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Importance and contribution of community, social and healthcare risk factors for Hepatitis C infection in Pakistan

Authors: *Adam Trickey[1,2], Margaret T May[1,2], Charlotte Davies[1], Huma Qureshi[3], Saeed Hamid[4], Hassan Mahmood[3], Quaid Saeed[5], Matthew Hickman[1,2], Nancy Glass[6], Francisco Averhoff[6], Peter Vickerman[1,2]

Affiliations:

1. School of Social and Community Medicine, University of Bristol, UK
2. National Institute of Health Research (NIHR) Health Protection Research Unit (HPRU) in Evaluation of Interventions
3. Pakistan Medical Research Council (PMRC), Islamabad, Pakistan
4. Department of Medicine, Aga Khan University, Karachi, Pakistan
5. National AIDS Control Programme, Islamabad, Pakistan
6. Centers for Disease Control and Prevention, Atlanta, USA

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***Corresponding Author information:**

Address: Canynge Hall, 39 Whatley Road, Bristol, BS8 2PS, United Kingdom

Email: adam.trickey@bristol.ac.uk **Telephone**: +44 117 928 7383

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Abstract

Pakistan has a high prevalence of hepatitis C virus (HCV) infection, estimated at 4.9% (2,290/46,843) in the 2007 national HCV sero-prevalence survey. We used data from this survey to assess the importance of risk factor associations with HCV prevalence in Pakistan.

Exposures were grouped as community (going to the barbers, sharing smoking equipment, having an ear/nose piercing, tattoo or acupuncture), healthcare (ever having haemodialysis, blood transfusion, or ≥5 injections in the last year), demographic (marital status and age), and socio-economic (illiterate or labourer). We used mutually adjusted multivariable regression analysis, stratified by sex, to determine associations with HCV infection, their population attributable fraction, and how risk of infection accumulates with multiple exposures. Strength of associations were assessed using adjusted odds ratios (aOR).

Community [aOR females 1.5(95% CI 1.2,1.8); males 1.2(1.1,1.4)] and healthcare [females 1.4(1.2,1.6); males 1.2(1.1,1.4)] exposures, low socio-economic status [females 1.6(1.3,1.80); males 1.3(1.2,1.5)], and marriage [females 1.5(1.2,1.9); males 1.4(1.1,1.8)] were associated with increased HCV infection. Among married women, the number of children was associated with an increase in HCV infection; linear trend aOR per child 1.06 (1.01,1.11). Fewer infections could be attributed to healthcare exposures (females 13%; males 6%) than to community exposures (females 25%; males 9%). Prevalence increased from 3% to 10% when cumulative exposures increased from 1 to ≥4 [aOR per additional exposure for females 1.5(1.4,1.6); males 1.2(1.2,1.3)].

A combination of community, healthcare and other factors appear to drive the Pakistan HCV epidemic, highlighting the need for a comprehensive array of prevention strategies.

Introduction

Hepatitis C virus (HCV) infection is a blood-borne pathogen that causes considerable morbidity and mortality globally[1, 2]. Recent estimates suggest that there are an estimated 80 million people living with HCV infection globally[3]. In developed countries, the primary mode of HCV transmission is injecting drug use[4, 5], but most of the HCV burden is concentrated in lower and middle income countries[1, 2], where most transmission is thought to be due to non-sterile healthcare and community practices[6, 7, 8, 9, 10, 11]. Healthcare practices associated with HCV-related risk include injections for medical purposes, blood transfusion, surgery, dental procedures, and receipt of intravenous infusions[10, 12, 13, 14, 15]. Community exposures found to be associated with HCV infection include barbering, tattooing, and ear and nose piercing[9, 12, 16, 17] .

The prevalence of HCV infection in most countries is low (<1%), but exceeds 4% in at least 12 countries including Egypt, Georgia, Nigeria, Russia, and Pakistan[3, 13, 18]. The burden of HCV is also concentrated, with about half (over 50 million) of all exposed adults (anti-HCV positive) living in six countries: Egypt, Pakistan, India, China, Russia and Nigeria[3].

Since the World Health Organisation (WHO) released its Global Health Strategy for eliminating viral hepatitis[19], there has been substantial interest in gaining a better understanding of how much HCV treatment scale-up is needed to reduce the transmission of HCV to low levels, especially in the highest prevalence settings such as Egypt, Georgia, and Pakistan[20 21]. However, to achieve large reductions in HCV transmission, it is also crucial to tackle the underlying risk factors that drive HCV transmission. Additionally, to effectively scale-up treatment it is also important to understand how to optimally target HCV testing interventions to minimize costs. This is especially true for countries with such a large burden of HCV as Pakistan, where there are an estimated 9 million people affected[18], and healthcare expenditure only makes up 0.9% of GDP (compared to 10.0% across the EU and 17.1% in USA[22]). Understanding what risk factors and markers are

predictive of HCV infection (eg. testing anti-HCV positive on a screening assay) could inform efficient, targeted screening recommendations that could reduce costs.

Recognised interventions for reducing HCV transmission among people who inject drugs (PWID) include opiate substitution therapy[23, 24, 25, 26, 27] and needle and syringe provision[25, 28], whereas modelling suggests that HCV treatment as prevention may also be an effective intervention[29, 30]. Beyond PWID, the focus globally for reducing HCV transmission has centred on behaviour change strategies (by WHO and the Safe Injection Global Network (SIGN)) to minimise unsafe injections[31]. During 2000 to 2010, these strategies succeeded in reducing reuse of injection equipment from 39.6% to 5.5% in the 71 countries assisted by WHO (including Pakistan)[32]. Recently, WHO launched a new global policy on injection safety to be piloted in a number of countries[33].

