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Epidemiological Aspects of Intrafamilial Spread of HCV Infection in Egyptian Population: A Pilot Study

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Abstract

Aim: Liver disease is a leading cause of morbidity and mortality among Egyptians. The major cause is infection with HCV, with 70 000 up to 140 000 newly reported cases annually. The objectives of this study were to determine the prevalence of anti-HCV antibodies among household contacts of HCV index cases and to identify the possible risk factors of transmission of HCV among Egyptian families. Material and Methods: The present external pilot study (double centre study) was performed on a convenient sample of 125 index cases and their 321 household family contacts recruited from Mansoura & Cairo University where 2 questionnaires were used to collect data from the index & their related contacts. The all were exposed to clinical examinations, routine laboratory testing & screening for the prevalence of Anti-HCV antibodies. Results: The prevalence of anti-HCV seropositivity among household contacts of index cases was found to be 13.7% which husbands of female index cases ranked first followed by wives of male index cases (36.36% versus 17.86% respectively, $P < 0.0001$) while sons & daughter followed later (6.84% & 4.94% respectively). When the distribution of household contacts by risky behaviour towards index cases was investigated, it was found that significant prevalence of anti-HCV antibodies positivity was detected between household contacts reporting their index cases having haematemsis &/or bleeding wound ($P < 0.05$), and household contacts giving IV injection to their index cases ($P < 0.05$) &

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household contacts visiting the same dentist as the index cases ($P < 0.01$) when compared to household contacts not exposed to the same risk factors. Conclusion: Transmission might occur during family contact and sexual behavior.

Keywords

HCV, Intrafamilial Transmission, Epidemiology

1. Introduction

Liver disease is a leading cause of morbidity and mortality among Egyptians. The major cause is infection with hepatitis C virus (HCV), with 70,000 up to 140,000 newly reported cases annually. Egypt has the highest prevalence of HCV worldwide. Prevalence of HCV was reported to be 13.9% among healthy populations and 78.5% among HCC cases. Adults have higher HCV prevalence (15.7%) than children (4.0%). Geographically, HCV prevailed more in the Nile delta (15.8%) than in Upper Egypt (9.02%) [1] [2].

The route of transmission of hepatitis C virus is still controversial and complicated. Transmission of blood or blood products leads to infection in the majority of cases. While the majority of intravenous drug users become infected by repetitive exposure to shared contaminated injection equipments. Needle-stick injuries in health-care settings represent another high risk category. HCV is less commonly transmitted through having sex with an infected person, being born to an HCV-infected mother, or sharing of personal items contaminated with infectious blood [3].

The household contacts of HCV seropositive patients had been shown to have an elevated risk of HCV infection [3] [4]. However, previous research has been inconclusive concerning the role of nonsexual household exposures entailing an increased risk of HCV transmission [5]. Significant clustering of HCV seropositivity among nonsexual contacts of HCV seropositive thalassemic patients had been reported [6].

2. Objectives

The objectives of this pilot study were 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 Egyptian families.

3. Methods

3.1. Patients Population

The study was performed on a convenient sample of 125 index cases and their 321 household family contacts recruited from different Egyptian governorates. The majority of index cases recruited (98 cases, 78.4%) were interviewed in Mansoura University Hospitals (inpatients and outpatients clinics of Tropical Medicine Department). The rest of index cases recruited (27 cases, 21.6%) were interviewed in Cairo University Hospitals (inpatients and outpatients clinics of Endemic Medicine Department. Pool areas for cases of Mansoura were restricted mostly to districts and villages of Dakahlia Governorate. Pool areas of Cairo cases encompassed almost all administrative governorates of Egypt (El-Giza, Helwan, El-Fayoum, Elmenya, Bani-Suef, El-Bahr-El-Ahmar, Kafr El-Sheikh, and El-Menoufeya).

3.2. Inclusion & Exclusion Criteria

Inclusion criteria included adult HCV positive cases and their close household contacts. Family members younger than 3 years old were excluded from the study

3.3. Study Design

All participants provided informed written consent. The research protocol was reviewed and approved by Medical Mansoura University Ethics Committee for Human Subject Research. Approval for this study was granted

by the research boards at the Mansoura University.

We obtained Institutional Ethical Review Committee approval and informed consent from the participating subjects. Seropositive HCV index cases & household contacts were asked to answer a questionnaire; Information collected included demographic data, awareness of modes of HCV transmission, degree of kinship of household contacts to index cases, and details of quotidian behavior towards index cases. HCV serostatus of each participant was determined by testing for anti-HCV antibodies (anti HCV Ab) using a commercial, enzyme-linked immunosorbent assay (ELISA) test from Abbott-Murex (Murex anti-HCV version 4.0). The Amplicor HCV RNA assay was used to detect HCV RNA in the index patient's serum and in the sera of corresponding HCV-seropositive household contacts in case the index patient was HCV RNA positive (Roche Diagnostic Systems, Indianapolis, IN).

