Epidemiol. Infect. (2013), **141**, 1831–1839. © Cambridge University Press 2012
doi:10.1017/S0950268812002312

Persisting role of healthcare settings in hepatitis C transmission in Pakistan: cause for concern

E. VER HOEVE[1], A. J. CODLIN[2], F. JAWED[2], A. J. KHAN[2], L. SAMAD[3], K. M. VATCHEVA[1], M. B. FALLON[4], M. ALI[3], S. K. NIAZ[3], J. B. McCORMICK[1] AND S. P. FISHER-HOCH[1]*

[1] *The University of Texas School of Public Health Brownsville Regional Campus, The University of Texas Health Science Center at Houston, Brownsville, TX, USA*
[2] *Interactive Research and Development (IRD), Karachi, Pakistan*
[3] *Indus Hospital, Karachi, Pakistan*
[4] *Division of Gastroenterology, Hepatology, and Nutrition, Department of Internal Medicine, The University of Texas Health Science Center at Houston, Houston, TX, USA*

Received 8 May 2012; Final revision 24 August 2012; Accepted 23 September 2012; first published online 1 November 2012

SUMMARY

Transmission of hepatitis C (HCV) in Pakistan is a continuing public health problem; 15 years ago it was linked to the practice of reusing therapeutic instruments in healthcare settings. We sought to examine current risk factors for HCV transmission in a hospital population in Karachi, Pakistan. We enrolled 300 laboratory-confirmed HCV-positive participants and 300 laboratory-confirmed HCV-negative participants from clinics at Indus Hospital. Independent and significant risk factors for both men and women were: receiving $\geqslant 12$ injections in the past year, blood transfusions, having had dental work performed, and delivery in hospital or transfusion for women. Interestingly, being of Mohajir origin or born in Sindh province were protective. Encouragingly, a strong protective effect was observed for those that reported bringing their own needle for injections (59%). The widespread reuse of therapeutic needles in healthcare settings in Karachi remains a major driver of the HCV epidemic.

Key words: Epidemiology, hepatitis C.

INTRODUCTION

The World Health Organization (WHO) estimates that hepatitis C virus (HCV) infects 3–4 million people and causes 366000 deaths annually [1, 2]. In addition, a further 130–170 million people are chronically infected with HCV. The majority of these chronic infections are asymptomatic, but as many as 80% will go on to develop liver disease including cirrhosis and liver cancer [2, 3]. The majority of the 3–4 million incident HCV cases reported each year globally are in low- and middle-income countries (LMICs) [4]. South Asia, in particular, is designated as a high burden area for HCV, with prevalence in the general population estimated to be 2·15% [2, 3]. According to the WHO's Global Burden of Disease Report in 2004, acute HCV infections were responsible for 119 disability-adjusted life years (DALYs) out of 23450 DALYs caused by infectious and parasitic diseases in LMICs found in the WHO's Eastern

* Author for correspondence: Dr S. Fisher-Hoch, 80 Fort Brown, Brownsville, TX, USA.
(Email: Susan.P.Fisher-Hoch@uth.tmc.edu)

Mediterranean region (which includes Pakistan) [5]. In Pakistan (estimated 2012 population: 189 million), an estimated 10 million people are infected with HCV with an average adult prevalence ranging from 2·5% to 25% [1, 3].

Several risk factors for HCV infection are uniquely prominent in Pakistan, most commonly, the reuse of equipment for therapeutic injections, unscreened blood transfusions, medical infusions, injecting drug use, sharing of razors and toothbrushes in the household, and being shaved by a barber, in addition to surgery, dental work, and sexual contact [1, 6, 7]. The major reported risk factor for HCV infection is the receipt of therapeutic injections using unsterilized, reused needles [7–10]. Pakistanis receive the highest number of injections *per capita* annually among LMICs, estimated to be between 8·2 and 13·6 per person annually [7]. The administration of injections by healthcare workers and receipt of injections by patients for even minor ailments is popular; many believe that injections provide quicker relief of symptoms, have greater effectiveness, and a lower frequency of side-effects compared to oral forms of medication [10].