In Pakistan, since 2005 a number of major hepatitis prevention and control programs[34, 35] have focused on ensuring safe blood transfusions, improving disposal of syringes, increasing public awareness, and educating healthcare professionals and barbers[36, 37, 38]; but unfortunately the effectiveness of these interventions in reducing HCV transmission in Pakistan is unknown.

In 2007, a large (n=46,843) national sero-prevalence survey for HCV was carried out in Pakistan, and found anti-HCV prevalence of 4.9% overall, 6.7% amongst adults (aged ≥16 years), which did not differ by sex[18]. HCV infection prevalence was higher in the more populous provinces of Punjab (6.7%) and Sindh (5.0%), than in the less populated provinces of North West Frontier (1.5%) and Baluchistan (1.1%). Previous analyses using this dataset have only considered univariate associations with HCV sero-prevalence meaning that these associations did not take into account the effects of other variables and were open to issues of confounding. In this report, we expand on these previous unadjusted analyses by undertaking a multivariable analysis of associations with exposures and risk factors for HCV infection. We estimate the population attributable fraction (PAF) of HCV due to grouped community or healthcare exposures and risk factors. The PAF assesses the proportion of prevalent infections attributable to different exposures, and depends both on the

strength of association with HCV infection and the population prevalence of the risk factor. We also assess the cumulative effect of multiple exposures on lifetime HCV-related risk.

Materials and methods

Data Collection

Survey methods and sampling frame have been described previously[18]. Briefly, the survey was conducted in four provinces with households drawn from primary sampling units (PSU), 138 urban and 212 rural. Included subjects gave consent to being tested.

Demographic information

Age, sex, marital status (never married, married, divorced/separated/widowed), and relationship with the survey responder were collected for all members of the household. Each person and household had a unique identifier and was labelled with the district and province. If a person's age was missing they were removed from the analysis. Age was grouped as 20-29, 30-39, 40-49 and 50-59 years. The district was used to categorise households as urban or rural.

Outcome variable

Sample testing for HCV was carried out using the rapid Advanced Quality One Step HCV Test (Bionike Inc.) system, which is estimated to have a sensitivity of 97.1% (95% confidence interval: 89.8–99.6%) and specificity of 96.3% (92.5–98.5%)[39]. Participants were only tested for antibodies to HCV (anti-HCV), not active infection.

Exposures and risk factors collected in the survey

Data were collected on whether participants had ever received haemodialysis, blood transfusion, had a history of surgery, had a family history of HCV infection, practised matam (ranges from ceremonial chest beating to self-flagellation with implements such as chains, and blades)[40, 41], had visited a dentist, had visited a barber, shared a toothbrush, shared smoking equipment, had

either a tattoo or acupuncture, had either an ear or nose piercing. The number of medical injections received in the last year (0, 1-4, 5-10, >10), and the type or syringe used (none, new disposable, re-used syringe, don't know) was recorded. Occupation was dichotomised as labourer or not, education was dichotomised as illiterate or not.

Derived variables – grouped exposures and risk factors (S-ES, healthcare, and community)

Risk factors and exposures that are surrogates for risk factors (for example, literacy as an indicator of socio-economic status) were grouped as socio-economic status (S-ES), healthcare risk, and community risk exposures. S-ES for all individuals was defined using data on the survey responder (assumed to be the head of the household). An individual was defined to have low S-ES if the head of the household was either a labourer or illiterate. Risk due to healthcare exposures was high if the person had previously had haemodialysis, a blood transfusion, or ≥5 injections in the last year. Lower numbers of yearly injections were not included as a healthcare risk exposure because 77% of the population reported at least 1 injection in the last year. Community exposures included going to the barber, sharing smoking equipment, having an ear or nose piercing, or having a tattoo or acupuncture. For each of the healthcare and community grouped risk/exposure variables, we counted the number of exposures and categorised them as 0, 1, or ≥2 risk factors. We also counted the total number of exposures (0, 1, 2, 3, 4 or ≥5 risk factors).

We also hypothesised that unsafe childbirth practices could be a risk factor for HCV acquisition in adult females. Although the survey did not directly ask respondents about their number of childbirths, it did list each household member and what their relationship was to the head of the household. Therefore, for females aged 20-59 years that described themselves as wife or head of household, and who identified themselves as married, the number of childbirths (0, 1, 2, 3, 4, ≥5 children) was estimated by counting the number of children in the household described as sons or daughters. We did not estimate number of childbirths for older females because of the increased

likelihood that some of their children will have left home. Age was grouped as 20-29, 30-39, 40-49 and 50-59 years in this analysis.

Statistical analysis

We tabulated HCV prevalence for the country, and by province and district. We also tabulated prevalence by age (0-19, 20-29, ≥30 years) and sex and cross-tabulated with the prevalence of risk factors/exposures for HCV acquisition.

Association of exposures and risk factors with HCV

We used logistic regression to estimate the unadjusted and mutually adjusted odds ratio (OR) (with 95% confidence intervals (CI)) for HCV infection for each exposure. Separate models were estimated for each age group (0-19, 20-29, ≥30 years) and sex to see how associations varied across these groups. We also estimated the association of age with HCV prevalence by fitting separate models for males and females that included age as a covariate. Robust standard errors accounted for clustering by household.

To assess which of social, healthcare, or community interventions might have more impact on HCV risk/exposure, we grouped variables into these domains and re-estimated mutually adjusted sex-specific models which were also adjusted for province, age, and marital status. We performed a separate analysis splitting the derived group variables into their individual components. We examined whether age modified the association of exposures with HCV infection by including the interaction with age as a continuous variable. We defined Population Attributable Fraction (PAF) (equation 1) as the proportional reduction in HCV that would occur if the risk factor were reduced to no exposure, and calculated this for each of the three factor domains[42]. We examined the relationship between HCV prevalence and the total number of risk factor exposures by fitting sex-specific models adjusted for age and province. Exposures included in this analysis were having >4

injections, haemodialysis, blood transfusions, going to the barber, ear/nose piercing, tattoo/acupuncture, sharing smoking equipment, marriage, illiteracy and being a labourer.

