Prevalence of HCV Infection in Household Contacts of Chronic Liver Diseases Cases in Egypt

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Background. Egypt has the highest prevalence of HCV infection worldwide. This project aimed at identifying the role of HCV transmission among household contacts to index cases in the persistent high incidence of HCV infection in Egypt. Methods. This cross-sectional study recruited 70 Egyptian cases with chronic liver diseases and their household contacts (140 contacts) from Qalubeyia Governorate. An interview questionnaire was used to collect information on sociodemographic characteristics and risk factors to HCV infection. HCV-RNA was tested using real-time polymerase chain reaction (PCR). Univariate and multivariate analyses were carried out to estimate the risk of HCV infection among contacts. Results. HCV viremia was detected in 85.7% of cases and 20% of contacts. HCV-RNA was detected in higher proportion of household contacts to cases than the general population. Contacts to HCV-positive cases were unlikely exposed to used syringe ($P < 0.02$) and unlikely to have history of Bilharziasis ($P < 0.001$) compared to contacts to HCV-negative cases. HCV-positive contacts were more likely older ($P < 0.001$) and married ($P = 0.008$) and had higher crowding index ($P = 0.04$) than HCV-negative contacts. Also, HCV-positive contacts were more likely exposed to blood transfusion ($P = 0.008$) and shaving at community barber ($P = 0.04$) and had history of Bilharziasis ($P = 0.01$). The strongest predictors for HCV infection among contacts were old age (OR, 95% CI: 1.08 to 1.15; $P < 0.01$) and blood transfusion (8.08, 1.75 to 37.3; $P = 0.007$). Conclusion. Nonetheless, household contacts to HCV cases are exposed to increased risk of HCV infection, and environmental exposure particularly blood transfusion remained a major source of HCV infection.

1. Introduction

In 2008, the Egyptian Demographic Health Survey reported that the prevalence of hepatitis C virus (HCV) infection was 14.7%, which was the highest prevalence of HCV in the world. [1] In 2013, the prevalence of HCV viremia was 7.3% due to the high mortality among old people with high prevalence of infection. [2] While in 2015, the prevalence of active HCV-infected cases was 4.4 [3].

A new era in the elimination of viral hepatitis has launched in 2015 when the United Nations General Assembly adopted the 2030 Agenda for Sustainable Development, which called on the international community to combat hepatitis. Viral hepatitis is a major public health challenge worldwide. The World Health Organization Eastern Mediterranean Region and the European Region have the highest reported prevalence of HCV particularly in the low- and middle-income countries. Globally, in 2015, the disease caused 1.34 million deaths. Each year, 1.75 million people newly acquire hepatitis C virus infection. These people are at risk of a slow progression to severe liver disease such as cirrhosis, hepatic decompensation, and hepatocellular carcinoma and death, unless they receive timely testing and treatment. [4].

Unsafe blood contact is the main source of HCV infection [5]. In Egypt, the main routes of HCV transmission have included the mass parenteral antischistosomal treatment from the 1950s to the 1980s, shared and reused needles, inadequate sterilization during dialysis, surgery, and dental care, and unsafe blood transfusion. Unsafe healthcare-related injections have been the major route of HCV transmission [6, 7]. Although the provision of safe injection practices was associated with reduced occurrence of HCV infection [8], the global incidence rate remained high (23.7 per 100,000) [4].

In Egypt, the prevalence of HCV infection is very high, and direct healthcare costs for hepatitis already consume 4% of the total health expenditure. Moreover, the indirect costs...
represent twice the direct costs. HCV treatment is highly cost-effective. That treating 328,000 HCV-infected patients annually by 2018 with the direct-acting antivirals (DAAs) could reduce the prevalence of infection by 94% and liver-related deaths by 75% by 2030 [9].

In Egypt, hepatitis C is just a problem in every family. The high prevalence of HCV infection and the clustering effect observed between HCV infections in households were linked to parenteral treatment for schistosomiasis [10]. However, the high incidence rate remained a pressing challenge to the already overstretched Egyptian healthcare system. Intrafamilial transmission has been accused for this high incidence. There are two patterns of intrafamilial transmission: horizontal transmission between patients infected with HCV and their household contacts sharing the same residential space due to shared behaviours and living conditions, and vertical transmission through the perinatal route. The perinatal transmission was found to have a minimal role [11, 12].

This project aimed to identify the role of intrafamilial transmission (transmission in relatives living in the same household) in the persistent high incidence of HCV infection in Egypt.

2. Subject and Methods

This cross-sectional study was conducted on cases with chronic liver diseases who were referred to the Molecular Biology Unit at Benha Faculty of Medicine, Qalubeya Governorate, Egypt, to test for HCV infection and their household contacts of both sexes and any age who were living in the same household with a case for at least one year were the candidates for the study.