4. Results

The prevalence of HCV seropositivity among household contacts of index cases was found to be 13.7%. No significant difference in prevalence was detected between males and females; and no gender predilection was found (**Table 1**). A statistically significant difference was found in prevalence of anti-HCV antibodies between different age groups with the age group ≥ 40 years showing the highest prevalence (44.45%) (**Table 2**).

When the relationship between HCV status and the degree of kinship to index cases were studied (**Table 3**), husbands of HCV seropositive female index cases ranked first followed by wives of male index cases (36.36% & 17.86% respectively, $P < 0.0001$) while sons & daughter followed later (6.84% & 4.94% respectively). However when the mean duration of marriage was calculated (**Table 4**), it was found that positive spouses had statistically significant longer duration of marriage than negative spouses ($P < 0.05$).

The study found high prevalence (16.98%) of chronic liver disease in index cases of anti-HCV positive household contacts (more than in their negative counterparts 12.02%, $P < 0.05$) (**Table 5**). On the other hand, (**Table 6**) shows that 92% of index cases participating were primary cases in their families. Clustering within families was observed in 10 HCV seropositive index cases (eight percent of a total of 125 primary cases).

When risky behaviour towards index cases was investigated (**Table 7**), it was found that a significant prevalence of anti-HCV antibodies positivity was detected between household contacts reporting their index cases to suffer an attack of haematemesis and/or a bleeding wound (20%) versus 10.45% in those whose index cases did not report history of bleeding ($P < 0.05$). A statistically-significant difference ($P < 0.05$) in the prevalence of anti-HCV positivity was also found between household contacts giving IV injection to their index cases (28%) compared to household contacts who did not report giving IV injection to their index cases (12.5%). Also a significant difference in prevalence of anti-HCV Ab positivity was detected between household contacts visiting the same dentist as the index cases compared to household contacts not visiting the same dentist as index cases ($P < 0.01$).

5. Discussion

Chronic infection with HCV presents a significant health problem worldwide with approximately 3% of the world population suffering from it, that is, more than 170 million people infected globally. Only 20% - 30% of

Table 1. Demographic data of participant household contact (n = 321).

	Index cases (n = 125) N (%)	**Household contacts (n = 321) N (%)**	**Total group (n = 446) N (%)**
University of recruitment			
Mansoura University	98 (78.4%)	217 (67.6%)	315 (70.6%)
Cairo University	27 (21.6%)	104 (32.4%)	131 (29.4%)
Total	125 (100%)	321 (100%)	446 (100%)
Gender Group	**Negative HCV cases**	**Positive HCV cases**	**Total**
Male	135 (84.37%)	25 (15.63%)	160 (100.0%)
Female	142 (88.2)	19 (11.8)	161 (100)
Total	277 (86.3)	44 (13.7)	321 (100)
Pearson Chi-Square	56.06	2	**<0.0001**

Table 2. Distribution of Anti-HCV among participant household contact according to the age.

Age Group	**Negative HCV cases**	**Positive HCV cases**	**Total**
≤19 Yrs	150 (96.16%)	6 (3.84%)	156 (100%)
20 - 39 Yrs	97 (87.39%)	14 (17.61%)	111 (100%)
≥40 Yrs	30 (55.55%)	24 (44.45%)	54 (100%)
Total	277 (86.3%)	44 (13.7%)	321 (100.0%)
Pearson Chi-Square	56.06	2	**<0.0001**

Table 3. Distribution of Anti-HCV among participant household contacts by degree of kinship to index cases (n = 321).

Degree of kinship to Index case	**Negative HCV cases**	**Positive HCV cases**	**Total**
Husband	14 (63.64%)	**8 (36.36%)**	22 (100%)
Wife	46 (82.14%)	**10 (17.86%)**	56 (100%)
Son	109 (93.16%)	**8 (6.84%)**	117 (100%)
Daughter	77 (95.06%)	**4 (4.94%)**	81 (100%)
Test of significance: Chi-square (*P*-value)	**22.49 (*P* < 0.0001)**		
Father	1 (50%)	1 (50%)	2 (100%)
Mother	3 (60%)	2 (40%)	5 (100%)
Brother	6 (54.55)	5 (45.45%)	11 (100%)
Sister	3 (60%)	2 (40%)	5 (100%)
Uncle	1 (100%)	0 (0.0%)	1 (100%)
Cousin	3 (60%)	2 (40%)	5 (100%)
Grand parents	2 (100%)	0 (0.0%)	2 (100%)
Other	11 (84.62%)	2 (15.38%)	13 (100%)
Total	277 (86.29%)	44 (13.71%)	321 (100.0%)

Table 4. Mean duration of marriage in household contacts husbands and wives (spouses) by anti-HCV status.