Equation 1: $$PAF = \frac{P_e(RR-1)}{P_e(RR-1)+1}$$

P_e = current prevalence of exposure (e.g. >4 medical injections)

RR = the adjusted relative risk of disease due to that specific exposure

In a separate analysis we investigated the importance of childbirth for HCV acquisition in wives aged 20-59 years, adjusting associations for age, province, S-ES, healthcare and community risk. We did this among married females, as only those who are married were assumed to have children in Pakistan.

Sensitivity analyses

As the prevalence of HCV was much higher in the more populated provinces (Punjab and Sindh compared to Baluchistan and North West Frontier), we performed sensitivity analyses (i) without adjusting for province, (ii) omitting Baluchistan and North-west Frontier provinces.

Analyses were conducted in part through the National Institute for Health Research Unit (NIHR HPRU) in Evaluation of Interventions (University of Bristol) in partnership with Public Health England.

Statistical analyses were performed in Stata 13.

Results

Overall 2,290/46,843 (4.9% [95% CI 4.7-5.1%]) of participants had HCV antibodies. The HCV prevalence was 4.8% (4.6-5.1%) and 4.9% (4.7-5.2%) for females and males, respectively. The prevalence of HCV was 6.7% (6.4-7.0%), 5.1% (4.6-5.5%), 1.1% (0.9-1.3%) and 1.5% (1.2-1.8%) in Punjab, Sindh, Baluchistan and the North-west Frontier, respectively.

Association of ungrouped exposures and risk factors with HCV

Table 1 summarises the exposures associated with HCV stratified by age categories (0-19, 20-29, ≥30 years) and gender, which can be seen in further detail in supplementary table 1. Prevalence of exposures and association with HCV infection varied by these different categories, with HCV infection rates being higher among married persons (both males and females) compared to never married, increasing with age, and with community and healthcare exposures.

Association of grouped exposures and risk factors with HCV

The HCV prevalence and the unadjusted and adjusted (for age, marital status, province, community, healthcare, S-ES) OR (95% CI) of HCV infection for the community, healthcare, and S-ES grouped exposures are shown in table 2, separately for males and females. Community, healthcare and S-ES exposures were all strongly associated with HCV infection. The increase in adjusted odds of prevalent HCV infection associated with one community exposure was similar to that associated with one healthcare exposure. Although the association of HCV infection with multiple healthcare exposures was much stronger than that due to multiple community factors, only a small proportion of the population was exposed to multiple healthcare exposures (females 0.8%; males 0.2%). Older age was associated with HCV infection, with a more than doubling of the rate among males aged ≥40 years compared with those aged 20-29 years. Ever (versus never) being married was also associated with HCV infection. Results from the sensitivity analyses – both those excluding provinces with very low prevalence (supplementary table 2) and those not adjusting for province (supplementary table 3) – were similar to the main analysis, which included all provinces and adjusted for province. A separate analysis where we did not group the exposures that comprised the community, healthcare, and S-ES variables (supplementary table 4) shows that a high percentage of those who had had haemodialysis or a blood transfusion had HCV infection but few individuals had undergone these procedures.

Population attributable fraction of HCV prevalence due to different exposures and risk factors

Most HCV infections were not attributable to an identified risk factor/exposure, although a greater proportion of HCV infections among females, 38% compared to 15% of males, were attributable to either a community or healthcare exposure, with community factors accounting for a greater proportion of HCV infections among both females and males (figure 1). The PAF suggests that prevention of exposure to community risks could potentially reduce HCV prevalence by 25% (95% CI: 13-35%) and 9% (2-16%) in females and males, respectively. In contrast, prevention of exposure to healthcare risks could potentially reduce HCV prevalence by 13% (8-19%) in females and 6% (2-10%) in males. Among both females and males, a high proportion of HCV appeared to be attributable to the exposures ever being married (19% and 23%, respectively) and low S-ES (13% and 23%, respectively).

Association of cumulative number of risk factors/exposures with HCV infection

The cumulative number of exposures increased with age, among both females and males (figure 2). Females accumulated risk factor exposures earlier than males. The prevalence of HCV infection also increased as the number of exposures increased (figure 3). The HCV prevalence for individuals with 0, 1, 2, 3, 4 and ≥5 lifetime exposures was 2%, 3%, 5%, 8%, 11% and 15%, respectively, with the majority of HCV infections (77%) being among individuals with two or more risk factor exposures. In Punjab and Sindh, the prevalence for individuals with ≥5 exposures was 13% and 17%, respectively. The aOR of HCV per additional exposure was 1.51 (1.41,1.61) for females and 1.21 (1.15,1.27) for males.

Association of childbirth with HCV infection

There were 5,556 married females aged 20-59 years old. There was an increase in HCV infection prevalence associated with the number of children; linear trend, aOR per child 1.06 (1.01,1.11).

Discussion

Main Findings

Our findings identified healthcare associated exposures, including childbirth, as an important category of risk associated with HCV infection in Pakistan. In addition, our findings also suggest that various community risk factors/exposures, low socio-economic status (S-ES), and marriage are associated with increased risk of HCV infection in the country. We estimate that the risk of HCV infection increases with cumulative lifetime healthcare exposures and accounts for 13% of female and 6% of male infections, whereas community exposures and low S-ES together account for over 20% and 10% of infections in females and males, respectively. Marriage also emerged as an important surrogate marker of risk for both sexes, accounting for about 20% of all prevalent infections; what factors in marriage contribute to HCV infection in Pakistan needs additional study. Unrecognized/unidentified risk factors beyond those associated with marriage, may also play an important role in transmission, as demonstrated by the large proportion of infections not attributable to either community or healthcare exposures identified in this survey. One potential important contributor could be injection drug use, which is a well-documented risk factor for HCV transmission, with injecting drug users having a very high prevalence of HCV infection[17, 43, 44, 45]; unfortunately this risk factor was not included in the survey. Alternatively, medical injections may be more important than our analysis suggests; there was a high prevalence in the population, amongst both HCV exposed and unexposed individuals, limiting the degree to which we could ascertain the association.

