Intrafamilial spread of Hepatitis C Virus in high socioeconomic population, in Menoufia Governorate

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Abstract: Objective: This study was done to study the intrafamilial spread of HCV in high socioeconomic population, and to determine the prevalence of anti-HCV antibodies among household contacts of HCV seropositive index patients and to identify the possible risk factors for HCV transmission among families. **Background:** HCV is a major public health problem world wide. Persistent HCV infection is a leading cause of serious liver disease including cirrhosis and hepatocellullar carcinoma. **Patients and Methods:** This study included 100 HCV positive cases of high socioeconomic population and their family members; they were selected from different areas in Menoufia Governorate. All participants were subjected to thorough history taking, clinical assessment, and detection of HCV antibodies by one-step test device. **Results:** our study reaveld that Prevalence of HCV in family members of HCV positive patient was 8.24% **Conclusion:** intrafamilial contact is an important factor in the transmission of HCV. Transmission might occur during family contact, sexual behavior, and the shared use of personal items. A wide scale national study is needed to clarify this important entity.
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1. Introduction

Hepatits C virus (HCV), is a member of the Flaviviridae family, has a single-stranded positive RNA genome with high genetic diversity. Six HCV genotypes, numbered 1–6, and a large number of subtypes have been described **(1).** It is estimated that approximately 130–210 million individuals, i.e. 3% of the world population are chronically infected with HCV **(2).** Egypt has the highest prevalence of HCV worldwide and the highest prevalence of HCV- 4, which is responsible for 90% of infections with a predominance of subtype 4a (90%). The origin of the HCV epidemic in Egypt was attributed to mass campaigns of parenteral anti-schistosomiasis treatment in the 1960–1970s **(3).** It is difficult to determine the number of new HCV infections, as most acute cases will not be noticed clinically, fewer than 25% of acute cases of HCV are clinically apparent **(4).**

Acute HCV infection is asymptomatic in 50–90% of cases, failure to spontaneously eradicate infection occurs in 50–90% of cases according to the route of transmission, the presence of symptomatic hepatitis, and to the age at which infection occurred; between 10% and 40% of patients with chronic HCV infection will develop cirrhosis **(5).** Death related to the complications of cirrhosis may occur, at an incidence of approximately 4% per year, whereas hepatocellular carcinoma (HCC) occurs in this population at an estimated incidence of 1–5% per year. Patients diagnosed with HCC have a 33% probability of death during the first year **(6).**

HCV is mostly transmitted through large or repeated direct percutaneous exposures to blood (e.g.transfusion or transplantation from infectious donors, injecting drug use) **(2).** Procedures performed by non-medical professionals and traditional healers have been identified as important risk factors for HCV transmission in Egypt **(7).** However the cause of transmission of HCV is unknown in about 20% of cases **(8).**

Diagnosis of chronic HCV infection is based on the presence of both anti-HCV antibodies, detected by enzyme immunoassays, and HCV RNA, detected by molecular assays **(9).** An over-the-counter antibody testing kit ("Hepatitis C Check") has been approved by the FDA. Data presented to the FDA suggest that the accuracy of the test is comparable to hospital laboratory-based antibody testing **(10).**

2. Patients and Methods

This is a cross- sectional analytic study. It was performed on a convenient sample of 100 index cases of high socioeconomic level and their 427 household family contacts. Patients were selected from Hepatology outpatient clinic of Shibin El-Kom Teaching Hospital in the period between November 2013 and March 2015. And gave oral consent to participate in the study (by the patient).

Inclusion criteria included, The age above 18 years (age of official marriage), Index patients and their control were living with their families, All patients and their families of high socioeconomic level according to Socioeconomic scoring system, Anti HCV Abs positive and HCV RNA positive.

Criteria for exclusion were patients with other causes of liver disease rather than HCV infection based on patient's history, laboratory or biopsy or who refuse to share in the study.

Members of the study group subjected to:

1. Thorough history taking: thorough history has been taken from all members of the study group with special emphasis on: Symptoms, and its duration, (e.g. abdominal pain, enlarged abdomen, lower limb edema, fatigue, loss of weight, jaundice). Special reference to host risk factors of HCV exposure in surgical words, blood transfusion, dental therapy, needle sticks injuries, parenteral anti schistosomiasis therapy, tattooing, circumcision and positive cases in the family habits of the patients as shaving.

