Tropical Medicine and International Health doi:10.1111/tmi.12410

VOLUME 20 NO 1 PP 89–97 JANUARY 2015

Hepatitis C virus acquisition among Egyptians: analysis of a 10-year surveillance of acute hepatitis C

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Abstract

OBJECTIVE To identify current risk factors for hepatitis C virus (HCV) acquisition among Egyptians.
METHODS Patients with acute HCV were identified through a surveillance system of acute hepatitis in four fever hospitals in Egypt between 2002 and 2012. Case–control analysis was conducted, cases being incident acute symptomatic HCV and controls being acute hepatitis A identified at the same hospitals. The questionnaire covered iatrogenic, community and household exposures to HCV in the 1–6 months prior to onset of symptoms. Multivariate models were built to identify risk factors associated with HCV acquisition among non-drug users and drug users separately.
RESULTS Among non-drug users, hospital admission was independently associated with acute HCV infection (OR = 4.2, 95% CI = 1.7–10.5). Several iatrogenic procedures, for example admission in a surgery unit, sutures, IV injections and IV infusions, highly correlated with hospital admission, were also associated with acute HCV infection and could have been used in the final model instead of hospital admission. Among drug users, identified risk factors were multiple sexual relations (OR = 4.0, 95% CI = 1.1–14.7), intravenous drug use (OR = 3.9, 95% CI = 1.2–13.0) and shaving at the barbershops (OR = 8.7, 95% CI = 2.4–31.4). Illiteracy and marriage were significant risk factors in both groups.
CONCLUSION Invasive medical procedures are still a major risk for acquiring new HCV infections in Egypt, as is illicit drug use in spreading HCV infection.

keywords acute hepatitis C, risk factors, epidemiology, Egypt

Introduction

Hepatitis C virus (HCV) is a leading cause of liver disease worldwide, as 130–170 million individuals are chronically infected and, of the more than 500 000 new cases of liver cancer that occur each year, 22% (>100 000) are attributable to HCV infection (Lavanchy 2011). Egypt has the highest worldwide prevalence (El-Zanaty & Way 2009). Previous research suggested that the Egyptian HCV epidemic resulted from the use of inadequately sterilised needles during mass campaigns to treat schistosomiasis between the 1960s and 1980s, establishing a large reservoir of chronic HCV infections and representing the world's largest iatrogenic transmission of blood-borne pathogens (Centers for Disease Control & Prevention 2012).

In 2008, a Demographic and Health Survey (DHS) was carried out in Egypt, providing for the first time a unique opportunity for HCV antibody testing on a nationwide representative sample of individuals (6052 women and 5074 men). It showed that 10% of the population aged 15–59 years had a chronic infection, which after inclusion of older age groups adds up to around 6 million chronic infections throughout the country (El-Zanaty &

Way 2009; Guerra *et al.* 2012). Men were more likely to be infected than women, and infection increased sharply with age, with higher prevalence in rural than urban areas.

Despite the government's efforts, the HCV epidemic in Egypt continues to grow. Incidence rates have been estimated at 2.4 per 1000 person-years (165 000 new infections annually), indicating a high level of ongoing transmission of HCV in this country (Mostafa *et al.* 2010; Centers for Disease Control & Prevention 2012).

Illicit use of injectable drugs is the main source of HCV infections in most developed countries (e.g. Western Europe, United States) while unsafe injections/transfusions and contaminated equipment used in healthcare-related procedures play a major role in HCV transmission in resource-limited settings (Alter 2007). However, recent studies showed that intravenous drug use appears to be a growing risk factor for acquiring new HCV infections in several resource-limited countries, including Egyptian urban areas (Razzaghi *et al.* 2000; Paez Jimenez *et al.* 2009; Kandeel *et al.* 2012). In Egypt, several exposures, such as unsafe injections, healthcare procedures and community exposures, have been associated with HCV infection (Habib *et al.* 2001; Arafa *et al.* 2005), but these studies were performed on prevalent cases in cross-sectional surveys without any information on the time of infection, making interpretation of the data difficult. Other studies, some with participants coming from the same study population (Paez Jimenez *et al.* 2009, 2010), have recruited incident cases (Paez Jimenez *et al.* 2009, 2010; Mostafa *et al.* 2010; Kandeel *et al.* 2012), but with insufficient power to allow proper significant testing of risks associated with rare exposures or stratification of the analysis by major risk groups. Yet, it is of utmost importance to identify the current risk factors for HCV infection in the population, in order to tailor prevention programmes and identify the critical interventions to implement. Therefore, we present here the results of a 10-year case–control study conducted in Egypt to identify the ongoing risk factors for acute HCV infection in urban settings.