Strengths and limitations

Our study was based on a very large sample size which included children as well as adults. Our results should be generalizable to the population of Pakistan as data were gathered from 100 districts in four provinces. However, the risk factor/exposure questions were limited in scope, often asking whether behaviours had ever occurred, which may have limited the degree to which we could ascribe elevated risk to them. HCV is a chronic condition, thus, infection could have resulted throughout the lifetime of the study subject, further limiting the ability to associate recent

exposures with infection. We were unable to determine why marriage and low S-ES were associated with increased prevalence of HCV infection – they may be surrogate markers for risk factors on which we did not have data, or possibly have an effect on healthcare utilization. We also lacked direct data on the number of childbirths amongst females, or where, including home or facility based deliveries, and what type of delivery was performed which limited the scope of our analyses on this risk factor. The survey did not enquire about female genital mutilation or male circumcision, both of which result in parenteral exposures. Our method for measuring the number of childbirths is likely to underestimate the total number as some children will have died or left home; however it should still be a useful proxy measure for the number of childbirths that a woman has had. It is possible that we may have overestimated risk associated with community risk factors, as accurate attribution of risk to specific medical/healthcare interventions, that are common in the population, to a chronic infection such as HCV may not reflect the risk of specific exposures.

We used anti-HCV prevalence to determine associations with HCV infection because testing for current HCV infection (eg PCR testing for presence of HCV RNA) was not performed. Further, we could not determine acute vs. chronic HCV infection; this is a universal problem; very few studies have assessed risk factors for recent, acute or incident HCV infections amongst the general population[9, 46, 47, 48]. This limits the degree to which we can determine current risk factors for HCV transmission as individuals with HCV antibody may have been infected in the distant past or more recently. Importantly, our analysis found similar associations with HCV prevalence in younger and older individuals suggesting similar risk factors may exist now as in the past. One exception was medical injections which was only associated with HCV infection among study subjects aged over 30 years. We cannot determine whether this is because cumulative exposure is more important or there has been a reduction in the risk due to medical injections in recent years.

Comparison with other studies

Our findings are consistent with previous studies examining risk factors for HCV infection[15, 16, 43, 45, 49, 50] in Pakistan. In agreement with some studies, we found the importance of healthcare and community exposures for HCV transmission, including medical injections, childbirth, attending barbers and ear/nose piercing[15, 16, 51, 52, 53, 54, 55, 56, 57]. However, not all studies are in agreement, and some did not find an association with piercing[16, 17, 43, 45, 49, 58], barbering or medical injections[17, 43], although these were much smaller surveys. Another study on women in Pakistan found higher S-ES was associated with a higher proportion of injections received using a new syringe, as opposed to re-use. This is one of the possible explanations of the protective association of S-ES on HCV infection that we found, and was confirmed in our dataset (results not shown)[59] This variable could also be a marker of accessing better quality health care which could also have a similar effect on reducing HCV risk.

As found in other studies in Pakistan and elsewhere[9, 12, 60, 61, 62, 63], marriage is associated with HCV infection for both sexes. The reasons for this are uncertain, with some studies suggesting sexual HCV transmission or shared use of personal items[12, 63]. For females in our study, the dominant exposures included ear and nose piercing, while a separate, restricted analysis also found childbirth to be an important exposure, possibly due to parenteral exposures[64]. For almost every female in Pakistan, ear and nose piercing is a cultural ritual which is undertaken in very early years of life (<5 years)[65]. Contact with barbers was associated with HCV infection among males. Barbering may be an important risk exposure among children as well as adults as every child (both male and female) undergoes head shaving until seven days of age[65]. Also, all male children undergo circumcision, which is mostly carried out by barbers in rural areas, but less so in urban areas[66].

Importantly for planning screening interventions, the cumulative number of risk factor exposures reported by an individual was highly predictive of HCV infection, with the sero-prevalence of HCV exceeding 10% among individuals with four exposures, and 15% in those with five or more; the effect was even more pronounced, 13% and 17% respectively, if they were from Punjab or Sindh.

Implications

Our results highlight the importance of HCV prevention interventions not only targeting potential healthcare risks/exposures in Pakistan, but also community settings and family behaviours where exposures may occur. These are likely to include barbering and ear piercing, and family behaviours such as sharing personal items like razors, toothbrushes, glass sharing, and practices associated with childbirth[16, 45, 49, 52]. More research is needed to better understand the main risk behaviours occurring in different settings. For instance, childbirth may be high risk only in certain settings, or when specific obstetric or gynaecological procedures are involved[50, 52, 67]. A recent meta-analysis found that caesarean section conferred a high risk for HCV infection (OR=3.35)[11], and other studies have documented the risk of HCV infection to both mother and child after normal labour[12, 68, 69].

A number of educational interventions have been undertaken in Pakistan over the past decade to tackle community and general[36] risk exposures such as barbering, tattooing and body piercing[36, 37, 38, 70]. For instance, in 2014/2015, the Health Foundation[71] developed an HCV educational intervention in Karachi, Pakistan, that aimed to educate the general public on healthcare and community risk factors through health educator volunteers and electronic and print media. A similar intervention is being done in Azad Kashmir in Northern Pakistan[72]. There is a need to better understand the effectiveness and impact of these interventions on practices and HCV transmission.