1.2. Inclusion Criteria. Cases with chronic liver diseases and aged ≥18 years old (to increase the likelihood of HCV infection) and their household contacts of both sexes and any age who were living in the same household with a case for at least one year were the candidates for the study.

1.3. Data Collection Tools. An interview questionnaire, which was reviewed and approved in previous studies [13–15], was used to collect information on personal data, socioeconomic characteristics, present and past health, and risk factors for exposure to HCV infection including history of surgical operations, dental procedures, blood transfusion, schistosomiasis treatment, contaminated needles or puncture, prior hospitalization, shared use of toothbrushes or shaving razors, common tools for nail trimming, circumcision, condom use, drug abuse, smoking, wet cupping (vigama), tattooing, and multiple sexual partners.

At the same visit, venous blood samples were collected to test for HCV-RNA using the quantitative real-time polymerase chain reaction (PCR). Extractation of viral RNA by the QIAamp Viral RNA mini kit was carried out using the QIAcube automatic extractor (QIAGEN GmbH). Amplification by TaqMan PCR master mix artus HCV RG RT-PCR kit (QIAGEN GmbH) was performed using the real-time PCR machine (Applied Biosystems StepOne Real-Time PCR System, San Diego, Ca, USA).

A pilot study was undertaken on 10 subjects (including equal numbers of males and females), and their questionnaires were not included in the study. Testing of the questionnaire was useful in estimating the time taken to answer the questions and understanding of the questions. This helped to reduce limitations of understanding as well as nonresponse to questions.

1.4. Statistical Analysis. Mean ± standard deviation (SD) and range were used to describe quantitative data, and frequency and percentage were used to describe qualitative data. Comparisons between the different study groups were carried out using the chi-square test and the Fisher exact test to compare proportions as appropriate. The Student t-test was used to measure the mean difference between two groups regarding parametric data. Multiple logistic regression analysis for HCV-positive contacts conditioned on being a contact of an HCV case and other potential risk factors was carried out. The risk of HCV infection was presented as odds ratio (OR) and 95% confidence interval (CI). Statistical significance was accepted at P < 0.05. All statistical analyses were conducted using STATA/SE version 11.2 for Windows (STATA corporation, College Station, Texas).

3. Results

Study participants comprised 70 cases with chronic liver diseases, their ages ranged between 19 and 78 years with a mean of 49.5 ± 11.7 years, and males constituted 60% of them. HCV-RNA was detected in 60 cases (85.7%). Household contacts comprised 140 cases, their ages ranged between 3 and 75 years with a mean of 33.28 ± 16.75 years, and males constituted 40.71% of them. HCV-RNA was detected in 28 households (20%). Detailed description of the characteristics of studied cases and their households and exposure to risk factors for HCV infection are shown in Table 1.