Methods

Participant recruitment and questionnaire

Study participants were identified through a surveillance system of acute hepatitis implemented between April 2002 and December 2012 in four fever hospitals in Egypt: two in Cairo (Abbassia and Imbaba Fever Hospitals), one in Alexandria (Alexandria Fever Hospital) and one in Assiut (Assiut Fever Hospital). Recruitment started in 2002 in Cairo, and in 2010 in Alexandria and Assiut. Fever hospitals are public infectious disease hospitals affiliated to the Ministry of Health (MOH). They serve low and middle socio-economic classes. Patients with recent symptoms (<3 weeks) suggestive of hepatitis (fever and/or jaundice) and alanine aminotransferase (ALT) more than three times the upper limit of normal (ULN) were invited to participate in the study. Patients with known pre-existing chronic liver disease were excluded.

All patients underwent a complete clinical assessment, and after giving informed consent, they answered orally administered standardised questionnaires covering socio-demographic characteristics, present and past health conditions, and exposure to potential risk factors for viral hepatitis during the 6 months preceding the onset of symptoms. Exposures were categorised as iatrogenic and community related. Iatrogenic exposures referred to history of invasive medical procedures [e.g. surgery, endoscopy, blood transfusion, intravenous (IV) infusions, injections], obstetrical procedures (women only) and dental treatment. Community exposures referred to shaving at barbershops, sharing razors or nail trimmers with family members, getting manicures or pedicures at beauty salons, tattooing and ear-piercing. Questions on high-risk behaviour such as having had more than one sexual partner or drug use (e.g. pills, sniffing or injecting) were only put to men, due to their sensitive nature.

We conducted a case–control analysis. Incident acute symptomatic hepatitis C patients were enrolled as cases either (i) before seroconversion, with negative anti-HCV antibody and positive HCV RNA laboratory results, or (ii) with rapid seroconversion: positive anti-HCV antibody, positive HCV RNA and ALT more than 10 times the ULN (i.e. ≥370 IU/l). The high ALT threshold was used to exclude ALT flares in patients with chronic hepatitis C (Hajarizadeh *et al.* 2012). The controls were recruited among hepatitis A patients (anti-HAV IgM positive) identified in the same fever hospitals. As age at infection profile of HAV and HCV is overlapping in the age group between 15 and 40 years of age, only subjects in this age group were included in the final analysis.

Approval for the study was obtained from the Institutional Review Board of the Egyptian MOH and the Ethics Committee of the Faculty of Medicine, Ain Shams University (Egypt).

Laboratory testing

A 20 ml of venous blood sample was collected. Patients were tested for standard liver functions [ALT, aspartate aminotransferase (AST), total and direct bilirubin, alkaline phosphatase] and for the following hepatitis markers:

anti-HAV IgM (HAVAB®, M EIA; Abbott Laboratories, Diagnostics Division, IL, USA); in patients with negative HAV IgM; anti-HBc IgM (CORZYME®, M rDNA; Abbott Laboratories); and HBs antigen (AUSZYME MONOCLONAL®, third-generation EIA; Abbott Laboratories). Anti-HCV antibody testing (AxSym HCV version 3.0) and HCV RNA testing using polymerase chain reaction (PCR) (nested reverse transcriptase PCR by in-house assay using 5′ UTR primers) (Abdel-Hamid *et al.* 1997) were done.

Statistical analysis

There is a strong association in our data set between HCV acquisition and illicit drug use [OR = 4.15 (3.08–5.60)]. As risk factors are different between drug users and non-drug users, our analytic choice was to build two separate models for these two populations. In this study, a 'drug user' is someone who declared to have used drugs (any type of drug, including pills) at some point in his life, and a 'non-drug user' is someone who declared that he never used drugs in his life. Sample size allowed a matched design for non-drug users; controls were then matched on age (±3 years), period of admission (three categories with grouping of similar total size: 2002–2004, 2005–2008 and 2009–2012) and hospital. For drug users, due to a smaller sample size, a matched design was not possible, so we adjusted on the following variables: age (5-year categories), hospital and period of admission.

