

HEPATITIS C IN A COMMUNITY IN UPPER EGYPT: I. CROSS-SECTIONAL SURVEY

MOHAMMED A. NAFEH, AHMED MEDHAT, MAGDA SHEHATA, NABIEL N. H. MIKHAIL, YOUSEF SWIFEE, MOHAMED ABDEL-HAMID, SUSAN WATTS, ALAN D. FIX, G. THOMAS STRICKLAND, WAGIDA ANWAR, AND ISMAIL SALLAM

Hepatitis C Prevention Project: Faculty of Medicine, Assiut University, Assiut, Egypt; Faculty of Medicine, Minia University Faculty of Medicine, Minia, Egypt; American University in Cairo, Cairo, Egypt; Egyptian Ministry of Health and Population, Cairo, Egypt; International Health Program, Department of Epidemiology and Preventive Medicine, University of Maryland School of Medicine, Baltimore, Maryland

Abstract. The prevalence of antibody to hepatitis C virus (anti-HCV) was determined in a cross-sectional survey in a village in Upper Egypt. Exposure and demographic characteristics were obtained through a questionnaire. Antibody to hepatitis C virus was assessed using a second generation enzyme immunoassay, and the presence of HCV RNA was tested using a reverse transcriptase–polymerase chain reaction. Collection of blood samples was targeted at those ≥ 5 years old, and obtained from 62.8%. This report describes the community, the HCV infection characteristics of the subjects, and evaluates some factors associated with presence of anti-HCV. Of the 6,031 participants, 522 (8.7%) were anti-HCV positive. Prevalence was higher among males than females (11.3% versus 6.5%; $P < 0.001$). It was greater among those > 30 years of age than among those ≤ 30 years of age (20.0% versus 3.6%; $P < 0.001$). Those who were less educated, farmed, provided health care, and were currently married had a significantly higher anti-HCV prevalence than those who were not; however, these associations were not significant after adjusting for age. Although active infections with *Schistosoma haematobium* were not associated with anti-HCV, a history of past infection was (age-adjusted risk ratio [RR] = 2.1, 95% confidence interval [CI] = 1.8, 2.4); 134 persons who had a history of receiving parenteral anti-schistosomal therapy had a higher age-adjusted RR (3.0; 95% CI = 2.5, 3.7) for anti-HCV than those who did not. Hepatitis C virus RNA was detected in 62.8% of the anti-HCV positive subjects, without significant variation by age, gender, education, or marital status. The prevalence of anti-HCV in Upper Egypt is high, albeit lower than in Lower Egypt, with continuing but limited transmission indicated by the lower prevalence in residents ≤ 30 years old.

INTRODUCTION

Recent investigations in Egypt have reported a strikingly high prevalence of antibodies to hepatitis C virus (anti-HCV) among blood donors,^{1–5} patients with exposure to blood products^{4,5} or with chronic liver disease,^{4–6} and subjects participating in rural community surveys.^{4,7} Antibody prevalence in blood donors ranged from 6% to 38% and averaged approximately 15%.^{1–5} In an investigation of 2,644 blood donors from 26 Egyptian governorates, those with the highest seroprevalence were located in the central and north-eastern Nile Delta and the Nile valley immediately south of Cairo.⁸ The high prevalence in the general Egyptian population suggests a difference in the transmission and natural history of HCV in Egypt compared with the United States and Europe and other developed and developing countries.

The purpose of this report is to describe the demographic characteristics and base-line prevalence of anti-HCV and HCV infection in a rural upper Egyptian community of approximately 11,000 inhabitants in which prospective investigations of risk factors for HCV infection and the natural history of HCV in the community are being performed.

MATERIALS AND METHODS

Community sample and study design. The study community was selected from among rural villages in Assiut governorate because it provided 1) convenient access to Assiut University Hospital, 2) cooperative village inhabitants, and 3) known local transmission of schistosomiasis, which was to be evaluated as an independent variable for HCV transmission. The community is located 15 km north of the city of Assiut and 375 km south of Cairo (Figure 1), and is composed of a mother village and a small satellite. A house-

to-house census of the entire village was performed by field teams during the preparatory phase, identifying and characterizing all residents: 11,227 individuals were living in 1,747 households. A household was defined as a unit sharing expenses, particularly food, and eating from a common pot, although not necessarily together.