Figure 1 shows the results of real-time PCR, and 6 out of 16 household contacts to HCV-negative cases (37.5%) had...
| Variable                        | Cases (number = 70) | Household contacts (number = 140) | Variable                        | Cases (number = 70) | Household contacts (number = 140) |
|--------------------------------|---------------------|----------------------------------|--------------------------------|---------------------|----------------------------------|
|                                | Number | %       | Number | %       | Number | %       | Number | %       | Number | %       | Number | %       |
| Sex                            | Females | 28 | 40.0 | 83 | 59.29 | History of blood transfusion | No | 59 | 84.29 | 127 | 90.71 |
|                                | Males   | 42 | 60.0 | 57 | 40.71 | Yes | 11 | 15.71 | 13 | 9.29 |
| Age (years)                    | Mean ± SD (range) (years) | 49.51 ± 11.71 (19–78) | 33.28 ± 16.75 (3–75) | Priorsr surgical procedures | No | 2 | 2.86 | 16 | 11.43 |
|                                | Housewife | 8 | 11.43 | 39 | 27.86 | Yes | 68 | 97.14 | 124 | 88.57 |
|                                | Specialist | 44 | 62.86 | 45 | 32.14 | No | 40 | 57.14 | 98 | 70.0 |
|                                | Medical/paramedical | 6 | 8.57 | 5 | 3.57 | Yes | 30 | 42.86 | 42 | 30.0 |
| Occupation                     | Student | 2 | 2.86 | 43 | 30.71 | Prior hospitalization | By medical personnel | 6 | 8.57 | 27 | 19.29 |
|                                | Worker | 10 | 14.29 | 8 | 5.71 | By nonmedical personnel | 63 | 90.0 | 89 | 63.57 |
|                                | Illiterate | 1 | 1.43 | 7 | 5.0 | No | 1 | 1.43 | 24 | 17.14 |
|                                | Read and write | 31 | 44.29 | 89 | 63.57 | No | 68 | 97.14 | 138 | 98.57 |
| Educational level              | Basic education | 8 | 11.43 | 20 | 14.29 | Yes | 2 | 2.86 | 2 | 1.43 |
|                                | Secondary school | 5 | 7.14 | 11 | 7.86 | Shaving at community | No | 7 | 10.00 | 59 | 42.14 |
|                                | High education | 25 | 35.71 | 13 | 9.29 | barber (males only) | Yes | 63 | 90.00 | 81 | 57.86 |
|                                | Single | 4 | 5.71 | 50 | 35.71 | Nail trimming | Private tool | 22 | 31.43 | 27 | 19.28 |
| Marital status                 | Married | 65 | 92.86 | 90 | 64.29 | Smoking Shisha | No | 60 | 85.71 | 134 | 95.71 |
|                                | Widow | 1 | 1.43 | 0 | 0.0 | Yes | 10 | 14.29 | 6 | 4.29 |
| Residence                      | Rural | 60 | 85.71 | 118 | 84.29 | Sharing razors | No | 24 | 34.29 | 60 | 42.86 |
|                                | Partners | 10 | 14.29 | 22 | 15.71 | Yes | 46 | 65.71 | 80 | 57.14 |
|                                | Parents | 37 | 26.43 | — | — | Exposed to used syringe** | Yes | 46 | 65.71 | 94 | 67.14 |
| Relation to cases              | Sons | — | — | 72 | 51.43 | Yes | 60 | 85.71 | 122 | 87.14 |
|                                | Siblings | — | — | 13 | 9.29 | Exposed to used toothbrush | Yes | 10 | 14.29 | 18 | 12.86 |
|                                | Others | — | — | 9 | 6.43 | Practice of tattooing | No | 56 | 80.0 | 126 | 90.0 |
| Crowding index (persons/room) | Mean ± SD (range) | 1.16 ± 0.66 (0.3–3) | | Practice of tattooing | Yes | 14 | 20.0 | 14 | 10.0 |
| HCV-RNA                        | Negative | 10 | 14.29 | 112 | 80.0 | Exposed to blood | No | 54 | 77.14 | 114 | 81.43 |
|                                | Positive | 23 | 32.86 | 12 | 8.57 | Yes | 16 | 22.86 | 26 | 18.57 |
|                                | UD | 37 | 52.86 | 16 | 11.43 | Exposed to blood | No | 54 | 77.14 | 128 | 91.43 |
|                                | Diarrhea | 15 | 21.43 | — | — | History of Bilharziasis | Yes | 16 | 22.86 | 12 | 8.57 |
|                                | Abdominal pain | 35 | 50.0 | — | — | No | 54 | 77.14 | 132 | 94.29 |
| Symptoms*                      | Easy fatigue | 30 | 42.86 | — | — | History of injection | Yes | 16 | 22.86 | 8 | 5.71 |
|                                | Yellow sclera | 9 | 12.86 | — | — | Yes | 16 | 22.86 | 8 | 5.71 |
|                                | Dark urine | 9 | 12.86 | — | — | Yes | 16 | 22.86 | 8 | 5.71 |

UD: undetermined; below detection level in patients who were under treatment for HCV; * more than one symptom was allowed; ** this included IV, IM, and needle stick injury.
The results of the study revealed that HCV infection remained the main cause of chronic liver diseases with a prevalence rate of 85.7% among cases, while the overall prevalence of HCV in the household contacts of both cases and controls was 20%.

Of the household contacts of HCV-infected patients, 22 out of the 124 contacts were HCV viremic (17.7%), compared to 6 out of the 16 contacts of HCV-negative cases (37.5%). The prevalence in both groups of contacts is much higher than the prevalence in the general population, which in similar age groups is in the range of 4%-5% viremic prevalence [3, 16]. This might suggest an increased risk of HCV infection among contacts to HCV-infected cases who serve as reservoirs of infection to their household contacts. This was also suggested by previous studies in Egypt [17, 18]. A prospective cohort of 6,734 anti-HCV-negative rural Egyptians detected 33 seroconversions. The strongest predictor for seroconversions was having anti-HCV-positive family member [17]. A comparative study of Egyptian families which included 90 families with index HCV-positive case (257 contacts) and 38 families with no index case (75 contacts) reported that 32 out of the 90 families with index cases had one or more HCV-positive contacts (38/257; 14.8%), while only two families with no index cases had HCV-positive contacts (3/75; 4%). Hence, intrafamilial transmission was thought to be a major underlying factor to the high prevalence of HCV infection in Egypt [18].