	Negative HCV cases	**Positive HCV cases**	T test (*P* value)
Mean duration of marriage in Years (SD)	18.83 ± 10.16	25.2 ± 9.85	**1.98 (<0.05)**

Table 5. Distribution of household contacts by presence of chronic liver disease (CLD) in index cases.

Chronic Liver Disease in Index Cases	**Anti-HCV negative household contacts (n = 277)**	**Anti-HCV positive household contacts (n = 44)**	**Total**
Absent	227 (87.98%)	31 (12.02%)	258 (100.0%)
Present	44 (83.01%)	9 (16.98%)	53 (100.0%)
Don't know	6 (60%)	4 (40%)	10 (100.0%)
Total	277 (86.3%)	44 (13.7%)	321 (100.0%)
Chi-square (Sig)	6.94 **(*P* < 0.05)**		

Table 6. Demographic data of index cases (125 cases).

Ranking of index cases among diagnosed cases in their families		
Primary case in his family	115	92%
Secondary case in his family	7	5.6%
Tertiary case in his family	3	2.4%
Total	125	100%
Antiviral treatment intake by primary cases		
Not started antiviral treatment	97	77.6%
On antiviral treatment now	16	12.8%
Stopped antiviral treatment	12	9.6%
Total	125	100.0%

HCV-infected individuals recover spontaneously [7].

Egypt has the highest prevalence of adult HCV infection in the world averaging 15% - 25% in rural communities [8] [9]. The number of Egyptians estimated to be chronically infected was 9.8%. The households' contacts of hepatitis C virus (HCV) seropositive patients have been shown to have an elevated risk of HCV infection [3] [10].

This pilot study gave an estimate of 13.7% (44/32) of HCV seroprevalence among household contacts of HCV seropositive index cases, which approximates the findings of EDHS [9] and other studies reporting that HCV seroprevalence is 16% and 20% among contacts of HCV-seropositive index patients [3] [10]. This may be translated into persistence of high risk of HCV transmission.

Many studies [11]-[15] suggested that the risk of sexual transmission of HCV should not be underestimated. Sexual transmission of viral diseases mediated by sexual secretions suggests a greater potential of male-to-female transmission. Bourlet *et al*. [16] reported that the seminal plasma of 4 of 32 (12.5%) subjects chronically infected with HCV was found to be positive for HCV RNA by the RT-PCR technique. Certainly, trauma to the mucosa as well as the high viremia levels during sexual intercourse increases the risk of viral transmission. Some studies stated that male-to-female transmission seems to be more common than female-to-male transmission [15] [17] [18]. On the contrary, other studies observed that the risk of sexually-acquiring HCV infection was extremely low [19]-[20]. In our study, husbands of HCV seropositive female index cases ranked first followed by wives of male index cases. It was stated that men married to anti-HCV-positive women had a higher incidence of HCV than men with an HCV negative wives [21]. Shedding of HCV RNA in the female genital tract is associated with the presence of blood (menstruation) [22].

In the present study, the prevalence of anti-HCV Ab positivity among wives was 17.8% (10/56), while the prevalence of anti-HCV Ab positivity among husbands was 36.4% (8/22); Anti-HCV positive spouses had longer duration of marriage than negative spouses (**Table 3** and **Table 4**). Many studies reported that the longer the duration of marriage, the higher the risk of HCV infection. The risk of HCV infection for the spouse was found to be increased after 15 years [23] [24]. Marriage did not only include a sexual relationship, but also other kinds of body contact and exposure to the same risk factors (*i.e*. sharing the same personal tools, exposure to blood of the index case by any means [25]. On the contrary, Terrault *et al*. [26] estimated the quantifiable risk for HCV infection among monogamous heterosexual couples, to be extremely low.

The present study showed high prevalence rates among offspring (6.8% for sons (8/117) and 4.94% for daughters (4/81)) of HCV seropositive patients. Similarly, studies from Japan revealed high prevalence rates among offspring of chronic HCV patients: 20.9% (14/67) in the study by Nishiguchi *et al*. [27]; 5.7% (three of 53) in the report of Nakashima *et al*. [28]; 16.9% (23/136) in the study by Hayashi *et al*. [29]; and 23.6% (13/55) in the study by Noguchi *et al*. [30]. In contrast, another three studies, two from Italy and one from Korea, presented low prevalence rates: 2.3% (one of 44) in the report of Napoli *et al*. [31]. 2.3% (three of 128) in the study of Demelia *et al*. [32] and 0% (none of 85) in the study of Kim *et al*. [33].