Consent procedure and participation. The Institutional Review Boards at both the University of Maryland-Baltimore and Assiut University reviewed and approved the research protocol and consent forms. Informed consent was obtained from all adult participants and from parents of participating minors.

All inhabitants five years of age or older in participating households were invited to participate and provide a blood sample. Some children less than five were also included if the parents indicated interest and gave consent; 86.7% of the households agreed to participate in the study. Questionnaire data and blood samples were obtained from 6,012 (62.8%) of the 9,581 village inhabitants five years of age or older and from 19 of 1,646 children less than five years old. Among those five years of age and older, the response among males (55.5%) was lower than that among females (70.4%). The primary reasons for not participating were 1) absence on each visit by the survey team, 1,376 (14.4%), 2) refusal to participate, 169 (1.8%), and 3) refusal to give a blood sample, 2,014 (21.0%).

Questionnaire and historical data. Questionnaires designed by a team of sociologists, epidemiologists, and clinicians familiar with modes of transmission of HCV and local customs were administered by trained survey teams. These questionnaires recorded data for sociodemographic characteristics, past and present medical histories, and potential risk factors for exposure to HCV. Adults and children

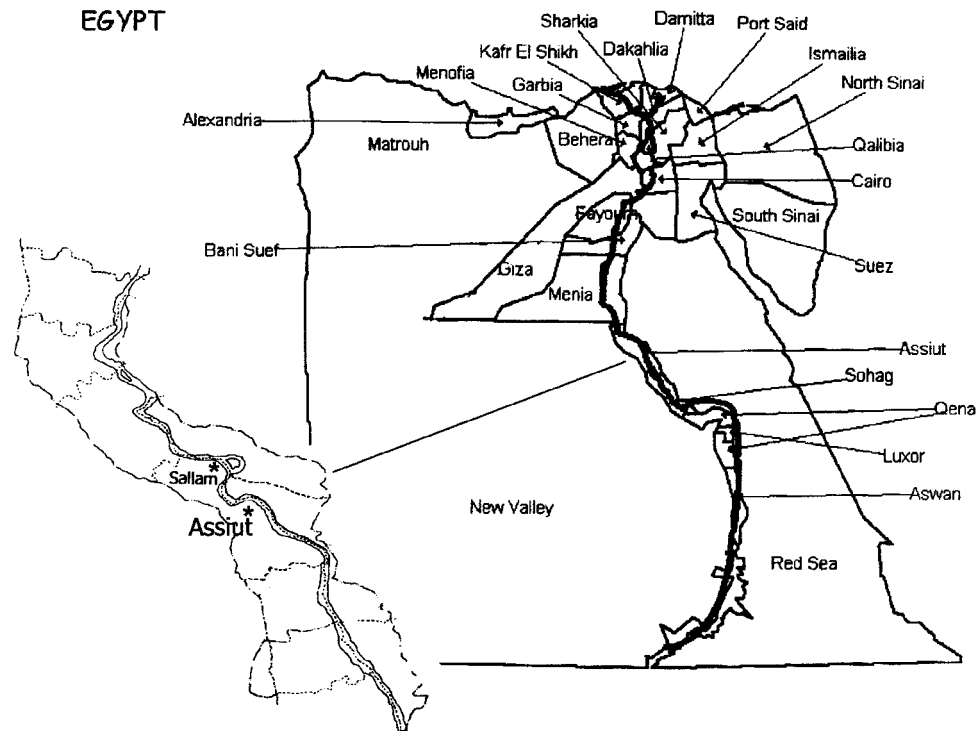


FIGURE 1. Map of Egypt showing Assiut Governorate and the site of the study community.

greater than 10 years of age were interviewed themselves, and usually the female head of the household provided information for children younger than 10 years of age. Education was categorized as no school, informal education (limited religious and traditional instruction by a village elder), school (having attended any amount of primary or secondary school), and university (having attended for any amount of time).