The lack of blood donor screening facilities and blood transfusion standards also contribute significantly to the spread of HCV in Pakistan [1, 3, 7, 11, 12]. The reported HCV prevalence in blood donors in Pakistan ranges from 1·2% to 7·5% nationwide and from 1·2% to 3·6% in Karachi [3]. The prevalence of HCV infection in people who have received multiple blood transfusions is significantly higher, occasionally reaching 60% [3]. Visiting the dentist is also a known risk factor for HCV. Men and women who have received dental treatment are respectively 1·25 and 1·31 times more likely to have a HCV infection than those who have not received dental treatment [4]. Similarly, 18·6% [95% confidence interval (CI) 14·7–22·5] of newly reported HCV cases attending one of five public sector tertiary-care hospitals located in Lahore, Peshawar, Karachi, Quetta, and Islamabad visited the dentist $\leqslant$6 months before the onset of symptoms [13].

The objective of this study was to determine key risk factors contributing to HCV transmission in 2011 in Karachi. Much of the previous data was obtained in rural or peri-urban communities [6, 10]. We hypothesized that the risk factors in a population in a large, urban centre with mixed ethnicities and cultures may be different from those in the overall Pakistani population or rural populations [14] suggesting a potential difference in risk factors in each region. The overall goal was to identify the underlying drivers and wider public health impact of HCV transmission in large urban agglomerations in the region and to gain a sense of whether progress has been made in mitigating any of the previously reported risk factors.

METHODS

Study setting and population

Indus Hospital is a high-quality, free of charge, tertiary-care facility located in a low-income area of Karachi. We designed a case-control study to assess the risk factors for acquiring HCV infection in patients newly and previously diagnosed with HCV at Indus Hospital. Most of these patients had been found to have elevated alanine aminotransferase levels thus triggering the need for an HCV antibody test. The remaining patients were identified through routine screening (blood donation, immigration, employment, medical assessment) where they were tested for HCV antibodies. None of the patients were acutely jaundiced. Six hundred participants (300 cases, 300 controls) were enrolled between 20 May 2011 and 15 March 2012.

Pakistan has five main ethnicities. Punjabis make up an estimated two-thirds of the population and originate from Punjab province where Lahore is located. Sindhis originate from Sindh province in which Karachi is located. The Pashtuns, a formerly nomadic people, are found in the North and Northwest, they also inhabit Afghanistan. The Balochi were also originally nomadic and hail from the Southwestern part of Pakistan (Balochistan). Mohajirs are of mixed ethnicity and are Muslim refugees or descendants of refugees from pre-partition India [15]. Published studies were used to estimate the lowest level of potential exposure to injections in cases and controls. Using a two-sided confidence level of 95%, a power of 80%, and a case:control ratio of 1:1, we estimated a minimum of 291 cases and 291 controls were required for the study. Allowing for a 3% refusal rate, we estimated that a total sample size of 300 participants in each study arm was required to detect the minimum effect.

Eligibility criteria

All participants enrolled in this study were laboratory-confirmed as being positive or negative for HCV antibodies using a chemiluminescence antibody immunoassay (Johnson and Johnson Vitros ECI, USA). If the antibody test was inconclusive, a confirmatory PCR (Johnson and Johnson) was performed. This information was recorded, stored, and confirmed by the hospital's Medical Information System (MIS).

An HCV-positive case was an Indus Hospital patient originating from the gastroenterology clinic with laboratory-confirmed HCV infection aged ⩾18 years. Only cases that had been diagnosed at Indus Hospital within the past year were enrolled. Controls were drawn from two sources of residents found either in the immediate catchment area of Indus Hospital or from individuals who attended the hospital for services. The first (30% of controls) source of HCV-negative controls were Indus Hospital patients recruited from hospital services with a negative laboratory-confirmed result within the past year. The second (70% of controls) source comprised participants from the community-based Indus Hospital Community Cohort (IHCC) with a negative laboratory-confirmed HCV result in the preceding year. The IHCC is a cohort consisting of a randomly selected sample from the Indus Hospital's catchment population for whom routine HCV antibody assays were available. All controls were aged ⩾18 years. HCV-positive cases who were on dialysis or who had been diagnosed with β-thalassaemia (and thus received frequent transfusions) were excluded from the study, as were HCV-negative controls who were healthy male blood donors.