Quantitative variables are presented as mean ± SD (range). Univariate ORs and 95% confidence intervals (95% CI) were estimated for each potential risk factor, using a conditional logistic regression model for the matched design and a logistic regression model for the adjusted design. Significance was assessed by the Wald test. Variables with *P*-values <0.20 were entered into a multivariate conditional logistic regression model for the matched design and a multivariate logistic regression for the adjusted design to simultaneously examine their independent effect. The final models were obtained through stepwise deletion of variables until all predictors left had *P*-values <0.05. Data were analysed using STATA 12.0 software (Stata Corporation, College Station, TX, USA).

Results

Between April 2002 and December 2012, 2493 acute hepatitis patients were recruited: 747 acutely infected with HAV, 1197 with HBV and 549 with HCV. The mean (±SD) age was 28.2 (±10.3) years; 73.8% were males. 87% presented with jaundice and 55% presented with fever. Socio-demographic and clinical characteristics of recruited patients are shown in Table 1.

According to our case definitions for acute hepatitis C in this study, 56 patients were diagnosed before seroconversion, and 198 were diagnosed after seroconversion.

Non-drug users

In total, 111 HCV cases and 111 HAV matched controls were included in this analysis (108 subjects from Abbassia, 88 from Imbaba, 20 from Alexandria and six from Assiut). The mean age of HCV cases was 26.6 ± 6.0 years, and 51.3% ($n = 57$) were males (Table 2). The mean age of controls was 25.4 ± 6.6, very similar to that of cases because of the matching design. The proportion of illiterates was higher among HCV cases (32.4%) compared with controls (13.5%) ($P < 0.001$). After splitting marriage into categories by duration of marriage, the risk of HCV was particularly increased for recent marriage of <1 year (OR = 9.7; 95% CI = 1.9–49.5) compared with singles.

In the univariate analysis among non-drug users, iatrogenic factors statistically associated with HCV infection were history of hospital admission, surgery, sutures, IV infusions and IV injections, but not intramuscular injections (Table 3). In women, birth delivery and caesarean section were associated with increased risk of infection. After studying various dental procedures separately, only gum treatment was associated with an increased risk of infection. None of the community exposures was associated with an increase in HCV risk (Table 4).

In the multivariate analysis, being recently married versus single (OR = 5.2; 95% CI = 0.9–30.2) and being illiterate (OR = 4.2; 95% CI = 1.7–10.5) were associated with HCV infection (Table 5). Hospital admission was independently associated with an increase in HCV risk (OR = 4.2; 95% CI = 1.7–10.5). Unsurprisingly, several iatrogenic risk factors were highly correlated with hospital admission, that is admission in surgery unit, sutures, IV injections and IV infusions, and remained significant in the model if added separately instead of hospital admission. We chose to present here the model with hospital admission as it was the most comprehensive variable related to healthcare procedures.

Drug users

As only men were asked questions about drug use, this analysis was restricted to men (Table 6). In total, 143 cases and 100 controls were included (102 subjects from Abbassia, 69 from Imbaba, 70 from Alexandria and two from Assiut). The mean age was 28.4 (±5.6) years for

Table 1 Socio-demographic and clinical characteristics of the recruited acute hepatitis A, B and C patients in the four fever hospitals, 2002–2012

	Acute A *N* = 747 *n* (%)	Acute B *N* = 1197 *n* (%)	Acute C *N* = 549 *n* (%)	Total *N* = 2493 *n* (%)
Age (years)*	21.1 ± 5.8 (15–62)	29.1 ± 9.1 (15–63)	36.1 ± 11.3 (15–65)	28.2 ± 10.3 (15–65)
Males	535 (71.6)	904 (75.5)	402 (73.2)	1841 (73.8)
Married	105 (14.0)	670 (55.9)	411 (74.8)	1186 (47.5)
Illiteracy	39 (5.2)	413 (34.5)	186 (33.8)	638 (25.5)
Fever	582 (77.9)	592 (49.4)	208 (37.8)	1382 (55.4)
Jaundice	663 (88.7)	1082 (90.3)	428 (77.9)	2173 (87.1)
Total Bilirubin (mg/dl)*	7.7 ± 4.7 (0.1–75)	10.6 ± 6.7 (0.2–92)	7.5 ± 6.2 (0.4–74)	9.0 ± 6.2 (0.1–92)
ALT (IU/l)*	1087.4 ± 943.7 (34–7693)	1106.4 ± 898.7 (25–7937)	767.1 ± 543.5 (63–4791)	1025.7 ± 856.0 (25–7937)

*Quantitative variables are presented as mean ± SD (range).