Laboratory methods. Hepatitis serology. Sera were separated, aliquoted, and labeled within 6 hr of collection, and stored at -70°C until testing. Serum samples from all subjects were tested for anti-HCV using a second generation enzyme immunoassay (EIA) with recombinant HCV antigen bound to beads as the solid phase (Abbott HCV EIA 2.0; Abbott Laboratories, North Chicago, IL). All steps were performed according to the manufacturer's instructions. Sera from 514 of the 523 with positive test results for anti-HCV were tested for HCV-RNA, which was amplified directly without isolation of RNA, using a one-step reverse transcription-polymerase chain reaction (RT-PCR) as described by Abdel Hamid and others.⁹ The primers of the RT-PCR are directed at the highly conserved region 5'-untranslated region (UTR) of the HCV genome.¹⁰ The cDNA fragment of the nested reaction was 231 basepairs (bp). The outer fragment flanked by the outer primers was 301 bp. All PCR testing were performed using a 96-plate format and a 9700 thermocycler (Perkin Elmer, Norwalk, CT). The RT-PCR amplicon was visualized by electrophoresis on a 2% agarose gel and staining with ethidium bromide.

Parasitologic examination. Parasitologic examination for *Schistosoma haematobium* was performed for the 4,814 individuals who provided urine samples. The remaining individuals either failed or refused to give urine samples at time

of examination. Nuclepore (Pleasanton, CA) filtration was used to quantify the ova in 10 ml of urine as described by Peters and others.¹¹

Statistical analysis. All data were entered into a Microsoft (Redmond, WA) Access database (Arabic version 97). Duplicate data entry was performed to ensure quality control. Data analysis was performed with a statistical package for personal computer (version 9; SPSS, Inc., Chicago, IL) using comparisons of means (Student's *t*-test) and proportions (chi-square test) when appropriate. Risk ratios (RRs) with 95% confidence intervals (CIs) were calculated to assess associations with anti-HCV positivity. Chi-square tests for trend were used to assess significance of trends for seropositivity across ordinal variables. Weighted Mantel-Haenszel RRs were used to adjust for age, using five-year strata. Age- and gender-adjustment of anti-HCV prevalence was based on the original census distributions for those five years and older in the entire village.

RESULTS

Comparison between participants and nonparticipants.

The mean age of participants five years and older was 25.1 years, and 54.9% were female (Table 1). Participants were more likely than nonparticipants to be female, participating males were younger than nonparticipating males, and participants had a slightly higher level of education than nonparticipants. Among those who were of legal age of marriage in Egypt, a slightly higher proportion of participants than nonparticipants were married (Table 1).

Seroprevalence by age and gender. The overall anti-HCV prevalence was 8.7% (95% CI = 8.0–9.5), with a higher ($P < 0.001$) prevalence among males than females, 11.3%

TABLE 1
Comparison of sociodemographic characteristics for respondents and nonrespondents

	Participants		Nonparticipants		<i>P</i>
	No. (%) [*]	Mean (SD)	No. (%) [*]	Mean (SD)	
Gender (≥ 5 years old)					< 0.001
Male	2,709 (45.1)		2,168 (60.9)		
Female	3,303 (54.9)		1,391 (39.1)		
Age (≥ 5 years)					
All		25.1 (16.2)		25.7 (18.7)	0.09†
Male		24.5 (16.9)		26.5 (17.9)	< 0.001†
Female		25.5 (15.7)		24.5 (19.8)	< 0.07†
Education (≥ 20 years)					
No school	1,421 (46.4)		1,153 (62.3)		< 0.001
Informal education	41 (1.3)		37 (2.0)		
School	1,501 (49.0)		603 (32.6)		
University	100 (3.3)		59 (3.2)		
Married‡	2,553 (60.1)		1,346 (57.0)		0.01

* Percent values represent the proportion of participants/nonparticipants in a specified category.

† *P* value for Student's *t*-test comparing mean age of participants to nonparticipants.

‡ Legal age of marriage in Egypt is 18 years for males and 16 years for females.

and 6.5%, respectively (Table 2). There was a substantial trend of increasing anti-HCV prevalence with age, with a marked increase in the fourth decade (Figure 2). Among those older than 30 years of age, males were more likely ($P < 0.001$) to be anti-HCV positive (28.4%) than females (13.6%); however, no gender difference was detected for anti-HCV prevalence among participants 30 years of age or younger (4.0% and 3.2%, respectively). The age- and gender-adjusted prevalence for the community was 9.2%.