Data management and analysis

Informed consent was obtained from all participants and a standardized questionnaire assessing demographic, behavioural, and medical risk factors for HCV infection was administered in Urdu by trained community health workers. Questionnaire data was digitized using standard double data entry and reconciliation methods. All participants were able to fully complete the questionnaire during the interview. (See Supplementary online material for questionnaire.) Descriptive statistics, odds ratios (ORs) and 95% confidence intervals (CIs) for demographic characteristics were generated using a simple logistic regression procedure. Demographic characteristics were considered significant if $P<0{\cdot}05$ or the 95% CI for the OR did not include 1·00. Three multivariable logistic regression models, one overall model and two gender-specific models were created. Interactions between the variables in these models were also analysed. The two sources of controls were combined to achieve the sample size required to detect the minimum effect; several variables also had too many levels to make stratification by control group possible. Moreover, the hospital controls were typically from the same community as the IHCC controls and both groups had visited Indus Hospital for many of their medical needs; however, a few patients were known to have travelled from places as far away as Afghanistan. The two control groups only significantly differed in age, birth place, past pregnancy, and ever having dental work performed. Therefore, bias between these two groups is limited. Furthermore, the case and control groups also originated from the same community which limits selection bias. With no non-responders or refusals, analysis regarding these two groups was not conducted. All statistical analyses were conducted using SAS version 9·2 (SAS Institute Inc., USA).

Ethical approval

This study was approved by the University of Texas Health Science Center Houston Committee for the Protection of Human Subjects, IRB- HSC-SPH-11-0257, and the Interactive Research and Development (IRD) Institutional Review Board, IRD_IRB_2011_05_002.

RESULTS

Study participants

The mean age (±S.D.) of the cases was 39·3 (±12·5) years and was significantly different from the mean age of the controls, 36·1 (±13·7) years. The mean income between both groups was not significantly different (Table 1). Those identifying themselves as Mohajir or Sindhi were significantly less likely to be HCV positive compared to all other ethnicities. Additionally, the education level of Sindhi or Mohajir participants was significantly higher than participants of other ethnicities. Sixty-two per cent of the participants were born in Karachi or Sindh province, while 20% were born in Punjab province. Participants born in Karachi/Sindh province were 0·37 (95% CI 0·24–0·58) times less likely to be HCV positive compared to all participants born elsewhere. Participants who were married were significantly more likely to be HCV positive (Table 2).

Table 1. *Mean and standard deviation of key continuous socio-demographic variables and their association with HCV status*

Continuous variables	HCV +, mean (S.D.)	HCV −, mean (S.D.)	*P* value*
Age (years)	**39·3 (12·5)**	**36·1 (13·7)**	**0·002**
Income (Pakistani rupees)	8803·2 (4943·9)	9310·4 (7731·6)	0·359

S.D., Standard deviation.
* Student's *t* test for equality of means.
Bold values indicate statistically significant variables ($P<0.05$).

Table 2. *Frequency and percentage of key categorical socio-demographic variables and their association with HCV status*

Categorical variables	Total, *n* (%)	HCV +, *n* (%)	HCV −, *n* (%)	OR (95% CI)
Gender				
Male	214 (35)	109 (51)	105 (49)	1·060 (0·759–1·480)
Female	386 (65)	191 (50)	195 (50)	Ref.
Ethnicity				
Mohajir/Sindhi	227 (37)	83 (37)	144 (63)	**0·414 (0·295–0·582)**
Other	373 (62)	217 (58)	156 (42)	Ref.
Birth place				
Karachi/Sindh	373 (62)	142 (38)	231 (62)	**0·373 (0·239–0·581)**
Islamabad/Punjab	121 (20)	92 (76)	29 (24)	**1·923 (1·084–3·410)**
Other	106 (18)	66 (62)	40 (38)	Ref.
Marital status				
Married	470 (78)	253 (54)	217 (46)	**2·059 (1·379–3·075)**
Not married	130 (22	47 (36)	83 (64)	Ref.
Education (years)				
No school/*madrassa*	299 (50)	147 (49)	152 (51)	0·837 (0·558–1·253)
Primary (1–5)/secondary (6–8)	163 (27)	79 (48)	84 (52)	0·814 (0·517–1·281)
Metric (9–10)/university	116 (26)	74 (54)	64 (46)	Ref.
Working status				
Currently working	199 (33)	93 (47)	106 (53)	0·822 (0·585–1·156)
Not currently working	401 (67)	207 (52)	194 (48)	Ref.
Occupation				
Labourer/skilled worker	268 (47)	134 (59)	134 (50)	1·163 (0·837–1·616)
Other	305 (53)	141 (46)	164 (54)	Ref.