A predesigned questionnaire was constructed including several parts to be filled by the patients themselves and their family members with special emphasis on the intrafamilial transmission.

2. Complete physical examination: with special emphasis on Signs of liver cell failure (e.g. jaundice, ascites, hepatomegaly, splenomegaly and lower limb edema).

3. Laboratory: HCV anti bodies by one step test device.

Sampling and methods

Blood Samples: Blood was collected from the patients by vacuum vein puncture (after taking their consent), using a dry 5-mL tube. The serum was separated, centrifuged, aliquoted and stored at -20ºC and HCV anti bodies by one step test device was done.

Statistical analysis:

The data collected were tabulated and analyzed by SPSS (statistical package for social science) version 17.0 on IBM compatible computer.

Two types of statistics were done.

Descriptive statistics e.g.mean (x) and standard deviation (SD).

Analytic statistics: Qualitative data expressed in number and percentage and analyzed by applying X2 test to study statistical relation between different variables. Logistic regression to predict the outcome in exposed.

Quantitative data are expressed to measure the central tendency of data and diversion around the mean.

P value > 0.05 was considered statistically non-significant.

P value < 0.05 was considered statistically significant.

P value < 0.001 was considered statistically highly significant **(11).**

3. Results:

The prevalence of HCV among high socioeconomic family members of HCV positive index cases in Menoufia governorate was found to be 8.24% (table 1) (fig.1).

The intra familial pattern of spread of HCV infection, about 41.67% was between spouses, 30.56% was from parent to their children and about 27.77% was between brothers and sisters. (table 2).

The intra spousal transmission of HCV infection, about 53.33% the index case was the wife and 46.67% the index case was the husband. (table 3) (fig.2).

There was statistical significant difference between positive and negative cases regarding age, and occupation and non statistical significant difference between positive and negative cases regarding gender (table 4).

There was statistical significant difference between positive and negative cases regarding using common tooth brushes and non statistical significant difference regarding using common towels, nail clippers and mosquito and flea bite. (table 5).

There was statistical significant difference between positive and negative cases regarding bilharzial treatment injection, multiple syringes and dental procedures and non significant difference regarding previous surgeries and blood transfusion (table 6).

There was statistical significant difference between positive and negative cases regarding using common shaving blades and non statistical significant difference regarding place of shaving (table 7).

Table 1: Prevalence of HCV in families of HCV positive patients

HCV	members of families of HCV positive subject (437)	%
Positive	36	8.24
Negative	401	91.76

Table 2: Intrafamilial pattern of spread of HCV infection.

Parameter	Positive cases (36)		P value
	No	%	
Between spouses	15	41.67	0.63
Parent to children	11	30.56	
Between brothers and sisters	10	27.77	

Table 3: Intraspousal transmission of HCV infection.

Parameter	index case of spouses (15)		P value
	No	%	
Wife	8	53.33	0.72
Husband	7	46.67	

Table 4: Sociodemographic data of negative and positive subjects of the families of HCV positive cases.

Parameter	Positive (36)	Negative (401)	Chi square test	P value
Age X ±SD	43.53±14.89	24.67±16.06	Mann Whitney test 6.79	< 0.001
Age groups in years <18 18-40 >40	 2.78% (n=1) 38.89% (n=14) 58.33% (n=21)	 7.48% (n=30) 48.13% (n=193) 44.39% (n=178)	3.04	0.22
Residence Urban Rural	 30.56% (n=11) 69.44% (n=25)	 57.36% (n=230) 42.64% (n=171)	9.59	0.0019
Gender Male Female	 52.78% (n=19) 47.22% (n=17)	 54.11% (n=217) 45.89% (n=184)	0.02	0.87
Occupation Not work or house wife Worker	 8.33% (n=3) 91.67% (n=33)	 13.47% (n=54) 91.03% (n=365)	6.69	0.035

Table 5: Risk factors of HCV of the studied group regarding daily practices.