Regarding viremic contacts of HCV-negative cases, the six contacts had past history of hospitalization, surgical procedures, and exposure to used syringe and were circumcised by nonmedical personnel, and three of them had past history of injection treatment for Bilharziasis (unpresented data). These increased the proportion of viremic contacts of HCV-negative cases.

4.2. HCV-Positive Household Contacts Were More Likely in Sexual Partners and Siblings. In the present study, HCV-positive household contacts were more likely in sexual partners and siblings. HCV positivity was more frequent in older, married contacts with higher crowding index. This corresponds to findings reported by concurrent studies in Egypt, which linked the familial transmission of HCV with advanced age (≥40) and sexual partners [18, 19]. Correspondingly, a cross-sectional study of 175 Italian HCV-positive patients and their family members found that HCV-positive family members accounted for 8.9% (23/259) with the highest prevalence in sexual partners (12.1%). The prevalence of anti-HCV was more likely in older family contacts [20]. Again in Italy over the period from 1975 to 2003, a total number of 2856 of HCV-infected index cases were invited with their family members (number =13,440) to take part in a study to investigate risk factors for HCV transmission. The overall prevalence of HCV infection in family members was 2.1%, with the highest prevalence in sexual partners (13.8%) followed by offspring (2.3%) and parents and siblings (2.1%) [21].

However, there were no significant differences in the prevalence of HCV infection between contacts to
| Variable | Household contacts to HCV-positive/UD cases (number = 124) | Household contacts to HCV-negative cases (number = 16) | OR (95% CI) | Variable | Household contacts to HCV-positive/UD cases (number = 124) | Household contacts to HCV-negative cases (number = 16) | OR (95% CI) |
|----------|------------------------------------------------------|------------------------------------------------------|-------------|----------|------------------------------------------------------|------------------------------------------------------|-------------|
| Sex      | Females 51 41.13 6 37.5 0.86 (0.24–2.81) | Males 73 58.87 10 62.50 0.86 (0.24–2.81) | Condom use No 122 98.39 16 100.0 — | Sex      | Females 51 41.13 6 37.5 0.86 (0.24–2.81) | Males 73 58.87 10 62.50 0.86 (0.24–2.81) | Condom use No 122 98.39 16 100.0 — |
| Age (years) | Mean ± SD (range) 32.89 ± 16.74 (3–75) | Mean ± SD (range) 36.25 ± 17.07 (12–62) | P = 0.45a | Shaving at community barber (males only) No 51 41.13 8 50.0 1.43 (0.43–4.68) | Shaving at community barber (males only) No 51 41.13 8 50.0 1.43 (0.43–4.68) | Shaving at community barber (males only) No 51 41.13 8 50.0 1.43 (0.43–4.68) |
