.8%) regarding SENV-H prevalence.

In our study, the coinfection with SENV& TTV was detected in 12.1% and 3.8% for hemodialysis patients and healthy blood donors respectively. This is in accordance with Afkari et al[27] who detected coinfections with SENV and TTV in 19.33% and 9.33% in hemodialysis and healthy blood donors respectively.

In results of this work, the coinfection of TTV with SENV-H, SENV-D and SENV-D/H was demonstrated in 15(18.3%), 6(16.7%) and 2(16.7%) in hemodialysis patients respectively with highly significant association between TTV and SENV-D and SENV-H. In controls, there was highly significant association between TTV and SENV-H coinfection 4(40%), and non-significant association between TTV and SENV-D coinfection 3(42.9%) nor SENV-D/H coinfection 1(50%). Also, Pirouzi et al.[28] reported Higher association between TTV and SENV-H, that SENV/TTV coinfection was detected in 43.33% of HIV patient group where 32.66% demonstrated SENV-H and 23.33% demonstrated SENV-D. Also, 21.33% of blood donors were TTV/SENV coinfected. In previously mentioned study[7], the SENV and TTV coinfection was detected in 26% in the hepatic patient group versus 4.65% in healthy blood donors.

Our results showed non-significant association between different SENV genotypes, TTV infections, HBV or HCV infections which coincide with Hosseini et al.[29] who reported that the frequency of SENV and its two genotypes were significantly low (P<0.05) in both hepatitis B and hepatitis C patients (56%) than that of healthy individuals (90.5%) tested. Magu et al.[30] reported in his results increased TTV DNA levels in hepatic tissue and appearance of TTV infection in post-transfusion hepatitis however the link between TTV and any hepatic affection is not analyzed yet.

In agreement with, Kobayashi[19], Hadeer Mohammed Ali[25] and Pirouzi[28], our results showed non-significant relation of TTV and SENV with age, sex, HBsAg, HCV antibody, DM, HTN, and history of previous surgery. But vary from them that duration of hemodialysis, history of blood transfusion and liver enzymes, AST and ALT, were significantly associated with SENV and TTV infection.

Regarding liver enzymes, AST, and ALT, Abd El-Hady et al.[3] reported that infection with SENV only didn't affect the level of AST or ALT in hemodialysis patients demonstrating that SENV had limited or no hepatic pathogenicity, that coincide with Schröter et al.[26] results. For khudair et al.[7] results, the elevation of AST and ALT among SENV infected participants was non-significant compared to participants that were coinfected with both SENV and TTV.

CONCLUSIONS

SENV and TTV are more prevalent in hemodialysis patients than controls. Duration of hemodialysis, history of blood transfusion, and elevated ALT and AST are significantly related to SENV and TTV infection. They have a non-significant role in increasing the severity of HBV or HCV infection among hemodialysis patients.

This manuscript has not been previously published and is not under consideration in the same or substantially similar form in any other reviewed media. I have contributed sufficiently to the project to be included as author. To the best of my knowledge, no conflict of interest, financial or others exist. All authors have participated in the concept and design, analysis, and interpretation of data, drafting and revising of the manuscript, and that they have approved the manuscript as submitted.

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Abbreviations:

SENV: SEN virus
SENV/H: SEN virus genotype H
SENV/D: SEN virus genotype D
SENV/H-D: both H and D genotypes of SEN virus
TTV: Torque Teno Virus
HD: hemodialysis
HCV: hepatitis C virus
HBV: hepatitis B virus
AST: aspartate transferase blood test
ALT: alanine amino transferase test

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