Seroprevalence by education and occupation. Anti-HCV prevalence was similar in adults who had no formal education (14.1%) and in those who had attended any type of school (14.4%). Those who had any education beyond high school had a seroprevalence of only 8.0%. Those who said they were farming were more likely ($P < 0.001$) to be anti-HCV positive than those who denied working in the fields. However, when adjusted for age and gender this difference was not significant. The 14 who worked in health

TABLE 2
Seroprevalence of antibody to hepatitis C virus (anti-HCV) by sociodemographic status*

Category	Total no.	Anti-HCV positive No. (%)	RR (95% CI)	Age-adjusted† RR (95% CI)	HCV PCR positive‡ No. (%)
All participants	6,031	522 (8.7)			323 (63.0)
Gender (M:F)			1.74 (1.47, 2.06)	1.90 (1.61, 2.23)	
Male	2,717	307 (11.3)			195 (64.6)
Female	3,314	215 (6.5)			128 (60.4)
Age (years)			0.18 (0.15, 0.22)	—	
≤ 30	4,164	149 (3.6)			83 (56.1)
> 30	1,867	373 (20.0)			240 (65.6)
Education (≥ 20 years)			1.81 (0.93, 3.55)§	1.05 (0.54, 2.04)§	
None	1,421	201 (14.1)			131 (66.2)
Informal	41	10 (24.4)			6 (60.0)
School	1,501	219 (14.6)			135 (62.8)
University	100	8 (8.0)			5 (62.5)
Employment (≥ 16 years)			1.49 (1.25, 1.78)	1.38 (1.16, 1.65)	
Practice agriculture					
Yes	1,972	289 (14.7)			185 (65.4)
No	1,784	175 (9.8)			105 (60.3)
Medical jobs			1.74 (0.64, 4.76)	1.60 (0.61, 4.19)	
Yes	14	3 (21.4)			1 (33.3)
No	3,742	461 (12.3)			289 (63.7)
Marital status			2.87 (2.30, 3.57)	1.02 (0.70, 1.47)¶	
Currently married	2,553	393 (15.4)			249 (64.5)
Not married	1,696	91 (5.4)			51 (56.0)

* RR = risk ratio; CI = confidence interval; PCR = polymerase chain reaction.

† Mantel-Haenszel weighted RR across five-year strata.

‡ HCV RNA among those who were anti-HCV seropositive (Total number tested was 514).

§ All categories compared to those with any university education.

¶ Mantel-Haenszel weighted RR across year-year strata between 15 and 35 years.

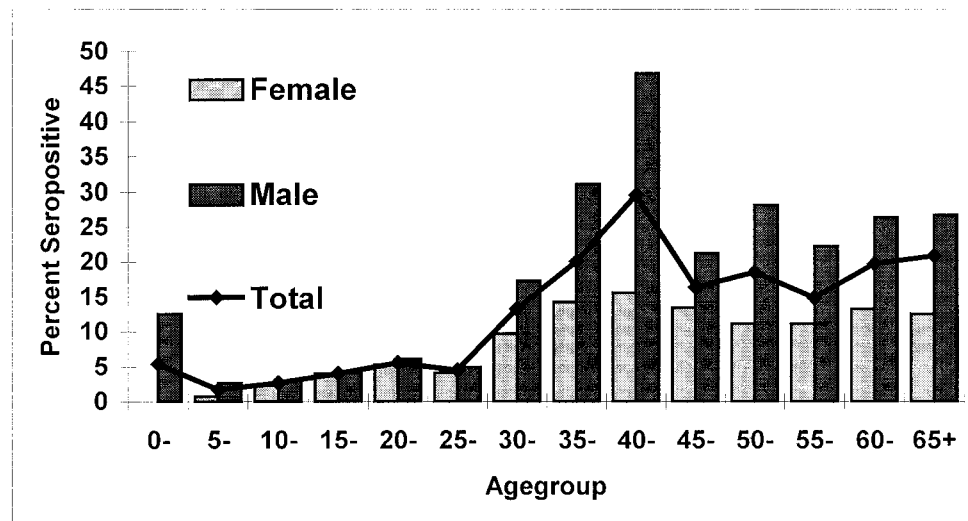


FIGURE 2. Anti-hepatitis C virus (HCV) seroprevalence by age and gender in the study community.

care were not more likely to be anti-HCV positive than their neighbors.