| Occupation | Medical/paramedical 4 3.23 1 6.25 0.33 (0.02–21.82) | Medical/paramedical 4 3.23 1 6.25 0.33 (0.02–21.82) | Circumcision No 23 18.55 1 6.25 5.23 (0.51–257.73) | Occupation | Medical/paramedical 4 3.23 1 6.25 0.33 (0.02–21.82) | Medical/paramedical 4 3.23 1 6.25 0.33 (0.02–21.82) | Circumcision No 23 18.55 1 6.25 5.23 (0.51–257.73) |
| Educational level | Basic/secondary education 30 24.19 1 6.25 4.70 (0.65–206.20) | Basic/secondary education 30 24.19 1 6.25 4.70 (0.65–206.20) | Nail trimming No 106 85.48 14 87.50 1.04 (0.20–10.24) | Educational level | Basic/secondary education 30 24.19 1 6.25 4.70 (0.65–206.20) | Basic/secondary education 30 24.19 1 6.25 4.70 (0.65–206.20) | Nail trimming No 106 85.48 14 87.50 1.04 (0.20–10.24) |
| Marital status | Unmarried 45 36.29 5 31.25 0.80 | Married 79 63.71 11 68.75 0.80 | Smoking shisha No 119 95.97 15 93.75 0.63 (0.06–31.77) | Marital status | Unmarried 45 36.29 5 31.25 0.80 | Married 79 63.71 11 68.75 0.80 | Smoking shisha No 119 95.97 15 93.75 0.63 (0.06–31.77) |
| Residence | Rural 103 83.06 15 93.75 3.06 | Rural 103 83.06 15 93.75 3.06 | Sharing razors Yes 52 41.94 8 50.0 1.38 (0.42–4.53) | Residence | Rural 103 83.06 15 93.75 3.06 | Rural 103 83.06 15 93.75 3.06 | Sharing razors Yes 52 41.94 8 50.0 1.38 (0.42–4.53) |
| Relation to cases | Sons 66 53.23 6 37.50 0.57 (0–5.17) | Sons 66 53.23 6 37.50 0.57 (0–5.17) | Exposed to used toothbrush No 106 85.48 14 87.50 1.04 (0.20–10.24) | Relation to cases | Sons 66 53.23 6 37.50 0.57 (0–5.17) | Sons 66 53.23 6 37.50 0.57 (0–5.17) | Exposed to used toothbrush No 106 85.48 14 87.50 1.04 (0.20–10.24) |
| Crowding index (person/room) | Mean ± SD (range) 1.15 ± 0.7 (0.28–3) | Mean ± SD (range) 1.1 ± 0.5 (0.6–1.67) | Practice of tattooing Yes 16 12.90 2 12.50 1.04 (0.20–10.24) | Crowding index (person/room) | Mean ± SD (range) 1.15 ± 0.7 (0.28–3) | Mean ± SD (range) 1.1 ± 0.5 (0.6–1.67) | Practice of tattooing Yes 16 12.90 2 12.50 1.04 (0.20–10.24) |
| History of blood transfusion | No 111 89.52 16 100.0 — | Yes 13 10.48 0 0.0 — | Exposed to blood No 102 82.26 12 75.00 0.65 (0.17–3.02 A) | History of blood transfusion | No 111 89.52 16 100.0 — | Yes 13 10.48 0 0.0 — | Exposed to blood No 102 82.26 12 75.00 0.65 (0.17–3.02 A) |
| Prior surgical procedures | No 15 12.10 1 6.25 0.48 | Yes 109 87.90 15 93.75 0.48 | History of Bilharziasis No 118 95.16 10 62.50 0.08 (0.02–0.39) | Prior surgical procedures | No 15 12.10 1 6.25 0.48 | Yes 109 87.90 15 93.75 0.48 | History of Bilharziasis No 118 95.16 10 62.50 0.08 (0.02–0.39) |
| Prior hospitalization | No 86 69.35 12 75.00 1.32 | Yes 38 30.65 4 25.00 1.32 (0.37–5.99) | History of injection treatment for Bilharziasis No 117 94.35 15 93.75 0.90 (0.10–43.10) | Prior hospitalization | No 86 69.35 12 75.00 1.32 | Yes 38 30.65 4 25.00 1.32 (0.37–5.99) | History of injection treatment for Bilharziasis No 117 94.35 15 93.75 0.90 (0.10–43.10) |