Conclusions

In summary, our results highlight the multitude of community and health care exposures that drive HCV transmission in Pakistan; similar risk factors for transmission have been identified from Egypt[8, 9, 11, 12, 73]. These findings underscore the urgent need for implementation of strategies to decrease HCV transmission in Pakistan and other countries with similar risk profiles. Treatment scale-up for HCV infection, with the new highly effective direct acting antivirals[74, 75], is planned in Pakistan, and many are already receiving treatment[76]. The finding from our study that HCV infection

is strongly associated with cumulative number of self-reported risk factors/exposures could help inform screening strategies to efficiently target individuals at highest risk for HCV infection. While scaling-up treatment is urgently needed to tackle the huge burden of HCV in Pakistan, policy makers should also remember the need for large-scale prevention interventions to curtail the continued transmission of HCV. Indeed, the low prevalence of HCV in many neighbouring countries[77, 78] suggests the required changes in behaviour should be possible with suitable interventions, including education campaigns, to improve knowledge on HCV transmission risks. These education campaigns need to be tailored to the local situation, which may require further research to identify the reasons why marriage, childbirth, and S-ES are associated with increased HCV risk in Pakistan.

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Disclaimer

The views expressed are those of the authors and do not necessarily represent those of the NHS, the NIHR, the Department of Health, Public Health England, or the Centers for Disease Control and Prevention, United States.

Disclosures

The authors have nothing to disclose.

Table 1: Variables significantly associated (p<0.05) with HCV infection, and associated adjusted odds ratios (95% confidence interval) of HCV infection, stratified by age category and gender. This table summarises supplementary tables 1a, 1b and 1c.

Males	OR (95% CI)	Females	OR (95% CI)
Aged 0-19 years:			
Barber (vs not)	1.74 (1.09, 2.78)	Tattoo or acupuncture (vs not)	12.4 (3.43, 44.5)
Ear or nose piercing (vs not)	2.67 (1.45, 4.92)	Ear or nose piercing (vs not)	1.61 (1.20, 2.15)
Labourer (vs not)	1.96 (1.21, 3.15)	Illiterate (vs not)	1.62 (1.19, 2.20)
Family history of HCV (vs not)	2.63 (1.35, 5.15)	Re-used syringe (vs none/new)	1.76 (1.18, 2.63)
Aged 20-29 years:			
Barber (vs not)	1.42 (1.00, 2.00)	Married (vs never)	1.58 (1.15, 2.19)
Ear or nose piercing (vs not)	2.21 (1.00, 4.91)	Other marital status (vs never)	3.77 (1.07, 13.3)
Labourer (vs not)	1.76 (1.19, 2.60)	Barber (vs not)	4.22 (1.01, 17.6)
Family history HCV (vs not)	2.73 (1.42, 5.25)	Tattoo or acupuncture (vs not)	3.37 (1.04, 11.0)
		Ear or nose piercing (vs not)	2.30 (1.40, 3.76)
		Family history of HCV (vs not)	1.95 (1.09, 3.50)
		Blood transfusion (vs never)	5.69 (1.71, 19.0)
Aged ≥30 years:			
Married (vs never)	1.60 (1.16, 2.22)	Illiterate (vs not)	1.43 (1.15, 1.78)
Barber (vs not)	1.45 (1.24, 1.70)	Labourer (vs not)	2.04 (1.29, 3.20)
Illiterate (vs not)	1.30 (1.11, 1.52)	5-10 injections (vs 0)	1.64 (1.16, 2.31)
Labourer (vs not)	1.40 (1.18, 1.67)	>10 injections (vs 0)	1.91 (1.31, 2.77)
<5 injections (vs 0)	1.71 (1.31, 2.24)	Re-used syringe (vs none/new)	0.64 (0.51, 0.81)
5-10 injections (vs 0)	1.67 (1.25, 2.24)	Family history of HCV (vs not)	2.57 (1.87, 3.53)
>10 injections (vs 0)	2.40 (1.71, 3.37)	Haemodialysis (vs never)	4.37 (1.61, 11.9)
Re-used syringe (vs none/new)	0.54 (0.44, 0.66)	Blood transfusion (vs never)	2.49 (1.55, 3.99)
Unknown syringe type (vs none/new)	0.42 (0.29, 0.61)		
Family history of HCV (vs not)	1.91 (1.38, 2.64)		

Table 2: Prevalence of risk factors/exposures and HCV infection, unadjusted and mutually adjusted odds ratio (95% CI) of HCV infection by sex.