Marital status. Marital status was associated with anti-HCV status (Table 2). Those who were married had a higher ($P < 0.001$) anti-HCV prevalence (15.4%) than those who were not (5.4%). However, the association was not significant after adjusting for age among those between 15 and 35 years old, with a Mantel-Haenszel RR of 1.02 (95% CI = 0.70–1.48). Age-adjustment was limited to this age group because there were very few unmarried individuals older than 35 years.

Relationship between HCV and schistosomiasis. The association of anti-HCV status with active schistosomiasis, self-reported history of prior schistosomal infection, and history of injection therapy for schistosomiasis was assessed. *Schistosoma haematobium* ova were detected in the urine of 196 (4.1%) of the 4,792 study subjects who provided urine samples, with a higher ($P < 0.001$) prevalence among males (9.5%) than females (2.3%); 1,576 (26.1%) individuals re-

ported having had laboratory confirmed schistosomiasis infection in the past. A history of injection therapy for schistosomiasis was reported by 134 (2.2% of all participants and 13.2% of anti-HCV positive participants). Active schistosomal infection was not associated with anti-HCV status: the risk ratio for anti-HCV in those with ova in their urine compared with those without active *S. haematobium* infections was 0.8 (95% CI = 0.5–1.4) (Table 3). Anti-HCV positivity was significantly associated with both a history of schistosomiasis and prior therapy with anti-schistosomal injection therapy. These relationships remained significant after adjusting for age. This adjustment is particularly important for exposure to parenteral therapy since only those older than 30 years were at risk (age adjusted RR = 2.9, 95% CI = 2.4–3.6).

HCV PCR. We tested 513 of the 522 who had anti-HCV for the presence of HCV RNA; 323 (62.8%) of them tested positive in the RT-PCR, without significant variation by age, gender, education, or marital status. Among anti-HCV-posi-

TABLE 3
Schistosomiasis and antibody to hepatitis C virus (anti-HCV) status*

Category	Total	Anti-HCV positive Number positive/category (%)		RR (95% CI)	Age-adjusted RR†
		Yes	No		
Current infection					
All	4,790	14/196 (7.1)	391/4,596 (8.5)	0.84 (0.5, 1.4)	1.61 (0.98, 2.65)
Males	2,073	11/134 (8.2)	220/1,939 (11.3)	0.72 (0.41, 1.29)	1.45 (0.83, 2.54)
Females	2,717	3/62 (4.8)	171/2,657 (6.4)	0.75 (0.25, 2.29)	1.34 (0.45, 3.98)
Past infection					
All	6,031	201/1,576 (12.8)	321/4,455 (7.2)	1.77 (1.50, 2.09)	2.05 (1.75, 2.41)
Males	2,717	180/1,291 (13.9)	127/1,426 (8.9)	1.57 (1.26, 1.94)	1.67 (1.35, 2.05)
Females	3,314	21/285 (7.4)	194/3,029 (6.4)	1.15 (0.75, 1.77)	1.71 (1.11, 2.61)
≤ 30 years old	4,164	53/1,172 (7.9)	96/2,992 (3.2)	1.40 (1.01, 1.95)	1.29 (0.93, 1.80)
> 30 years old	1,867	148/404 (36.6)	225/1,463 (15.4)	2.38 (2.00, 2.84)	2.48 (2.06, 2.97)
Injection therapy					
All	6,031	69/134 (51.5)	453/5,897 (7.7)	6.70 (5.56, 8.08)	3.03 (2.50, 3.66)
Males	2,717	62/117 (53.0)	245/2,600 (9.4)	5.62 (4.57, 6.92)	2.12 (1.72, 2.61)
Females	3,314	7/17 (41.2)	208/3,297 (6.3)	6.53 (3.64, 11.69)	3.72 (2.04, 6.78)

* RR = risk ratio; CI = confidence interval.