UD: undetermined; below detection level in patients who were under treatment for HCV; *Student t-test; P: probability; OR (95% CI): odds ratio (95% confidence interval); *P < 0.05; **P < 0.01.
| Variable                      | HCV-positive/UD (number = 28) | HCV-negative (number = 112) | OR (95% CI) | Variable                      | HCV-positive/UD (number = 28) | HCV-negative (number = 112) | OR (95% CI) |
|-------------------------------|-------------------------------|----------------------------|-------------|-------------------------------|-------------------------------|----------------------------|-------------|
|                               | Number | %       | Number | %       |                              | Number | %       | Number | %       |                              | Number | %       | Number | %       |                              |
| **Sex**                       |        |         |        |         |                              |        |         |        |         |                              |        |         |        |         |                              |
| Females                       | 14     | 50.0    | 69     | 61.6    | 1.60 (0.64–4.01) | No     | 28     | 100.0 | 110     | 98.21 | 0 (0–7.84) |                              |
| Males                         | 14     | 50.0    | 43     | 38.3    | 1.00                          | Yes    | 0      | 0      | 2       | 1.79  |                           |
| **Age (years)**               |        |         |        |         |                              |        |         |        |         |                              |        |         |        |         |                              |
| Mean ± SD (range)             | 47.96± 13.87 (16–75) | 29.58± 15.36 (3–65) | **P < 0.001** | No | 7 | 25.00 | 52 | 46.43 | 2.6 | *(0.96–7.79)* |                              |
| House wife                    | 7      | 25.0    | 32     | 28.57   | 2.52 (0.83–8.25) | Yes    | 21     | 75.0  | 60     | 53.57 |                           |
| Specialist                    | 16     | 57.14   | 29     | 25.89   | 1.14 (0.02–14.19) | No     | 4      | 14.29 | 23     | 20.54 | 1.00                        |
| **Occupation**                |        |         |        |         |                              |        |         |        |         |                              |        |         |        |         |                              |
| Medical/paramedical           | 1      | 3.57    | 4      | 3.57    | 0.11 (0.002–0.94)* | No     | 2      | 7.14  | 22     | 19.64 | 0.52 (0.04–1.13) |                              |
| **Educational level**         |        |         |        |         |                              |        |         |        |         |                              |        |         |        |         |                              |
| Illiterate/read and write     | 19     | 67.86   | 77     | 68.75   | 1.00                          | Private tool | 4      | 14.29 | 22     | 19.64 | 1.47 (0.44–6.39) |                              |
| Basic/secondary education     | 6      | 21.43   | 25     | 22.32   | 0.97 (0.28–2.91) |        |        |        |        |                              |        |         |        |         |                              |
| High education                | 3      | 10.71   | 10     | 8.93    | 1.21 (0.19–5.36) |        |        |        |        |                              |        |         |        |         |                              |
| Unmarried                     | 4      | 14.29   | 46     | 41.07   | 4.18 (1.30–17.54)** |        |        |        |        |                              |        |         |        |         |                              |
| Married                       | 24     | 85.71   | 66     | 58.93   | 1.64                          |        |        |        |        |                              |        |         |        |         |                              |
| Urban                         | 22     | 78.57   | 96     | 85.71   | 1.00                          |        |        |        |        |                              |        |         |        |         |                              |
| Rural                         | 6      | 21.43   | 16     | 14.29   | 0.47 (0.07–0.50) |        |        |        |        |                              |        |         |        |         |                              |
| Partners                      | 9      | 32.14   | 28     | 25.00   | 1.00                          |        |        |        |        |                              |        |         |        |         |                              |
| Parents                       | 6      | 21.43   | 3      | 2.68    | 6.22 (1.02–44.40)* |        |        |        |        |                              |        |         |        |         |                              |
| **Relation to cases**         |        |         |        |         |                              |        |         |        |         |                              |        |         |        |         |                              |
| Sons                          | 3      | 10.71   | 69     | 61.61   | 0.13 (0.02–6.00)** |        |        |        |        |                              |        |         |        |         |                              |
| Siblings                      | 9      | 32.14   | 4      | 3.57    | 7.00 (1.45–37.43)** |        |        |        |        |                              |        |         |        |         |                              |
| Others                        | 1      | 3.57    | 8      | 7.14    | 0.39 (0.01–3.72) |        |        |        |        |                              |        |         |        |         |                              |
| **Crowding index (person/room)** | 1.9± 0.6 | 1.67± 0.5 | **P = 0.04** | Practice of tattooing | No | 27 | 96.43 | 107 | 95.54 | 0.79 |                           |
| History of blood transfusion  | 21     | 75.0    | 106    | 94.64   | 5.89                          | Exposed to blood | No | 19 | 67.86 | 97 | 86.61 | 3.06 (1.01–8.75)* |
| Prior surgical procedures     | 7      | 25.0    | 6      | 5.36    | 1.09                          | Exposed to blood | No | 9 | 32.14 | 15 | 13.39 |                           |
| Prior hospitalization         | 3      | 10.71   | 13     | 11.61   | Yes | 22 | 78.57 | 106 | 94.64 | 4.82 (1.15–19.63)* |                              |
| Yes                           | 25     | 89.29   | 99     | 88.39   | 6 | 21.43 | 6 | 5.36 | 2.57 |                           |
| No                            | 16     | 57.14   | 82     | 73.21   | 2.05 (0.78–5.23) |        |        |        |        |                              |        |         |        |         |                              |