Risk factors	Positive cases (36)	Negative cases (401) % (No)	Chi square test	P value
Common tooth brush Yes No	 80.55% (n=29) 19.45% (n=7)	 57.61% (n=231) 42.39% (n=170)	7.22	0.0072
Towels Yes No	 58.33% (n=21) 41.67% (n=15)	 69.58% (n=279) 30.42% (n=128)	1.58	0.208
Nail clipper Yes No	 61.11% (n=22) 38.89% (n=14)	 70.07% (n=281) 29.93% (n=126)	0.96	0.326
Mosquito or flea bite Yes No	 91.67% (n=33) 8.33(n=3)	 95.26%(n=382) 4.74% (n=25)	0.27	0.604

Table 6: Risk factors of the studied group regarding past history.

Risk factors	Positive cases (36)	Negative cases (401)	Chi square test	P value
Bilharzial treatment by injection Yes No	 80.56% (n=29) 19.44% (n=7)	 6.48% (n=26) 93.52% (n=375)	7.95	0.0048
Multiple syringes Yes No	 83.33% (n=30) 16.67% (n=6)	 3.74% (n=15) 96.26% (n=386)	12.07	< 0.001
Previous surgery Yes No	 52.78% (n=19) 47.22% (n=17)	 42.64% (n=171) 57.36% (n=230)	0.28	0.595
Blood transfusion Yes No	 83.33% (n=30) 16.67% (n=6)	 17.21% (n=69) 82.79% (n=332)	0.01	0.93
Dental procedures Yes No	 55.56% (n=20) 44.44% (n=16)	 26.43% (n=106) 83.57% (n=295)	13.65	< 0.001
Tattooing Yes No	 0.0% (n=0) 100% (n=36)	 0.0% (n=0) 100% (n=401)	====	=====

Table 7: Risk factors of the studied group regarding shaving.

Risk factors	Positive cases (36) % No	Negative cases (401) % No	Chi square test	P value
Shaving Outside home Inside home	 86.11% (n=31) 13.89% (n=5)	 93.52% (n=375) 6.48% (n=26)	2.75	0.097
Common shaving blades Yes No	 55.56% (n=20) 44.44% (n=16)	 31.67% (n=127) 68.33% (n=274)	8.44	0.0036

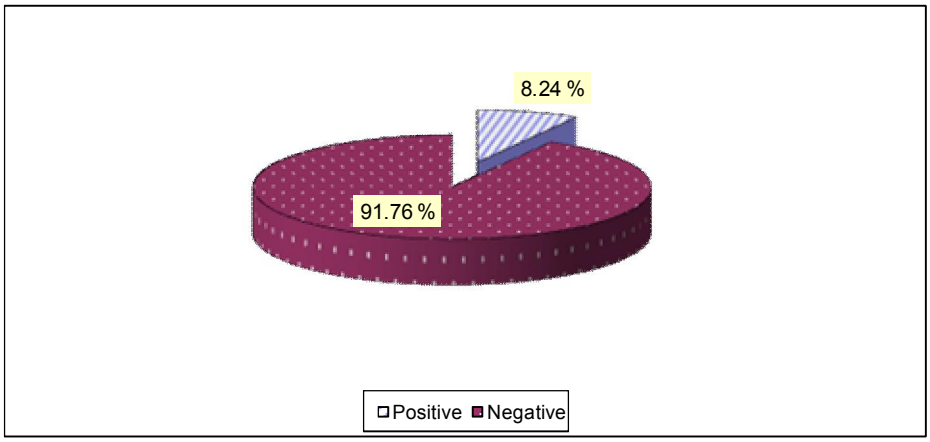

Figure (1): Prevalence of HCV in families of HCV positive patients.