Risk Factor	OR (95% CI) for HCV infection					OR (95% CI) for HCV infection				
	Males					Females				
	Freq.	HCV Prev.	Unadjusted	Adjusted	Adj. p-value	Freq.	HCV Prev.	Unadjusted	Adjusted	Adj. p-value
Never married	15,293	2%	1	1		12,707	2%	1	1	
Ever married	9,032	9%	4.14 (3.65, 4.70)	1.43 (1.14, 1.78)	p=0.002	9,811	8%	3.53 (3.07, 4.06)	1.54 (1.23, 1.94)	p<0.001
Community risks 0	17,306	3%	1	1		6,796	3%	1	1	
Community risks 1	6,105	9%	2.73 (2.41, 3.10)	1.22 (1.06, 1.41)	p=0.006	15,492	6%	2.18 (1.85, 2.58)	1.46 (1.21, 1.76)	p<0.001
Community risks ≥2	914	12%	4.10 (3.30, 5.10)	1.34 (1.06, 1.69)	p=0.013	230	10%	3.82 (2.41, 6.07)	2.07 (1.25, 3.44)	p=0.005
S-ES risks 0	14,166	4%	1	1		10,389	3%	1	1	
S-ES risks ≥1	10,159	7%	1.84 (1.64, 2.07)	1.33 (1.17, 1.51)	p<0.001	12,129	6%	2.00 (1.75, 2.30)	1.55 (1.33, 1.81)	p<0.001
Healthcare risks 0	17,570	4%	1	1		15,660	4%	1	1	
Healthcare risks 1	6,701	6%	1.45 (1.28, 1.65)	1.21 (1.06, 1.39)	p=0.005	6,675	7%	1.75 (1.54, 1.99)	1.40 (1.22, 1.61)	p<0.001
Healthcare risks ≥2	54	20%	5.57 (2.86, 10.83)	3.31 (1.69, 6.47)	p<0.001	183	22%	7.16 (5.00, 10.26)	4.17 (2.84, 6.14)	p<0.001
Punjab (Province)	13,186	7%	1	1		11,926	7%	1	1	
Sindh	4,640	5%	0.73 (0.63, 0.86)	0.69 (0.59, 0.82)	p<0.001	4,221	5%	0.75 (0.64, 0.89)	0.67 (0.56, 0.79)	p<0.001
Baluchistan	3,831	1%	0.15 (0.11, 0.22)	0.16 (0.11, 0.22)	p<0.001	3,766	1%	0.16 (0.11, 0.22)	0.14 (0.10, 0.19)	p<0.001
North West Frontier	2,668	1%	0.18 (0.13, 0.27)	0.19 (0.13, 0.28)	p<0.001	2,605	2%	0.24 (0.17, 0.33)	0.20 (0.14, 0.29)	p<0.001
Age 0-9	5,309	2%	0.36 (0.27, 0.49)	0.48 (0.35, 0.66)	p<0.001	5,013	2%	0.39 (0.30, 0.50)	0.63 (0.46, 0.85)	p=0.003
Age 10-19	6,360	2%	0.59 (0.47, 0.74)	0.77 (0.60, 0.99)	p=0.041	5,808	2%	0.48 (0.38, 0.60)	0.69 (0.53, 0.89)	p=0.005
Age 20-29	4,420	4%	1	1		4,272	5%	1	1	
Age 30-39	2,831	7%	1.90 (1.54, 2.34)	1.53 (1.20, 1.95)	p<0.001	2,910	8%	1.84 (1.52, 2.23)	1.47 (1.20, 1.81)	p<0.001
Age 40-49	2,292	11%	3.17 (2.60, 3.88)	2.43 (1.90, 3.09)	p<0.001	2,109	9%	1.88 (1.54, 2.31)	1.40 (1.12, 1.75)	p=0.003
Age 50-59	1,479	11%	3.04 (2.43, 3.80)	2.41 (1.85, 3.14)	p<0.001	1,289	10%	2.20 (1.75, 2.76)	1.55 (1.21, 1.98)	p<0.001
Age 60+	1,634	11%	3.06 (2.47, 3.79)	2.22 (1.71, 2.88)	p<0.001	1,117	9%	1.90 (1.48, 2.43)	1.25 (0.96, 1.63)	p=0.10

S-ES: socio-economic status

FIGURE LEGENDS

FIGURE 1: Population attributable fraction of HCV infection due to community and healthcare risks.

FIGURE 2: Proportion of the population experiencing different numbers of exposures for HCV infection by age and sex. Exposures included in this analysis were having >4 injections, haemodialysis, blood transfusions, going to the barber, ear/nose piercing, tattoo/acupuncture, sharing smoking equipment, marriage, illiteracy and being a labourer.

FIGURE 3: Proportion of population, HCV prevalence, and proportion of infections among individuals with different numbers of exposures.

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Supplementary table 1: Prevalence of risk factors/exposures and HCV infection, unadjusted and mutually adjusted odds ratio (95% CI) of HCV infection by age and sex.