OR, Odds ratio; CI, confidence interval.
Bold values indicate statistically significant variables ($P<0.05$).

Risk factors

A univariable analysis of all the risk factors showed that participants that: received ⩾12 injections in the past year, received ⩾12 medical infusions in the past year, ever had a blood transfusion, were hospitalized for an accident or disease, or ever had dental work performed were all significantly more likely to be HCV positive. Participants who received a blood transfusion were 2·21 (95% CI 1·42–3·43) times more likely to be HCV positive compared to those who did not receive a transfusion. Participants who received ⩾12 injections were 8·02 (95% CI 3·94–16·32) times more likely to be HCV positive compared to those who received 1–4 injections in the past year. Participants who brought their own needle for injections were 0·29 (95% CI 0·0·19–0·43) times less likely to be HCV positive compared to those who did not bring their own needle. Those who ever had dental work done were 1·97 (95% CI 1·35–2·89) times more likely to be HCV positive compared to those who did not have dental work done in the past year (Table 3). Being shaved by a barber, sharing a toothbrush in the household, being sexually active, and having a tattoo were not found to be significant.

Women who had ever been pregnant, received a blood transfusion during pregnancy, or gave birth in a government or private hospital were all significantly

Table 3. *Frequency and percentage of key risk factors and their association with HCV infection*

Categorical variables	Total, *n* (%)	HCV +, *n* (%)	OR (95% CI)
Hospitalized for accident/disease	94 (16)	60 (64)	**1·964 (1·245–3·097)**
Ever received blood transfusion	145 (24)	95 (66)	**2·317 (1·570–3·419)**
Injections			
Received ⩾12 injections in the past year	116 (23)	82 (71)	**5·566 (3·215–9·634)**
Received 5-11 injections in the past year	81 (16)	35 (43)	1·756 (0·985–3·131)
Received 1–4 injections in the past year	129 (25)	39 (30)	Ref.
Medical infusions			
Received ⩾12 medical infusions in the past year	34 (6)	24 (71)	**2·399 (1·064–5·407)**
Received 5–11 medical infusions in the past year	41 (7)	23 (56)	1·278 (0·631–2·586)
Received 1–4 medical infusions in the past year	132 (24)	66 (50)	Ref.
General practitioner administered injection/infusion	267 (65)	146 (55)	0·762 (0·506–1·145)
Brought own needle for injection/infusion	252 (59)	104 (41)	**0·286 (0·189–0·432)**
Piercing	386 (64)	191 (50)	0·944 (0·676–1·318)
Piercing location			
Jeweller's	12 (4)	2 (17)	0·212 (0·045–1·000)
At home from an ear piercer	35 (10)	18 (51)	1·799 (0·772–4·191)
Friend or family member	288 (86)	132 (46)	Ref.
Sexually active	373 (64)	178 (48)	0·816 (0·583–1·143)
Ever had dental work	257 (43)	166 (65)	**2·866 (2·049–4·009)**
Ever pregnant*	322 (91)	177 (55)	**8·545 (2·930–24·921)**
Number of pregnancies*			
4–6	124 (38)	65 (52)	0·842 (0·488–1·454)
⩾7	109 (34)	62 (57)	1·009 (0·574–1·772)
1–3	90 (28)	51 (57)	Ref.
Received a blood transfusion during pregnancy*	57 (21)	39 (68)	**2·864 (1·538–5·335)**
Place of delivery*			
Government hospital	76 (29)	44 (58)	**2·087 (1·184–3·678)**
Private hospital	49 (18)	29 (59)	**2·201 (1·135–4·267)**
Friend/family member's home or maternity home	141 (53)	56 (40)	Ref.
Mode of delivery*			
Vaginal delivery	237 (89)	105 (44)	**0·133 (0·045–0·394)**
Caesarean section/use of instruments	28 (11)	24 (86)	Ref.

OR, Odds ratio; CI, confidence interval.
* Women only.
Bold values indicate statistically significant variables ($P<0{\cdot}05$).

more likely to be HCV positive than those who had never been pregnant, receive a blood transfusion, or had a birth at a friend's or family member's home. Additionally, women who had a vaginal delivery were significantly less likely to be HCV positive compared to those who had a Caesarean section (Table 3).