Table 2 Socio-demographic characteristics of acute HCV cases and matched HAV controls among non-drug users, 2002–12

	Acute HCV cases (*n* = 111) *n* (%)	Matched HAV controls* (*n* = 111) *n* (%)	OR (95% CI)	*P*-value
Mean age (years)	26.6 ± 6.0	25.4 ± 6.6	NA	NA
Males	57 (51.3)	69 (62.2)	1.6 (0.9–2.7)	0.1
Education				
Ability to read and write	74 (66.7)	96 (86.5)	1	**0.001**
Illiteracy	36 (32.4)	15 (13.5)	3.6 (1.7–7.9)	
Marriage duration				
Single	41 (36.9)	65 (58.6)	1	**0.002**
Less than one year	11 (9.9)	2 (1.8)	9.7 (1.9–49.5)	
One year or longer	57 (51.3)	39 (35.1)	4.1 (1.7–9.6)	

OR, odds ratio; CI, confidence interval; NA, not applicable.
*Matching on age (±3 years), period of admission and hospital.
The bold *P*-values mean significant *P*-values

Table 3 Healthcare-related risk factors in acute HCV cases and matched HAV controls among non-drug users, 2002–12

	Acute HCV cases (*n* = 111) *n* (%)	Matched HAV controls* (*n* = 111) *n* (%)	OR (95% CI)	*P*-value
Hospital admission	33 (29.7)	9 (8.1)	4.4 (1.9–10.1)	**<0.001**
Surgery	15 (13.5)	4 (3.6)	3.7 (1.2–11.3)	**0.02**
Sutures	27 (24.3)	10 (9.0)	3.6 (1.5–8.3)	**0.003**
Intravenous injections	14 (12.6)	5 (4.5)	3.2 (1.1–10.0)	**0.04**
Intramuscular injections	30 (27.0)	20 (18.0)	1.7 (0.9–3.2)	0.1
Intravenous infusions	36 (32.4)	10 (9.0)	4.7 (2.1–10.7)	**<0.001**
Endoscopy	4 (3.6)	0	–	–
Blood transfusion	4 (3.6)	1 (0.9)	4.0 (0.4–35.8)	0.2
Birth delivery†	17 (15.3)	4 (3.6)	4.2 (1.4–12.6)	**0.009**
Caesarean section†	10 (9.0)	1 (0.9)	10.0 (1.3–78.1)	**0.03**
Teeth extraction	12 (10.8)	13 (11.7)	1 (0.4–2.7)	1
Gum treatment	9 (8.1)	1 (0.9)	9.0 (1.1–71.0)	**0.04**
Catheter	9 (8.1)	3 (2.7)	3.0 (0.8–11.1)	0.1

OR, odds ratio; CI, confidence interval.
*Matching on age (±3 years), period of admission and hospital.
†Men were considered as non-exposed.
The bold *P*-value mean significant *P*-values

Table 4 Community exposures in acute HCV cases and matched HAV controls among non-drug users, 2002–2012

	Acute HCV cases (n = 111) n (%)	Matched HAV controls* (n = 111) n (%)	OR (95% CI)	P-value
Shaving at barbershops†	40 (36.0)	45 (40.5)	0.8 (0.5–1.4)	0.4
Sharing razor blades†	8 (7.2)	7 (6.3)	1.2 (0.4–3.5)	0.8
Tattoo	1 (0.9)	1 (0.9)	–	–
Multiple sexual partners†				
No	83 (74.8)	72 (64.9)	1	0.3
Yes	1 (0.9)	1 (0.9)	1.0 (0.1–16.0)	
No answer	27 (24.3)	38 (34.2)	0.6 (0.3–1.1)	

OR, odds ratio; CI, confidence interval.
*Matching on age (±3 years), period of admission and hospital.
†Women were considered as non-exposed.