† Mantel-Haenszel weighted RR, by five-year age groups.

tive subjects who both submitted urine samples and had serum tested for HCV RNA, the proportion with active *S. haematobium* infections was not different ($P = 0.62$) between those who were HCV RNA positive (8 of 252, 3.2%) and those who were HCV RNA negative (6 of 145, 4.1%).

DISCUSSION

Although very high for most other areas of the world, the prevalence of anti-HCV in our community is consistent with other studies that showed the prevalence in rural communities in Upper Egypt was approximately 10%, which was much lower than in inhabitants of villages in Lower Egypt.^{4,7,8,12,13} Among the reasons for this geographic variation in prevalence of HCV infection in Egypt may be the difference in the intensity and duration of intravenous tartar emetic schistosomiasis control programs in Upper and Lower Egypt, with the programs in Lower Egypt affecting a larger proportion of the population over a longer period of time and administering a greater number of doses. These control programs are believed to have infected a large proportion of the exposed population with HCV from the 1950s until the early 1980s, establishing a large reservoir of infection in adults in rural Egyptian communities. In Upper Egypt where *S. haematobium* is endemic, parenteral treatment campaigns for schistosomiasis were used less intensely and started later and discontinued earlier.¹³

Our data support this hypothesis. Males, who more frequently have schistosomiasis than females,^{14–17} and those more than 30 years of age who had risk of exposure to parenteral antischistosomal therapy,¹³ had much higher anti-HCV infection rates than females and those 30 years of age and younger, respectively. The gender difference in anti-HCV prevalence being present only in adults more than 30 years of age further supports this, as does the finding that active *S. haematobium* infections did not increase the risk for anti-HCV or for HCV RNA. However, a history of schistosomiasis increased the risk by 2.5-fold, and those who reported a history of therapy for schistosomiasis were almost three times as likely to have anti-HCV than those who did not.

There was a trend for those who were less educated, farmed, married, or provided health care to more likely be anti-HCV positive than those who did not meet these criteria. However, when adjusted for age and gender, none of these variables were significantly associated with anti-HCV status. If, following more extensive analysis, marriage proves to be a risk for HCV infection, it does not necessarily have to be entirely due to sexual exposures since married couples have frequent common exposures, other than sexual, which could transmit HCV.

The HCV RNA prevalence of 62.8% among our subjects having anti-HCV is lower than the 80–85% commonly referred to in the literature.¹⁸ However, this level is consistent with a previous report demonstrating HCV RNA among 62.5% of ELISA-positive Egyptian blood donors.¹ There are several potential reasons for this: among these are differences in subject population and reduced sensitivity of the RT-PCR method used for detecting genotype four strains (the predominant genotype in Egypt) or for detecting lower levels of viremia.⁹ Most reports of a higher prevalence of HCV

RNA among anti-HCV positive individuals were from subjects reporting previous blood transfusions or intravenous drug use, or were among patients with liver disease.^{19–21} As was recently pointed out by Kenny-Walsh in a report of women infected from HCV-contaminated anti-D immune globulin, those with less intensive exposures to HCV may have a lower prevalence of chronic infection.²² Only 55% of these women who were anti-HCV positive were also HCV RNA positive. An additional possibility is that the sera were not adequately processed, handled, and stored and had lost some of their RNA activity. This is unlikely. Blood was centrifuged and the sera were separated into five aliquots within 6 hr of venipuncture. It was kept frozen at -70°C in Assiut until it was transported in a truck with a freezer locker (ice cream transporter) to Shibin El Kom where it was placed in a -80°C freezer in the Liver Institute until individual aliquots were thawed for RT-PCR testing.

Subjects who chose to participate were different from those who declined in some characteristics, most notably gender, age, and educational background. Participants were more likely to be female and participating males were slightly younger than non-participating males. However, the age and gender adjusted prevalence of anti-HCV (9.2%) is not substantively different from the unadjusted prevalence (8.7%), and there was no evidence for confounding by educational background after adjusting for age. We have no reason to believe this village is substantially different from others in the area, and the prevalence of anti-HCV is consistent with that of other studies.⁸

Herein, we have described the baseline cross-section prevalence of anti-HCV and HCV-RNA in 6,031 inhabitants of a village in Upper Egypt. The prevalence of anti-HCV in Upper Egypt is high, albeit lower than in Lower Egypt, with continuing but limited transmission. Subsequent assessments of risk factors for prevalent and incident infection and the natural history of HCV in the community are underway.