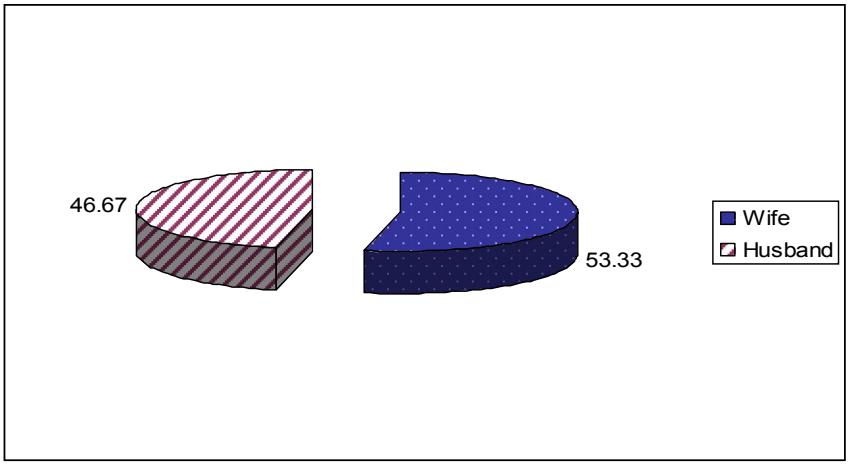

Figure (2): Intra spousal transmission of HCV infection.

4. Discussion:

Egypt has the highest prevalence of recorded HCV worldwide, estimated nationally at 14.7%, which is attributed to extensive iatrogenic transmission during the era of PAT mass-treatment campaigns **(11).**

Intrafamilial transmission is possible, and transmission between spouses is often assumed to be sexual. However, other routes of transmission between married couples and other family members are possible. Some studies have found high rates of infection among non spouse household transmission. It is supported by the fact that HCV RNA has often been found in the saliva of patients with or without serum HCV RNA **(8).**

Mostafa et al., (12) recommended screening of families of infected HCV subjects as an essential part of case management for early detection and their further management.

In this study prevalence of HCV among high socioeconomic family members of HCV positive index cases is about 8.24%. and this agree with many studies; one was performed in Italy by **La Torre et al., (13)** that demonstrated prevalence of 8.9%, and an earlier study performed also in Italy by **Brusaferro et al., (14)** that demonstrated prevalence of 10.3%, but the earliest study was performed in Egypt by **Paez Jimenez et al., (15)** and showed a prevalence 4.3%, However the social level is not determined in these studies.

In our study it was found that mean age of HCV positive index patients was above 40 years (43.53±14.89).

In a previous study, similar results were obtained where anti HCV prevalence was much higher among individuals older than 20 years of age with the highest level (56.7%), in those over 40 years **(16).**

Prevalence of chronic HCV infection in Egypt is higher among men than women (12% and 8%, respectively), **(17)** and that agreeed with our study which found that in family members the prevalence in-between males was higher than females (52.78 and 47.22% respectively).

Alter., (19) found the prevalence of HCV among males is higher than among females (7.8 %, 6.9%), also the same is in the National survey (15.5%, 15.0%) for same age groups. These differences between both sexes of each study are slight and are of no statistical significance. The different rates of HCV among females and males in both studies may be due to the different proportions of the sexes in each study.

In our study prevalence of HCV positive is higher among family members residing in rural versus urban areas (69.44% versus 30.56%).

Community based studies for measuring the prevalence of HCV among Egyptians have been performed mostly involving rural inhabitants. One of these studies was carried on 1000 subjects More than half (57.1%) of farmers were positive **(7)**. The intrafamilial exposure was not a significant factor in HCV incidence as the prevalence of HCV positive subjects was 8.24% in those persons with positive family history. In other cohort study in Egypt, the strongest predictor of incident HCV infection was having an anti-HCV positive family member. Among those, the incidence was 5.8/1000 per year, compared with 1.0/1000 per year ($P < 0.01$) among those with no positive family members. The highest incidence rate (14.1/1000 PY) was in children younger than 10 years who were living in households with an anti-HCV–positive parent. The study did not determine the factors responsible for this association **(19).**

In similar study, it was found that, among subjects older than 20 years, the small group with at least some university education had a lower prevalence than the remaining subjects **(16).**