Table 5 Multivariate analysis showing factors independently associated with acute HCV among non-drug users using controls matched on age (±3 years), period of admission and hospital, 2002–2012

	Adjusted OR (95% CI)	P-value
Illiteracy	3.5 (1.4–8.6)	0.007
Marriage duration		0.05
Single	1	
Less than one year	5.2 (0.9–30.2)	
One year or longer	2.9 (1.2–7.2)	
Missing	0.6 (0.1–3.9)	
Hospital admission*	4.2 (1.7–10.5)	0.002

OR, odds ratio adjusted by all other covariates shown in the Table; CI, confidence interval.
*Several variables related to hospital admission (i.e. admission in surgery unit, sutures, intravenous injections, intravenous infusions) were significantly correlated and could be added in the model instead of hospital admission.

cases and 22.8 (±4.2) years for controls. More than a quarter of cases were illiterate, but only 6% of controls. Almost 50% of cases and 90% of controls had never been married. The logistic regression analysis identified five independent risk factors associated with an increase in HCV risk: multiple sexual partners (OR = 4.0; 95% CI = 1.1–14.7), intravenous drug use (OR = 3.9; 95% CI = 1.2–13.0) and shaving at barbershops (OR = 8.7; 95% CI = 2.4–31.4) (Table 6). Being recently married versus single (OR = 15.6; 95% CI = 1.2–199.7) was again associated with HCV transmission, as was being illiterate (OR = 4.8; 95% CI = 1.5–15.3).

Discussion

This 10-year case–control study on incident acute hepatitis showed that factors associated with acquiring new HCV infections differed between drug users and non-drug users. Iatrogenic exposures were associated with HCV acquisition in non-drug users, whereas community behaviours, rather than iatrogenic procedures, were responsible for HCV acquisition among drug users.

A key strength of this study is the recruitment of incident HCV cases, allowing detailed assessment of exposures in a well-defined time period, between 1 and 6 months prior to onset of symptoms. The use of incident cases allowed for the identification of factors associated with current HCV acquisition, making our findings particularly relevant for ongoing prevention programmes. However, the study has some limitations: by focusing on symptomatic cases, one may wonder whether focusing on symptomatic cases might have biased the study towards the identification of risk factors more prone to lead to symptomatic forms of infection. However, we have not found in the literature evidence of factors associated with symptomatic forms of infection, except for older age (Fabris *et al.* 2008). Moreover, epidemiology textbooks recommend that control groups do not share risk factors with cases. This may not be entirely true for patients with acute hepatitis A because a minority of them (e.g. injecting drug users, men who have sex with men) may have been infected because of behaviours related to their belonging to these risk groups. Another limitation concerns the avoidance of sensitive questions about behaviours (mainly drug use and multiple sexual partners) with women. As a result, we were not able to study these behaviours in women. Even in men, there were numerous missing data for these sensitive questions among non-drug users and likely 'socially desirable' answers to these questions, so the interpretation of these results should be cautious.

The findings from this study highlight the importance of invasive healthcare procedures as a major risk factor

Table 6 Multivariate analysis showing factors independently associated with acute HCV among drug users, 2002–2012

	Acute HCV cases (n = 143) n (%)	HAV controls (n = 100) n (%)	Adjusted OR n = 234* (95% CI)	P-value
Illiteracy				
No	104 (73.8)	94 (94.0)	1	0.008
Yes	37 (26.2)	6 (6.0)	4.8 (1.5–15.3)	
Marriage				
Single	70 (49.6)	90 (90.0)	1	0.01
Less than 1 year	9 (6.4)	1 (1.0)	15.6 (1.2–199.7)	
One year or longer	56 (39.7)	9 (9.0)	3.7 (1.3–10.7)	
Missing	6 (4.3)	0	–	
Multiple sexual partners				
No	64 (45.4)	56 (56.0)	1	0.04
Yes	22 (15.6)	7 (7.0)	4.0 (1.1–14.7)	
No answer	55 (39.0)	37 (37.0)	1.7 (0.7–4.4)	
Illicit drug use				
Oral only	21 (14.9)	22 (22.0)	1	0.02
Sniffing	53 (37.6)	34 (34.0)	1.3 (0.4–4.1)	
Intravenous drug	58 (41.1)	10 (10.0)	3.9 (1.2–13.0)	
Missing	9 (6.4)	34 (34.0)	0.5 (0.1–1.8)	
Shaving at barbershops				
No	9 (6.4)	21 (21.0)	1	0.001
Yes	132 (93.6)	78 (78.0)	8.7 (2.4–31.4)	
Missing	0	1 (1.0)	–	

OR, odds ratio adjusted by age (5-year categories), hospital, period of admission and all other covariates shown in the Table; CI, confidence interval.