Acknowledgments: Members of the Assiut University Hepatitis C Prevention Project field team and the village rural health unit assisted in collecting the data and samples from the subjects. Serologic testing was performed at the Liver Institute (Menoufiya University). This investigation could not have been performed without the careful project management of Mar-Jan Ostrowski.

Financial support: The Hepatitis C Prevention Project is supported by the United States Agency for International Development grant no. 263-G-00-96-00043-00.

Author's addresses: Mohammed A. Nafeh, Ahmed Medhat, Magda Shehata, and Yousef Swifee, Department of Tropical Medicine, Faculty of Medicine, Assiut University, Assiut, Egypt. Mohamed Abdel-Hamid and Nabil N. H. Mikhail, Hepatitis C Prevention Project, 10 Kasr El-Aini Street, Cairo, Egypt. Susan Watts, Social Research Center, American University in Cairo, PO Box 2511, 11511 Cairo, Egypt. Alan D. Fix and G. Thomas Strickland, International Health Program, Department of Epidemiology and Preventive Medicine, University of Maryland School of Medicine, 660 West Redwood Street, Baltimore, MD, 21201. Wagida Anwar and Ismail Sallam, Egyptian Ministry of Health and Population, 3 Magless El Shaab Street, Cairo, Egypt.

Reprint requests: G. Thomas Strickland, Department of Epidemiology and Preventive Medicine, School of Medicine, University of Maryland-Baltimore, 660 West Redwood Street, Baltimore, MD 21201.