Regarding interspousal spread of HCV infection; it was (41.67%) of the HCV positive group. This result coincides with the study performed by **Boghdadi et**

al., (20) it was found the risk of sexual transmission between spouses was 18%., where 17.4% from wife to husband and 18.6% from husband to wife and Sexual intercourse numbers above 5 of husbands of index females is more risky to acquire HCV infection from their wives with a sensitivity of 76.1% and specificity of 71.2% and Husbands of HCV positive wives with sexual intercourse numbers more than 5 times per month is 12 times risky to acquire HCV infection than others. and with the result of study **Chang et al., (21),** which demonstrated a close pattern (28%). But many other studies demonstrated a lower prevalence of interspousal spread; **Plancoulaine et al., (22)** demonstrated a result of (19.8%), **Brusaferro et al., (14)** demonstrated a result of (15.4%), and **Tahan et al., (23)** demonstrated a result of only (2%).

It was found that HCV index cases having marital duration longer than 12.5 years were more risky to transmit HCV infection more than those married for shorter duration of < 12.5 years.

As regards spread from parents to offsprings; (30.56%) 11 siblings of HCV +ve index cases are HCV +ve. In the study done by **Plancoulaine et al., (22)**, the result was (11.6%), which is smaller than ours as we can't exclude the possibility of other sources of HCV acquisition as dental or surgical procedures.

Many other studies demonstrated a lower prevalence of this kind of spread; **Chang et al., (21)** demonstrated a result of (6.9%), **Brusaferro et al., (14)** demonstrated a result of (4.3%), and **Minola et al., (24)** demonstrated a result of (2.3%).

As regards the prevalence of spread between siblings; 10 HCV +ve cases (27.8%) were due to transmission among siblings. This result was similar to the study done by **Plancoulaine et al., (22)**, that demonstrated a similar result (20.1%), and the study done by **Akhtar et al., (25)**, that demonstrated a very close result of (19.8%).

As concerning using common bath towels, we found that 21 patients (58.33%) of the 36 HCV positive patients in our study shared bath towels, and 15 patients (41.67%) didn't.

In the study done by **Piao et al., (26)**, 46 HCV positive patients (23.0%) did share common bath towels, and the majority 154 (77.0%) didn't.

As concerning using common nail clippers, we found that 22 (61.11%) did share nail clippers, and 14 patients (38.89%) didn't.

In this particular concern the study done by **Piao et al., (26)** coincided with our study and demonstrated a similar result; 133 patients (66.5%) did share nail clippers, and 67 patients (33.5%) didn't.

As concerning using common shaving blades, we found that 20 (55.56%) did share shaving blades, and 16 patients (44.44%) didn't.

In the study done by **Piao et al., (26)**, 15 patients (7.5%) did share razors, and 185 (92.5%) didn't.

In our study 52.78 % of subjects who underwent surgical operations in a family with HCV +ve case have anti HCV positive results, and this is close to that was found by **Piao et al., (26)**, about 49 % was HCV +ve.

Regarding dental maneuvers, our study showed that dental procedures was a risk factor of HCV transmission as 55.56 % of the positive family members underwent dental maneuvers. This was in agreement with **Alam et al., (27)** who found that people sharing unsterile medical or dental equipment are at high risk of contracting HCV.

In our study, 80.56 % of HCV positive family members had previously treated by anti bilharzial treatment injection, which matches with the results by **Rao et al., (28)** which suggested that familial clustering of HCV is largely due to parenteral treatments for schistosomiasis experienced in common by a family.

This study showed that the multiple syringes exposure was a risk factor for HCV infection, as we found that 83.33% of HCV positive cases had history of multiple syringe exposure. According to data collected by the Egyptian Demographic Health Survey in 2008, 18.5% received one or more injections in the last six months **(17)**, which meets with our results.

Regarding obstetric history, our study showed that 60% of HCV +ve of female family members had previous labor, and 66.7% of them were at hospital, 44% were by CS. This results meet with thy study done by **Hillemanns et al., (29),** which showed that 42% of 31 anti-HCV positive patients had a cesarean section which was twice the rate of that in the HCV-negative group (p=0.004).

5. Conclusion:

Interfamilial contact is an important factor in the transmission of HCV. Transmission might occur during family contact, sexual behavior, and the shared use of personal items. A wide scale national study is needed to clarify this important entity.

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