In the multivariable analysis we created a combined model consisting of both men and women before building gender-specific models. The combined model showed that participants who ever had dental work performed, ever had a blood transfusion, or received ⩾12 injections were significantly more likely to be HCV positive. Participants who brought their own needle or were born in Sindh province were significantly less likely to be HCV positive (Table 4). The female-only model revealed that women who received ⩾12 injections, ever had dental work performed, or received a blood transfusion while pregnant were significantly more likely to be HCV positive. Women who brought their own needle for their injection or medical infusion as well as those who identified themselves as being of Mohajir or Sindhi ethnicity were significantly less likely to be HCV positive (Table 4). The male-only model revealed that men who brought their own needle or were born in Sindh province were significantly less likely to be HCV positive. Additionally, men who had ⩾12 injections in the past year were significantly more likely to be HCV positive compared to those who had 1–4 injections in the past year (Table 4). No significant interactions were detected in any of these three models.

Table 4. *Multivariable models for risk factors associated with HCV status (n=308)*

Categorical variables	OR	95% CI
Both sexes (*n*=438)		
Ever had dental work performed	**2·095**	**(1·201–3·655)**
Brought own needle for injection	**0·376**	**(0·210–0·673)**
Received ⩾12 injections in the past year	**4·469**	**(2·349–8·499)**
Received 5–11 injections in the past year	1·483	(0·746–2·951)
Ever received a blood transfusion	**2·397**	**(1·201–4·785)**
Hospitalized for an accident or disease	1·153	(0·569–2·335)
Mohajir or Sindhi ethnicity	0·570	(0·319–1·019)
Currently working/worked as a labourer	1·006	(0·576–1·757)
Born in Sindh Province	**0·226**	**(0·102–0·501)**
Born in Northern areas	0·532	(0·210–1·345)
Male gender	*1·153*	*(0·993–2·335)*
Females only (*n*=130)		
Received ⩾12 injections in the past year	**5·479**	**(1·832–16·388)**
Received 5–11 injections in the past year	1·435	(0·406–5·075)
Hospitalized for an accident or disease	0·616	(0·156–2·444)
Mohajir or Sindhi ethnicity	**0·255**	**(0·086–0·757)**
Vaginal mode of delivery	0·173	(0·011–2·749)
Brought own needle	**0·154**	**(0·053–0·452)**
Ever had dental work performed	**3·325**	**(1·226–9·021)**
Baby delivered at Government hospital	0·884	(0·265–2·949)
Baby delivered at private hospital	1·676	(0·480–5·848)
Received transfusion while pregnant	**5·541**	**(1·272–24·137)**
Males only (*n*=123)		
Brought own needle	**0·325**	**(0·130–0·809)**
Received ⩾12 injections in the past year	**2·813**	**(1·055–7·499)**
Received 5–11 injections in the past year	0·748	(0·265–2·109)
Born in Sindh province	**0·253**	**(0·077–0·828)**
Born in Northern areas	0·608	(0·154–2·405)
Ever received blood transfusion	2·468	(0·577–10·558)
Hospitalized for an accident or disease	1·829	(0·641–5·213)
Ever had dental work performed	*2·097*	*(0·918–4·791)*

OR, Odds ratio; CI, confidence interval.
Bold values indicate statistically significant variables ($P<0{\cdot}05$). Italicized values indicate borderline significant variables.

DISCUSSION

Fifteen years after the original reports on the risks of HCV transmission in Pakistan, a wide range of poor practices in healthcare settings continues to drive the HCV epidemic in Karachi. Despite some efforts by government and non-governmental organizations to raise awareness regarding the risks of HCV transmission, it remains common in healthcare settings, particularly due to the reuse of syringes and needles for therapeutic injections. Administering and receiving unsafe and unnecessary injections for a variety of minor ailments remains embedded in the health practice and culture. A synergistic response is created through this prevailing belief in the power of injections and the tendency of providers to give injections for financial gain [10].

Our findings suggest that HCV transmission is primarily occurring in healthcare settings of all types and remains dominated by the use of needles or contaminated blood products and instruments. We found that receiving therapeutic injections was still independently and strongly associated with HCV status and was closely related to the number of injections an individual was receiving. The epidemic of therapeutic injections in Pakistan is both well established and well known such that this finding is neither new nor unique [7–10]. What is new, and most disturbing, is that despite efforts, the practice has continued unabated in Karachi during the 15 years since the problem was first reported.