UD: undetermined; below detection level in patients who were under treatment for HCV; *Student t-test; P: probability; OR (95% CI): odds ratio (95% confidence interval); **P < 0.05; ***P < 0.01.
HCV-positive and HCV-negative cases. This contradicts the above suggestion. But, the high prevalence of HCV infection among contacts to HCV-negative patients could be explained by the past history of hospitalization, surgical procedures, exposure to used syringe, circumcision by nonmedical personnel, and prior injection treatment for Bilharziasis.

Moreover, it was found that HCV-positive contacts were more likely exposed to sources of infections such as shaving at common barber, infected blood, and Bilharziasis. Thus, the risk of HCV infection increased with environmental exposure to potential sources of infection. Correspondingly, the risk of HCV infection was increased among sexual partners of the Italian index cases who were intravenous drug users (23.6%) compared to cases who acquired infection through transfusions (7.8%), which suggests a parenteral route of transmission [21].

In addition, a controlled historical cohort study was conducted in Iran to investigate the intrafamilial transmission of HCV infection among sexual and nonsexual contacts. Only 2.9% (7/270 subjects) of contacts to HCV cases and 1.1% (3/270 subjects) of contacts to noninfected controls had anti-HCV antibodies. Of these, two subjects among the unexposed group proved to be HCV-infected during the recombinant immunoblot assay (RIBA) and PCR, and both of them were IV drug users. Thus, there was no intrafamilial risk for HCV transmission, and sexual contact was more likely to stimulate the immune system rather than increasing the risk of HCV infection [22].

Moreover, in the present study, we found that risky behaviours such as using nonsterile syringes and exposure to Bilharzial infection were less frequent among household contacts to HCV-infected case. This might reflect their awareness about the ways of HCV transmission.

In this study, HCV infection in household contacts to index cases was associated with past history of blood transfusion. However, in this study, whether this transfusion was before or after blood donor screening policy was not verified, but still blood transfusion represents a main risk for HCV infection, which emphasizes more efforts for safe blood transfusion. Similarly, 72% of subjects with history of blood transfusion (54/75 subjects) were HCV positive in the cross-sectional survey of one thousand healthy blood donors volunteered in Kaser Al Ani hospital blood bank, Cairo, Egypt [23]. Correspondingly, transfusion was commonly reported as the main rout of HCV transmission among blood donors in Iran [24, 25] and in USA [26], in asymptomatic urban population of the State of Mexico with at least one risk factor [27], and in HCV-infected patients who were identified between 2001 and 2008 in the Northern California, USA [28].

However, in Egypt, the main risk factor for HCV infection was the traditional injection treatment of schistosomiasis [29–31].

### 4.3. Limitations
The main limitations of this study were the unknown duration of the disease for index case and recall bias due to the cross-sectional nature of the study, which also makes it inaccessible to assess the time relationship between exposure to risk factors including the index case and outcome (HCV seropositivity) unlike the prospective cohort design. Further large-scale prospective studies to investigate the viral sequencing between cases and contacts (seroconversion) are recommended to prove or disprove the contact transmission.

As far as information bias is concerned, this type of error could be avoided by using a well-established means of collecting data on past exposures and risk factors. Regarding selection bias, we collected information regarding the contacts of the index patients attending Benha Faculty of Medicine, and we believe that our population is a random sample of patients with HCV.

Another limitation of the study refers to the lack of assessment for HCV genotypes, so we were unable to address whether family members share the same genotype, and differing genotypes have differing rates of transmission.

### 5. Conclusion
The controversy on the intrafamilial transmission of HCV infection can be due to the different methods used to detect anti-HCV antibodies (first and second generations ELISA have lower sensitivity than the third-generation assays), different geographic areas, viremia levels, and sexual behaviours of the target population.

Finally, it can be concluded that household contacts to HCV cases are exposed to increased risk of HCV infection. This is favoured by environmental exposures to other sources of infections. Nonetheless, contacts to HCV patients are more likely aware of the different ways of HCV transmission and avoid exposure to sources of infection. In addition, prolonged exposure to infected cases can stimulate the immune system.

### Data Availability
The data used to support the findings of this study are available from the corresponding author upon request.
Conflicts of Interest

The authors declare that they have no conflicts of interest.

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References

[1] F. El-Zanaty and A. Way, *Egypt Demographic and Health Survey 2008*, Ministry of Health, El-Zanaty and Associates, and Macro International, Cairo, Egypt, https://dhsprogram.com/pubs/pdf/fr220/fr220.pdf, 2009.

[2] H. Razavi, I. Waked, C. Sarrazin et al., “The present and future disease burden of hepatitis C virus (HCV) infection with today’s treatment paradigm,” *Journal of Viral Hepatitis*, vol. 21, no. s1, pp. 34–59, 2014.

[3] Ministry of Health and Population/Egypt, *El-Zanaty and Associates/Egypt, International ICF. Egypt Health Issues Survey 2015, Cairo, Egypt. Ministry of Health and Population/ Egypt and ICF International*, https://dhsprogram.com/pubs/pdf/FR313/FR313.pdf, 2015.

[4] World Health Organization, “Global hepatitis report,” 2017, p. 141, 2017.

[5] C. Estes, M. Abdel-Kareem, W. Abdel-Razek et al., “Epidemiological aspects of intrafamilial spread of HCV infection in Egyptian population: a pilot study,” *Open Journal of Gastroenterology*, vol. 4, no. 5, pp. 228–236, 2014.

[6] J. Pepin, C. N. A. Chakra, E. Pepin, V. Nault, and L. Valiquette, “Evolution of the global burden of viral infections from unsafe medical injections, 2000-2010,” *PLoS One*, vol. 9, no. 6, Article ID e99677, 2014.