Supplementary table 1a: Males and females aged 0-19 years

	Males Aged 0-19					Females aged 0-19				
		HCV	OR (95% CI)		P		HCV	OR (95% CI)		P
Risk factor	**N (%)**	**N (%)**	**Unadjusted**	**Adjusted**	**value**	**N (%)**	**N (%)**	**Unadjusted**	**Adjusted**	**value**
Marital status (v. never)	11518 (99)	220 (1.9)	1	1		10415 (96)	219 (2.1)	1	1	
Married	129 (1.1)	4 (3.1)	1.64 (0.60,4.51)	1.15 (0.44,3.00)	0.78	392 (3.6)	12 (3.1)	1.47 (0.82,2.65)	1.11 (0.61,2.02)	0.74
other	22 (0.2)	1 (4.5)	2.45 (0.32,18.4)	2.17 (0.26,18.1)	0.47	14 (0.1)	0 (0)	NA	NA	
Urban (v. rural)	4463 (38)	80 (1.8)	0.89 (0.66,1.19)	0.91 (0.67,1.25)	0.56	4360 (40)	79 (1.8)	0.77 (0.55,1.06)	0.85 (0.58,1.22)	0.37
Community risk										
Barber	587 (5.2)	24 (3.9)	2.21 (1.44,3.40)	1.74 (1.09,2.78)	0.02	22 (0.2)	0 (0)	NA	NA	
Sharing smoking eqpt.	49 (0.4)	1 (2.0)	1.06 (0.15,7.73)	0.60 (0.09,4.11)	0.60	15 (0.1)	0 (0)	NA	NA	
Sharing a toothbrush	86 (0.7)	2 (2.3)	1.21 (0.30,4.90)	1.21 (0.31,4.79)	0.78	75 (0.7)	2 (2.7)	1.26 (0.30,5.30)	1.15 (0.27,4.85)	0.85
Tattoo or acupuncture	24 (0.2)	0	NA	NA		11 (0.1)	3 (27)	17.4 (4.38,69.2)	12.4 (3.43,44.5)	<0.001
Ear or nose piercing	268 (2.3)	13 (4.9)	2.69 (1.47,4.91)	2.67 (1.45,4.92)	0.002	6151 (57)	155 (2.5)	1.56 (1.17,2.08)	1.61 (1.20,2.15)	0.001
Matam	23 (0.2)	1 (4.3)	2.32 (0.37,14.7)	1.31 (0.18,9.52)	0.79	8 (0.1)	0 (0)		NA	
Socio-economic status										
Illiterate	3809 (33)	78 (2.1)	1.10 (0.83,1.46)	1.03 (0.76,1.39)	0.85	4406 (41)	122 (2.8)	1.65 (1.24,2.20)	1.62 (1.19,2.20)	0.002
Labourer	575 (4.9)	25 (4.4)	2.48 (1.61,3.80)	1.96 (1.21,3.15)	0.006	175 (1.6)	2 (1.1)	0.53 (0.13,2.10)	0.42 (0.10,1.69)	0.22
Healthcare risk										
No. of injections (v. 0)	3447 (30)	61 (1.8)	1	1		2996 (28)	59 (2.0)		1	
<5 injections	5934 (51)	108 (1.8)	1.03 (0.73,1.44)	0.88 (0.62,1.26)	0.49	5617 (52)	130 (2.3)	1.18 (0.84,1.65)	0.92 (0.65,1.29)	0.61
5-10 injections	1905 (16)	48 (2.5)	1.43 (0.95,2.16)	1.03 (0.65,1.63)	0.89	1838 (17)	37 (2.0)	1.02 (0.67,1.55)	0.69 (0.44,1.08)	0.10
>10 injections	383 (3.3)	8 (2.1)	1.18 (0.56,2.50)	0.89 (0.41,1.94)	0.768	370 (3.4)	5 (1.4)	0.68 (0.27,1.70)	0.50 (0.20,1.29)	0.15
Syringe use (v. none/new)	9826 (84)	173 (1.8)	1	1		9118 (84)	176 (1.9)	1	1	
Re-used syringe	1201 (10)	37 (3.1)	1.76 (1.14,2.74)	1.50 (0.99,2.28)	0.056	1096 (10)	37 (3.4)	1.74 (1.13,2.67)	1.76 (1.18,2.63)	0.006
Unknown syringe type	642 (5.5)	15 (2.3)	1.33 (0.72,2.44)	1.29 (0.71,2.34)	0.40	607 (5.6)	18 (3.0)	1.52 (0.64,3.60)	1.47 (0.62,3.50)	0.38
Dentist	31 (0.3)	0	NA	NA		44 (0.4)	2 (4.6)	2.19 (0.52,9.22)	2.47 (0.58,10.5)	0.22
Family history HCV	205 (1.8)	10 (4.9)	2.68 (1.36,5.29)	2.63 (1.35,5.15)	0.005	213 (2.0)	4 (1.9)	0.88 (0.32,2.36)	0.93 (0.34,2.55)	0.89
Haemodialysis	10 (0.1)	0	NA	NA		13 (0.1)	0 (0)	NA	NA	
Blood transfusion	16 (0.1)	0	NA	NA		19 (0.2)	2 (11)	5.43 (1.24,23.73)	11.5 (0.96,138)	0.054
History of surgery	132 (1.1)	1 (0.8)	0.38 (0.05,2.73)	0.35 (0.05,2.62)	0.31	104 (1.0)	3 (2.9)	1.37 (0.43,4.33)	0.59 (0.08,4.36)	0.60
TOTAL	**11669 (100)**	**225 (1.9)**				**10821 (100)**	**213 (2.0)**			