We are not clear, however, as to why people in this population seek injections to this extent, or how much the use of injections may be driven by practitioners. We have previously shown that, when asked, patients will generally say that the practitioner recommended the injection, whereas when practitioners are questioned, they say it was requested by the patient [10]. These health-seeking and healthcare behaviours need to be explored in a targeted study. What is clear is that many healthcare practitioners lack training, resources or good intentions and put themselves and their patients at risk for HCV [10, 16, 17]. Although the purchase of clean needles and syringes by patients is clearly an effective protection, the poverty and low levels of health literacy make the purchase of new or cleaned needles impractical for many, and not cost-effective for health practitioners working in the competitive private healthcare sector [16, 17]. Sadly, even the purchase of new syringes does not always guarantee safety from HCV transmission. Clinical laboratories often dump used syringes at community waste sites or laboratory housekeeping staff steal the used syringes only to have healthcare waste dealers repackage the discarded or stolen syringes and sell them as new [9]. Nevertheless, it was encouraging to find that a significant number of people were well enough informed to bring their own needle for an injection and were consequently significantly less likely to be HCV positive. However, it is also clear that this understanding is not implemented widely enough to make a major impact on transmission.

In accord with this study, dental procedures have previously been reported as a significant risk factor for HCV in Pakistan [4, 18–20]. Contaminated dental equipment must be assumed to be the source of HCV infection along with possible use of unclean needles for major and minor dental surgeries [21–23]. Similar to health practitioners without formal education administering unsafe injections, unqualified dental practitioners also administer unsafe procedures to their patients [8]. In the univariable analysis, participants who were hospitalized for an accident or disease were more likely to be HCV positive, a finding consistent with other reports and further evidence implicating medical procedures as a source of transmission [4, 18].

All three multivariable models suggest that participants who had ever received a blood transfusion were more likely to be HCV positive. There is a large demand for blood transfusions in Pakistan often by women with pregnancy-related complications and because of widespread anaemia; blood transfusions are regularly administered at a number of blood banks run by private institutions, non-governmental organizations, government institutions, or semi-government organizations [12, 24, 25]. Blood banks in Pakistan and those in other developing countries often operate below WHO standards, thereby acting as a potential source of bloodborne pathogen infection [12, 14, 25]. As a result of the early efforts of our group, regulations were established in Sindh province many years ago regulating safety in blood banks and requiring HCV screening. However, implementation and enforcement remains problematical and blood banks continue to be a frequent source of HCV infection [12]. Furthermore, no centralized system or programme is currently in place that regulates blood transfusions in Karachi [25]. One major problem is that HCV assays are prohibitively expensive for most Pakistanis, with the cost of screening for reagents alone about US$10 per test. This unacceptable situation needs to be addressed.

Regardless of gender, receiving $\geqslant 12$ therapeutic injections in the past year was highly associated with HCV infection. Nevertheless, both gender and ethnicity (including place of birth) impacted the likelihood of being HCV positive. In this study we determined that risk factors for transmission differed between genders. The univariable analysis showed that for women, mode of child birth, receiving a blood transfusion during pregnancy, having delivery at a government or private hospital and a history of pregnancy were all associated with positive HCV status. There is little published data available on place and type of delivery, although that which has been published is likely to have significant implications for HCV transmission [4, 18]. However, in our multivariable analysis simply having a blood transfusion during pregnancy remained independently significant. Although we cannot exclude that HCV might have been transmitted through contaminated needles, blood products, or instruments used during a Caesarean section or other obstetric procedure, it is clear that giving birth in a healthcare setting considerably increases the risk to women [4, 18].

Although the risk factors identified in this large study are common in Pakistanis and have been reported elsewhere, considerable regional variations, and possible temporal trends justified the need to better determine risk factors on which to base intervention strategies. Interestingly, both the overall and male multivariable models showed that those born in Sindh province compared to those born in Punjab province were significantly less likely to be HCV positive. This finding could be related to varying cultural practices among Pakistani ethnicities and potentially reflect differing socioeconomic conditions. Additionally, the female model showed that participants of Sindhi or Mohajir ethnicity were less likely to be HCV positive. The significant difference in education level seen between those of Mohajir/Sindhi ethnicity and all other ethnicities may contribute towards this observed protective effect. Even though we did gather some data, our study was not designed to accurately detect differences in ethnicities. This would require further detailed questionnaires and genetic analyses and a much larger sample size.