REFERENCES

1. Saeed AA, al-Admawi AM, al-Rasheed A, Fairclough D, Bacchus R, Ring C, Garson J, 1991. Hepatitis C virus infection in Egyptian volunteer blood donors in Riyadh. *Lancet* 338: 459–460.
2. Kamel MA, Ghaffar YA, Wasef MA, Wright M, Clark LC, Miller FD, 1992. High HCV prevalence in Egyptian blood donors (letter). *Lancet* 340: 427.
3. Darwish MA, Raouf TA, Rushdy P, Constantine NT, Rao MR, Edelman R, 1993. Risk factors associated with a high seroprevalence of hepatitis C virus infection in Egyptian blood donors. *Am J Trop Med Hyg* 49: 440–447.
4. Abdel-Wahab MF, Zakaria S, Kamel M, Abdel-Khaliq MK, Mabrouk MA, Salama H, Esmat G, Thomas DL, Strickland GT, 1994. High seroprevalence of hepatitis C infection among risk groups in Egypt. *Am J Trop Med Hyg* 51: 563–567.
5. Bassily S, Hyams KC, Fouad RA, Samaan MD, Hibbs RG, 1995. A high risk of hepatitis C infection among Egyptian blood donors: the role of parenteral drug abuse. *Am J Trop Med Hyg* 52: 503–505.
6. Waked IA, Saleh SM, Moustafa MS, Raouf AA, Thomas DL, Strickland GT, 1995. High prevalence of hepatitis C in Egyptian patients with chronic liver disease. *Gut* 37: 105–107.
7. Darwish MA, Faris R, Clemens JD, Rao MR, Edelman R, 1996. High seroprevalence of hepatitis A, B, C, and E viruses in residents in an Egyptian village in The Nile Delta: a pilot study. *Am J Trop Med Hyg* 54: 554–558.
8. Arthur RR, Hassan NF, Abdallah MY, el-Sharkawy MS, Saad MD, Hackbart BG, Imam IZ, 1997. Hepatitis C antibody prevalence in blood donors in different governorates in Egypt. *Trans R Soc Trop Med Hyg* 91: 271–274.
9. Abdel-Hamid M, Edelman DC, Highsmith WE, Constantine NT, 1997. Optimization, assessment, and proposed use of a direct nested reverse transcription-polymerase chain reaction protocol for the detection of hepatitis C virus. *J Hum Virol* 1: 58–65.
10. Okamoto H, Okada S, Sugiyama Y, Yotsumoto S, Tanaka T, Yoshizawa H, Tsuda F, Miyakawa Y, Mayumi M, 1990. The 5'-terminal sequence of the hepatitis C virus genome. *Jpn J Exp Med* 60: 167–177.
11. Peters PA, Warren KS, Mahmoud AA, 1976. Rapid, accurate quantification of schistosome eggs via nuclepore filters. *J Parasitol* 62: 154–155.
12. Hibbs RG, Corwin AL, Hassan NF, Kamel M, Darwish M, Edelman R, Constantine NT, Rao MR, Khalifa AS, Mokhtar S, Fam NS, Ekladius EM, Bassily SB, 1993. The epidemiology of antibody to hepatitis C in Egypt. *J Infect Dis* 168: 789–790.
13. Frank C, Mohamed MK, Strickland GT, Lavanchy D, Arthur RR, Magder LS, El Khoby T, Abdel-Wahab Y, Aly Ohn ES, Anwar W, Sallam I, 2000. The role of parenteral antischistosomal therapy in the spread of hepatitis C virus in Egypt. *Lancet* 355: 887–891.
14. El-Khoby T, Galal N, Fenwick A, Barakat R, El-Hawey A, Nooman Z, Habib M, Abdel-Wahab F, Gabr NS, Hammam HM, Hussein MH, Mikhail NNH, Cline BL, Strickland GT, 2000. The epidemiology of schistosomiasis in Egypt: summary findings in nine governorates. *Am J Trop Med Hyg* 62 (suppl): 88–99.
15. Ghaffar YA, Fattah SA, Kamel M, Badr RM, Mahomed FF, Strickland GT, 1991. The impact of endemic schistosomiasis on acute viral hepatitis. *Am J Trop Med Hyg* 45: 743–750.
16. Kamel MA, Miller FD, el Masry AG, Zakaria S, Khattab M, Esmat G, Ghaffar YA, 1994. The epidemiology of *Schistosoma mansoni*, hepatitis B and hepatitis C infection in Egypt. *Ann Trop Med Parasitol* 88: 501–509.
17. Hamman HM, Allam FAM, Moftah FM, Abdel-Aty MA, Hany AH, Abd-El-Motagaly KF, Nafeh MA, Khalifa R, Mikhail NNH, Talaat M, Hussein MH, Strickland GT, 2000. The epidemiology of schistosomiasis in Egypt: Assiut Governorate. *Am J Trop Med Hyg* 62 (suppl): 73–79.
18. Alter MJ, Mast EE, Moyer LA, Margolis HS, 1998. Hepatitis C. *Infect Dis Clin North Am* 12: 13–26.
19. Alter MJ, Margolis HS, Krawczynski K, Judson FN, Mares A, Alexander WJ, Hu PY, Miller JK, Gerber MA, Sampliner RE, L. ME, J. BM, 1992. The natural history of community-acquired hepatitis C in the United States. The Sentinel Counties Chronic non-A, non-B Hepatitis Study Team. *N Engl J Med* 327: 1899–1905.
20. Shakil AO, Conry-Cantilena C, Alter HJ, Hayashi P, Kleiner DE, Tedeschi V, Krawczynski K, Conjeevaram HS, Sallie R, Di Bisceglie AM, 1995. Volunteer blood donors with antibody to hepatitis C virus: clinical, biochemical, virologic, and histologic features. The Hepatitis C Study Group. *Ann Intern Med* 123: 330–337.
21. Esteban JI, Lopez-Talavera JC, Genesca J, Madoz P, Viladomiu L, Muniz E, Martin-Vega C, Rosell M, Allende H, Vidal X, Gonzalez A, Hernandez JM, Esteban R, Guardia J, 1991. High rate of infectivity and liver disease in blood donors with antibodies to hepatitis C virus. *Ann Intern Med* 115: 443–449.
22. Kenny-Walsh E, 1999. Clinical outcomes after hepatitis C infection from contaminated anti-D immune globulin. Irish Hepatology Research Group. *N Engl J Med* 340: 1228–1233.