[7] F. El-Bendary, G. Esmat, M. Neamatallah et al., “Epidemiology of hepatitis C virus infection and its modes of transmission in a cohort of initially asymptomatic blood donors,” *Journal of Infectious Diseases*, vol. 206, no. 5, pp. 654–661, 2012.

[8] A. Fani, M. Sofian, M. Adeli, and P. Fani, “Intrafamilial transmission of hepatitis C virus infection in Iran,” *Iranian Journal of Clinical Infectious Diseases*, vol. 4, no. 3, pp. 157–161, 2009.

[9] H. I. Awadalla, M. H. Ragab, N. A. Nassar, and M. A. H. Osman, “Risk factors of hepatitis C infection among Egyptian blood donors,” *Central European Journal of Public Health*, vol. 19, no. 4, p. 217, 2011.

[10] S. M. Alavian, B. Gholami, and S. Masarrat, “Hepatitis C risk factors in Iranian volunteer blood donors: a case-control study,” *Journal of Gastroenterology and Hepatology*, vol. 17, no. 10, pp. 1092–1097, 2002.

[11] A. Kandeel, M. Genedy, S. El Refai, A. L. Funk, A. Fontanet, M. H. Ragab, and T. Omran, “Risk factor analysis of hepatitis C virus infection among Egyptian health-care workers in a national liver diseases referral centre,” *Bulletin of the World Health Organization*, vol. 89, no. 9207, pp. 887–891, 2000.

[12] S. K. AbdulQawi, M. A. Metwally, I. Raghi, M. AbdelHamid, and A. Shaheen, “Prospective study of prevalence and risk factors for hepatitis C in pregnant Egyptian women and its transmission to their infants,” *Croatian Medical Journal*, vol. 51, no. 3, pp. 219–228, 2010.

[13] T. El-Zanaty and A. Way, *Egypt Demographic and Health Survey 2008*, Ministry of Health, El-Zanaty and Associates, and Macro International, Cairo, Egypt, https://dhsprogram.com/pubs/pdf/fr220/fr220.pdf, 2009.

[14] M. Habib, M. K. Mohamed, F. Abdel-Aziz et al., “Hepatitis C virus infection in a community in the Nile Delta: risk factors for seropositivity,” *Hepatology*, vol. 33, no. 1, pp. 248–253, 2001.

[15] A. Kandeel, M. Genedy, S. El Refai, A. L. Funk, A. Fontanet, and M. Talaat, “The prevalence of hepatitis C virus infection in Egypt 2015: implications for future policy on prevention and treatment,” *Liver International*, vol. 37, no. 1, pp. 45–53, 2017.

[16] M. K. Mohamed, M. Abdel Hamid, N. N. Mikhail et al., “Intrafamilial transmission of hepatitis C in Egypt,” *Hepatology*, vol. 42, no. 3, pp. 683–687, 2005.

[17] M. Z. Omar, M. A. Metwally, H. M. El-Feky, I. A. Ahmed, M. A. Ismail, and A. Idris, “Role of intrafamilial transmission in high prevalence of hepatitis C virus in Egypt,” *Hepatic Medicine: Evidence and Research*, vol. 9, pp. 27–33, 2017.

[18] M. El-Bendary, G. Esmat, M. Neamataallah et al., “Epidemiological aspects of intrafamilial spread of HCV infection in Egyptian population: a pilot study,” *Open Journal of Gastroenterology*, vol. 4, no. 5, pp. 228–236, 2014.

[19] A. Kandeel, M. Genedy, S. El Refai, A. L. Funk, A. Fontanet, M. H. Ragab, and T. Omran, “Risk factor analysis of hepatitis C virus infection among Egyptian health-care workers in a national liver diseases referral centre,” *Bulletin of the World Health Organization*, vol. 89, no. 9207, pp. 887–891, 2000.

[20] S. Romero-Figueroa, E. Ceballos-Salgado, L. Santillan-Arreygue, M. Rubio-Lezama, and J. J. Garduno-Garcia, “Risk factor analysis of hepatitis C virus infection among Hispanic and Asian American patients,” *Journal of Viral Hepatitis*, vol. 19, no. 2, pp. e105–e111, 2012.
[30] A. Medhat, M. Shehata, L. S. Magder et al., “Hepatitis c in a community in Upper Egypt: risk factors for infection,” *American Journal of Tropical Medicine and Hygiene*, vol. 66, no. 5, pp. 633–638, 2002.

[31] N. N. Mikhail, D. L. Lewis, N. Omar et al., “Prospective study of cross-infection from upper-GI endoscopy in a hepatitis C-prevalent population,” *Gastrointestinal Endoscopy*, vol. 65, no. 4, pp. 584–588, 2007.