Mohamed *et al*. [34] suggested a person-to-person HCV transmission within families. This explanation was further supported by the fact that the genetic sequence of the 18 children matched the sequence of a virus found

Table 7. Distribution of household contacts by risky behavior towards index cases.

Risky Behavior (Yes-No)	Index cases (n = 125)	Positive Household Contacts/ All Household Contacts.		Z-test (Sig.)
		n/N	%	
Helped Index case during an attack of haematemesis or a bleeding wound				
(Yes)	29	22/110	**20**	2.2 ($P < 0.05$)
NO	96	22/211	**10.4**	
Helped primary case during other bleeding episodes				
(Yes)	10	8/55	**14.55**	−0.02 ($P > 0.05$)
NO	115	36/266	**13.53**	
Precautions taken against transmission				
(No)	96	42/303	**13.8**	−0.02 ($P > 0.05$)
YES	29	2/18	**11.1**	
Have been soiled with blood during help of primary case				
(Yes)	6	4/23	**17.39**	0.22 ($P > 0.05$)
NO	119	40/298	**13.42**	
Change of soiled clothes and hand hygiene				
(No)	122	42/302	**13.9**	0.07 ($P > 0.05$)
YES	3	2/19	**10.53**	
Give index case Intravenous Injection				
(Yes)	8	7/25	**28**	1.86 ($P < 0.05$)
NO	117	37/296	**12.5**	
Accompanied index patient during hospital-stay				
(Yes)	9	6/25	**24**	1.26, $P > 0.05$
NO	116	38/296	**12.81**	
Use of thee same shaving razors and scissors as index case				
(Yes)	50	14/67	**20.9**	1.72, $P > 0.05$
NO	75	30/254	**11.8**	
Use o the f same tooth brushes as primary case				
(Yes)	10	2/17	**11.7**	−0.12, $P > 0.05$
NO	115	42/304	**13.82**	
Visit same dentists as primary case				
(Yes)	50	18/76	**23.68**	2.70, $P < 0.01$
NO	75	26/245	**10.61**	

in one of their parents. Test of significance calculated for percentage distribution of anti-HCV positivity among husbands, wives, sons, and daughters proved to be highly significant.

The prevalence of anti-HCV Ab positivity was significantly high in subjects aged ≥40 years old (44.45%). Similarly, other studies found that anti-HCV Ab positivity increased with the length of the household contact re-

lationship [25] [26] [35]. Arafa *et al*. [36] stated that the prevalence of HCV antibodies in rural area of Egypt increased from 2.7% in those <20 years of age to more than 40% in males whose age ranged from 40 - 54 years.

The rate of HCV transmission among households ranged from 0% to 11% [17] [19] [21] [37]-[39]. Interestingly, in the present study, anti-HCV positive household contacts adopted more risky behaviors than anti-HCV negative household contacts. It was found that having an index case with history of haematemesis &/or other bleeding episodes, giving IV injections to the index case, and visiting the same dentist as index case were statistically considered as risk factors for household contacts to acquire HCV infection. This could lead us to consider that habits constructing the profile of family household contact behaviour were confounding factors for intra-familial HCV transmission. In addition to family contact and sexual behaviour, the shared use of personal items such as razor blades, toothbrushes, nail clippers and manicure cutters might be important factors for the intra-familial transmission of HCV [12] [19]. This opinion did not agree with a Brazilian study, where the authors concluded that the risk of transmission of HCV did not increase with long periods of living together, sexual activity and sharing of personal items [38]. Comparison between sex partners and other family members residing with the same household, having an HCV carrier as a reference, showed that intrafamilial contact is an important factor in the transmission of HCV. Cultural habits differ from one population to another and can interfere in the results of epidemiological studies that involve HCV transmission.

Research on the role of the familial environment in the spread of HCV had been inconclusive up till now [40]. Reportedly, intrafamilial nonsexual HCV transmission is uncommon and related to the length of exposure and the stage of HCV infection in the index subjects [10] [25], whereas other researchers demonstrated a relatively high incidence of intrafamilial HCV transmission [39]. Transmission might also occur during a common background environmental exposure from outside the household [41]-[43]. In the current study, 16.98% of anti-HCV positive household contacts reported having their index cases suffering from chronic liver disease compared to 12.02% of anti-HCV positive household contacts having their index cases not suffering from CLD.

6. Conclusion

In 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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