*Seven participants with missing data: six cases with missing information on duration of marriage and one control with missing information on shaving at barbershops. We had only two patients from Assiut hospital, so we dropped them from the analysis.

for acquiring new HCV infections in Egypt. Admission in surgery unit, sutures, IV injections and IV infusions were found to be associated with HCV infection. This finding is consistent with previous studies with different designs in Egypt (Habib *et al.* 2001; Paez Jimenez *et al.* 2009; Kandeel *et al.* 2012). Mass antischistosomiasis campaigns created a huge HCV reservoir in rural areas in Egypt. From this reservoir, in the last decades, HCV spread to the rest of the community through invasive medical procedures and particularly injections (Arafa *et al.* 2005). It has been estimated that worldwide, approximately 2 million HCV infections are acquired annually from contaminated healthcare injections and may account for up to 40% of all HCV infections (Hauri *et al.* 2004). The frequency of therapeutic injection use is high in Egypt. Approximately 280 million injections were administered in Egypt in 2001, of which an estimated 8% (23 millions) might have been unsafe (Talaat *et al.* 2003). Several studies in Egypt showed that receiving injections increases HCV risk (Arafa *et al.* 2005; Mostafa *et al.* 2010; Kandeel *et al.* 2012), while another study specified IV injections as a risk exposure to HCV infection (Paez Jimenez *et al.* 2009). In our findings, only IV injections were associated with acquisition of HCV infection. Promoting through mass media reduction of unnecessary injections and increasing the safety of injections are utmost priorities for Egypt.

The high correlation of the HCV-associated invasive procedures with hospital admissions suggests that many infections took place in hospitals, despite the important efforts deployed by the MOH for infection control in hospitals in the past 10 years. Some limitations of the infection control programme may be economical (elevated cost of sterilisation procedures and of disposable material) and in the capacity to reach hospital facilities outside of the MOH coverage.

We did not find any association with other potential modes of acquisition, such as cosmetic procedures (e.g. tattooing, body piercing, manicure and pedicure) as they were uncommonly reported in our study. Very few studies have suggested an increase in the risk of HCV infection associated with these procedures (Mariano *et al.* 2004; Carney *et al.* 2013). While this does not hinder their role in HCV acquisition, it does suggest that even if there is a risk of acquiring HCV related to these procedures, they have a little contribution to HCV spread in

this population and are unlikely to be major sources of new HCV infections in Egypt, considering the very limited number of exposed individuals.

Drug users are a specific population with various high-risk behaviours for HCV acquisition. In our study, IV drug use (IVDU) emerged as an independent risk factor for HCV transmission among drug users, being responsible for an approximately fourfold increased risk of incident HCV infection. Sharing the drug solution, syringes or other drug preparation equipment (such as water, drug mixing containers and cotton filters) all increase the risk of transmission if any of these components are infected with HCV (Centers for Disease Control & Prevention 2002). Moreover, fewer sharing partners are necessary to sustain HCV transmission than are necessary for other blood-borne viruses (Murray *et al.* 2003). In recent years, IVDU has increased in the Middle East, Africa and South-East Asia, posing an additional threat and a new challenge to public health authorities for the implementation of harm reduction programmes (Lavanchy 2011; Nelson *et al.* 2011). Indeed, Soliman *et al.* (2010) reported that more than half of the DU in Cairo injected with used needles or syringes. Prevalence of HCV antibody among IVDU in 77 countries in Europe, Asia and North America has surpassed 50% in some countries and almost reached 90% in others (Nelson *et al.* 2011). We are not aware of recent estimates of HCV prevalence among drug users in Cairo, but it will probably be high considering the background prevalence in the population. An additional worry is the high level of drug use among controls in this study (10%), which suggests a high prevalence of this risky behaviour. Little information regarding drug use is available in Egypt, not only because it is a new phenomenon but also because of the lack of funds to study it in a systematic way (Kandeel *et al.* 2012). Moreover, religious and cultural impediments make IVDU an under-investigated population in the Middle East (Ramia *et al.* 2012).