Several limitations were present in this study. Since the exposure variables refer to past events recall bias is an issue and using detailed questions to verify answers would be difficult to design. We utilized a technique which assists participants in recall by asking questions that serially increase the time span over which injections were received [6]. Many culturally taboo variables such as alcohol and drug consumption (both of which are illegal) were subject to respondent bias and were not thought sufficiently accurate for analysis. With limited personnel, participants were only enrolled during the afternoons on Mondays, Wednesdays and Fridays, thereby making it difficult to match controls and cases for age and gender. By enrolling controls from both the hospital and the community we attempted to minimize selection bias by using two comparison groups, but the sample was not randomly representative of the community. Although the overall sample size was adequate, stratifying for sex reduced power, and this may have limited the results of multivariable analyses. Furthermore, the sampling frame was not designed to properly assess ethnic and socioeconomic differences. The strength of our study was in detailed information and rigorous analyses and the importance of the messages that emerged.

Much of current HCV detection involves screening and treating for chronic disease. This approach at the individual patient level cannot impact a generally invisible epidemic where the preclinical interval may last for several years [2]. As complications from HCV begin to present themselves after the subclinical period, the real devastation of this epidemic will take its toll. Many studies have found that HCV awareness in Pakistan is very low, although when asked, many people perceive hepatitis as one of the leading health threats. Assessment of HCV knowledge at a family medicine clinic in Karachi reported in 2002 that about 50% and 46% of males and females, respectively, did know that HCV could be transmitted by needles and injections [7, 26]. These data are supported by our observation that a considerable number of patients reported taking their own needles for injections. In order to prevent new cases of HCV in Pakistan, a population-level preventative approach must be expanded through the development of communication messages and behavioural interventions specifically tailored to this population. Use of cell phones to reinforce behaviour might be particularly effective since cell phone use is widespread even in the poorest communities.

Healthcare practitioners at all levels are clearly an important target for HCV education with messages emphasizing the disastrous consequences of this infection and the simple procedures needed to avoid transmission. For some practitioners, it may be necessary to provide financial incentives or equipment (e.g. clean, single-use needles) to induce changes in their medical practices and to offset a decrease in their profits. Making practitioners legally responsible for transmission might be a useful step to curb the practice of reusing needles for injections, but would be difficult to monitor and enforce. The risks to the practitioners, themselves, should be emphasized and could add to the motivation. We need to gather more detailed data on key places where high-risk injections, blood transfusions, dental work, and deliveries occur. Determining transmission within such centres remains a difficult problem but could be addressed through a HCV surveillance programme. Access to effective and affordable treatment for HCV infection may become a reality in the future, but public education, HCV surveillance in high-risk settings, and market interventions promoting auto-disable syringes need to be prioritized now. Until this happens, HCV transmission through unsafe injection use, dental procedures, and blood transfusions will remain a major public health challenge in Karachi, in Pakistan and throughout the region.

SUPPLEMENTARY MATERIAL

For supplementary material accompanying this paper visit http://dx.doi.org/10.1017/S0950268812002312.

ACKNOWLEDGMENTS

The authors acknowledge the contribution of the HCV field work team at Indus Hospital who were responsible for all data collection and entry as well as the funding provided by existing grants at Indus Hospital. The authors are grateful for the support provided by Indus Hospital. We acknowledge the training and support provided by faculty and staff to E.V.H. and A.C. from the Hispanic Health Research Center and Clinical Research Unit in Brownsville, funded by MD000170 P20 from the National Center on Minority Health and Health Disparities (NCMHD), and the Centers for Translational Science Award 1U54RR023417-01 from the National Center for Research Resources (NCRR).

DECLARATION OF INTEREST

None.

REFERENCES

1. **Ali SA, *et al.*** Hepatitis B and hepatitis C in Pakistan: prevalence and risk factors. *International Journal of Infectious Diseases* 2009; **13**: 9–19.
2. **World Health Oragnization.** Hepatitis C. WHO fact sheet no. 164. 2011.
3. **Jafri W, Subhan A.** Hepatitis C in Pakistan: magnitude, genotype, disease characteristics and therapeutic response. *Tropical Gastroenterology* 2008; **29**: 194–201.
4. **Janjua NZ, *et al.*** Health care risk factors among women and personal behaviours among men explain the high prevalence of hepatitis C virus infection in Karachi, Pakistan. *Journal of Viral Hepatitis* 2010; **17**: 317–326.
5. **World Health Organization.** The global burden of disease: 2004 update, 2008.
6. **Luby SP, *et al.*** The relationship between therapeutic injections and high prevalence of hepatitis C infection in Hafizabad, Pakistan. *Epidemiology and Infection* 1997; **119**: 349–356.
7. **Waheed Y, *et al.*** Hepatitis C virus in Pakistan: a systematic review of prevalence, genotypes and risk factors. *World Journal of Gastroenterology* 2009; **15**: 5647–653.
8. **Ali I, *et al.*** Prevalence of HCV among the high risk groups in Khyber Pakhtunkhwa. *Virology Journal* 2011; **8**: 296.
9. **Abdul MS, *et al.*** Recycling of injection equipment in Pakistan. *Infection Control and Hospital Epidemiology* 2003; **24**: 145–146.
10. **Khan AJ, *et al.*** Unsafe injections and the transmission of hepatitis B and C in a periurban community in Pakistan. *Bulletin of the World Health Organization* 2000; **78**: 956–963.
11. **Hamid S, *et al.*** PSG consensus statement on management of hepatitis C virus infection –2003. *Journal of the Pakistan Medical Association* 2004; **54**: 146–150.
12. **Luby S, *et al.*** Evaluation of blood bank practices in Karachi, Pakistan, and the government's response. *Health Policy and Planning* 2000; **15**: 217–222.
13. **Centers for Disease Control and Prevention.** Establishment of a viral hepatitis surveillance system – Pakistan, 2009–2011. *Morbidity and Mortality Weekly Report* 2011; **60**: 1385–1390.
14. **Sievert W, *et al.*** A systematic review of hepatitis C virus epidemiology in Asia, Australia and Egypt. *Liver International* 2011; **31** (Suppl. 2): 61–80.
15. **Worldmark Encyclopedia of Nations.** (http://www.encyclopedia.com/topic/Pakistan.aspx). Accessed 19 July 2012.
16. **Kermode M.** Unsafe injections in low-income country health settings: need for injection safety promotion to prevent the spread of blood-borne viruses. *Health Promotion International* 2004; **19**: 95–103.
17. **Luby S, *et al.*** Long-term improvement in unsafe injection practices following community intervention. *International Journal of Infectious Diseases* 2005; **9**: 52–59.
18. **Khan UR, *et al.*** Case-control study of risk factors associated with hepatitis C virus infection among pregnant women in hospitals of Karachi-Pakistan. *Tropical Medicine and International Health* 2008; **13**: 754–761.
19. **Akhtar S, *et al.*** Hepatitis C virus infection in asymptomatic male volunteer blood donors in Karachi, Pakistan. *Journal of Viral Hepatitis* 2004; **11**: 527–535.
20. **Bari A, *et al.*** Risk factors for hepatitis C virus infection in male adults in Rawalpindi-Islamabad, Pakistan. *Tropical Medicine and International Health* 2000; **6**: 732–738.
21. **Qureshi H, *et al.*** Determination of risk factors for hepatitis B and C in male patients suffering from chronic hepatitis. *BMC Research Notes* 2009; **2**: 212.
22. **Al-Jamal M, *et al.*** Hepatitis C virus (HCV) infection in hemodialysis patients in the south of Jordan. *Saudi Journal of Kidney Diseases and Transplantation* 2009; **20**: 488–492.
23. **Piazza M, *et al.*** Detection of hepatitis C virus-RNA by polymerase chain reaction in dental surgeries. *Journal of Medical Virology* 1995; **45**: 40–42.
24. **World Health Organization.** Global database on blood safety report 2004–2005. 2008.
25. **Kassi M, *et al.*** Safe blood transfusion practices in blood banks of Karachi, Pakistan. *Transfusion Medicine* 2011; **21**: 57–62.
26. **Khuwaja AK, Qureshi R, Fatmi Z.** Knowledge about hepatitis B and C among patients attending family medicine clinics in Karachi. *Eastern Mediterranean Health Journal* 2002; **8**: 787–793.