Another contribution to HCV acquisition among drug users in our study was multiple sexual partners. While these results should be taken with caution considering the large proportion of participants who did not reply to this sensitive question, it is worth noting that sexual transmission is a controversial mode of HCV transmission that has received considerable attention among healthcare providers and the lay public (Tohme & Holmberg 2010). The extent to which HCV is transmitted by sexual activity and under what circumstances is one of the most debatable aspects of the epidemiology of hepatitis C. Outbreaks of acute hepatitis C have been well documented among HIV-positive men who have sex with men (Yaphe *et al.* 2012). On the other hand, sexual transmission in heterosexual long-term relationships seems extremely low (Thursz & Fontanet 2013). Increased HCV risk associated with multiple sexual partners has been previously documented among drug users. Whether it is related to under-reported associated drug use or an independent risk factor in itself is unresolved. In our study, questions about other risky sexual practices were not asked because of their sensitive nature and social unacceptance in the Egyptian community, but they might pose an unrecognised mechanism for HCV acquisition.

Quite puzzling was the ninefold increase in HCV risk associated with shaving at barbershops among drug users, while no elevation in risk existed for the same behaviour among non-drug users. Our hypothesis to this finding is that certain barbershops could be used as a place for drug users gathering or could be used as drop in places for having intravenous injections from the barber. Indeed, the so-called health barbers were a primary source of medical care in the past and continue to provide injections at a much lower cost than formal medical providers (Talaat *et al.* 2003). However, we did not find in the literature evidence linking barbershops and drug users. This needs further exploration in future studies.

Marriage emerged as a risk factor for acute HCV infection among drug users and non-drug users, supporting the possibility that HCV is transmitted between spouses. Interspousal transmission has been addressed in different studies and achieved somewhat conflicting results. Magder *et al.* (2005), through mathematical modelling, estimated that 6% of infected individuals in rural areas of Egypt acquired infection from their spouses. In line with our results, studies from Karachi and Cameroon showed that interspousal transmission played a role in HCV transmission (Qureshi *et al.* 2007; Njouom *et al.* 2011). However, limited or no evidence of HCV transmission between partners was found in other studies (Tahan *et al.* 2005; Del Corno & Civardi 2006). Here, the risk of HCV transmission was higher among the recently married (<1 year) and decreased afterwards. Paez Jimenez *et al.* (2009) had suggested that upon first encounters with an HCV-infected spouse, the most susceptible individuals would become infected, while others would remain susceptible to a low degree to infection for the rest of their lives. Still, we were not able to identify the exact routes of transmission, whether sexual, exchange of grooming items, sharing needles or other routes. This needs to be further investigated in additional studies.

Illiteracy was a significant risk factor for HCV infection in our two models. However, controls being acute

hepatitis A cases aged between 15 and 40 years, they likely belong to higher socio-economic levels with higher standards of hygiene leading to late acquisition of HAV infection. The evidence for an association between HCV infection and lower education level comes from other studies, one in which family controls of HCV patients were used (Paez Jimenez *et al.* 2009), and from the national DHS (Guerra *et al.* 2012). The type of healthcare-serving patients with a low socio-economic level and the likelihood of reuse of unsterilised material in this context might explain the observed relation (Guerra *et al.* 2012).

In conclusion, this study confirms the major role of healthcare-related exposures in the current acquisition of HCV in the Egyptian community, despite the Egyptian government's efforts to control HCV transmission in healthcare settings. It also highlights the important role of illicit drug use in spreading HCV infection. Efforts need to be intensified on both the prevention and treatment fronts, to reduce the reservoir of HCV. National healthcare awareness and infection control programmes should be strengthened to prevent further transmission. Prevention programmes must be implemented to discourage drug use and limit acquisition among drugs users. Finally, ongoing monitoring of the epidemiology of HCV infection is crucial for understanding the dynamics of transmission and preventing future infections.

Acknowledgements

We are indebted to the clinicians and non-medical staff at Abassia, Imbaba, Alexandria and Assiut fever hospitals for help with patient recruitment and the study participants for their time and trust. The study was funded by the *Agence Nationale de Recherche sur le SIDA et les hepatites virales*, France.

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