NA – not applicable – no cases of HCV infection

Supplementary table 1b: Males and females aged 20-29 years

	Males Aged 20-29					Females aged 20-29				
		HCV	OR (95% CI)		P		HCV	OR (95% CI)		P value
Risk factor	**N (%)**	**N (%)**	**Unadjusted**	**Adjusted**	**value**	**N (%)**	**N (%)**	**Unadjusted**	**Adjusted**	
Marital status (v. never)	3121 (71)	108 (3.5)	1	1		1870 (44)	63 (3.4)	1	1	
Married	1284 (29)	64 (5.0)	1.45 (1.05,1.99)	1.31 (0.94,1.82)	0.11	2373 (56)	138 (5.8)	1.77 (1.31,2.40)	1.58 (1.15,2.19)	0.005
Other	15 (0.3)	0 (0)	NA	NA		29 (0.7)	3 (10)	3.31 (0.98,11.2)	3.77 (1.07,13.3)	0.039
Urban (v. rural)	1897 (43)	69 (3.6)	0.89 (0.64,1.22)	0.89 (0.64,1.23)	0.47	1799 (42)	77 (4.3)	0.83 (0.62,1.11)	0.85 (0.61,1.17)	0.31
Community risk										
Barber	1823 (41)	90 (4.9)	1.59 (1.17,2.17)	1.42 (1.00,2.00)	0.047	26 (0.6)	3 (12)	2.62 (0.78,8.87)	4.22 (1.01,17.6)	0.048
Sharing smoking eqpt.	217 (4.9)	12 (5.5)	1.48 (0.82,2.67)	1.12 (0.60,2.10)	0.72	37 (0.9)	4 (11)	2.44 (0.85,7.02)	1.45 (0.47,4.55)	0.52
Sharing a toothbrush	72 (1.6)	5 (6.9)	1.87 (0.77,4.51)	1.57 (0.62,3.97)	0.34	29 (0.7)	2 (6.9)	1.48 (0.33,6.58)	1.61 (0.36,7.12)	0.53
Tattoo or acupuncture	47 (1.1)	3 (6.4)	1.70 (0.53,5.46)	1.18 (0.36,3.88)	0.78	24 (0.6)	4 (17)	4.05 (1.35,12.17)	3.37 (1.04,11.0)	0.043
Ear or nose piercing	111 (2.5)	8 (7.2)	1.94 (0.93,4.07)	2.21 (1.00,4.91)	0.051	3349 (78)	181 (5.4)	2.23 (1.44,3.46)	2.30 (1.40,3.76)	<0.001
Matam	14 (0.3)	1 (7.1)	1.91 (0.33,11.0)	1.92 (0.36,10.1)	0.44	6 (0.1)	0 (0)	NA	NA	
Socio-economic status										
Illiterate	1168 (26)	47 (4.0)	1.05 (0.74,1.48)	0.93 (0.64,1.35)	0.72	2129 (50)	111 (5.2)	1.21 (0.91,1.61)	0.99 (0.71,1.38)	0.91
Labourer	817 (19)	51 (6.2)	1.92 (1.35,2.72)	1.76 (1.19,2.60)	0.005	88 (2.1)	5 (5.7)	1.21 (0.48,3.03)	1.14 (0.45,2.88)	0.78
Healthcare risk										
No. of injections (v. 0)	1049 (24)	35 (3.3)	1	1		798 (19)	31 (3.9)	1	1	
<5 injections	2032 (46)	80 (3.9)	1.19 (0.79,1.79)	1.13 (0.64,1.99)	0.68	2043 (48)	82 (4.0)	1.03 (0.67,1.60)	0.79 (0.43,1.45)	0.45
5-10 injections	1090 (25)	42 (3.9)	1.16 (0.73,1.86)	1.06 (0.57,1.99)	0.85	1122 (26)	68 (6.1)	1.60 (1.02,2.49)	1.11 (0.58,2.14)	0.75
>10 injections	249 (5.6)	15 (6.0)	1.86 (0.98,3.53)	2.03 (0.92,4.48)	0.08	309 (7.2)	23 (7.4)	1.99 (1.13,3.51)	1.43 (0.67,3.02)	0.36
Syringe use (v. none/new)	1600 (36)	62 (3.9)	1	1		1341 (31)	57 (4.3)	1	1	
Re-used syringe	2559 (58)	103 (4.0)	1.22 (0.82,1.81)	0.91 (0.57,1.46)	0.7	2656 (62)	131 (4.9)	1.28 (0.85,1.94)	0.96 (0.59,1.56)	0.87
Unknown syringe type	261 (5.9)	7 (2.7)	0.80 (0.32,1.98)	0.52 (0.20,1.36)	0.18	275 (6.4)	16 (5.8)	1.53 (0.80,2.92)	1.11 (0.54,2.29)	0.78
Dentist	49 (1.1)	0 (0)	NA	NA		52 (1.2)	2 (3.9)	0.80 (0.19,3.30)	0.75 (0.17,3.30)	0.70
Family history HCV	132 (3.0)	14 (10)	3.10 (1.63,5.92)	2.73 (1.42,5.25)	0.003	163 (3.8)	16 (9.8)	2.27 (1.30,3.97)	1.95 (1.09,3.50)	0.025
Haemodialysis	6 (0.1)	1 (17)	4.96 (0.58,42.7)	7.77 (0.98,61.6)	0.052	6 (0.1)	1 (16.7)	4.00 (0.47,34.44)	2.36 (0.14,38.8)	0.55
Blood transfusion	9 (0.2)	0 (0)	NA	NA		56 (1.3)	8 (14)	3.42 (1.60,7.31)	5.69 (1.71,19.0)	0.005
History of surgery	151 (3.4)	2 (1.3)	0.32 (0.08,1.32)	0.27 (0.06,1.16)	0.078	185 (4.3)	11 (6.0)	1.28 (0.68,2.38)	0.44 (0.16,1.25)	0.13
TOTAL	**4420 (100)**	**172 (3.9)**				**4272 (100)**	**204 (4.8)**			

NA – not applicable – no cases of HCV infection

Supplementary table 1c: Males and females aged ≥30 years

	Males aged ≥ 30 years					Females aged ≥ 30 years				
		HCV	OR (95% CI)		P value		HCV	OR (95% CI)		P value
Risk factor	**N (%)**	**N (%)**	**Unadjusted**	**Adjusted**		**N (%)**	**N (%)**	**Unadjusted**	**Adjusted**	
Marital status (v. never)	654 (7.9)	39 (6.0)	1	1		422 (5.6)	23 (5.5)			
Married	7310 (89)	739 (10)	1.77 (1.28,2.44)	1.60 (1.16,2.22)	0.004	6317 (85)	569 (9.0)	1.70 (1.11,2.61)	1.52 (0.98,2.34)	0.060
Other	272 (3.3)	27 (9.9)	1.73 (1.05,2.85)	1.43 (0.85,2.38)	0.18	686 (9.3)	61 (8.9)	1.68 (1.02,2.76)	1.41 (0.85,2.35)	0.19
Urban (v. rural)	3257 (40)	330 (10)	1.07 (0.92,1.24)	1.17 (0.99,1.37)	0.060	3039 (41)	255 (8.4)	0.92 (0.77,1.09)	0.96 (0.79,1.16)	0.67
Community risk										
Barber	3580 (44)	441 (12)	1.66 (1.43,1.92)	1.45 (1.24,1.70)	<0.001	49 (0.7)	4 (8.2)	0.92 (0.33,2.57)	1.00 (0.35,2.84)	1
Sharing smoking eqpt.	991 (12)	132 (13)	1.50 (1.23,1.83)	1.23 (0.99,1.54)	0.061	126 (1.7)	10 (7.9)	0.89 (0.46,1.72)	0.72 (0.37,1.40)	0.33
Sharing a toothbrush	161 (2.0)	22 (14)	1.46 (0.93,2.29)	1.29 (0.79,2.09)	0.31	62 (0.8)	8 (13)	NA	NA	
Tattoo or acupuncture	78 (1.0)	8 (10)	1.06 (0.51,2.20)	0.87 (0.40,1.89)	0.73	46 (0.6)	1 (2.2)	0.23 (0.03,1.68)	0.20 (0.03,1.55)	0.12
Ear or nose piercing	159 (1.9)	14 (8.8)	0.89 (0.51,1.54)	1.01 (0.58,1.76)	0.98	6087 (82)	562 (9.2)	1.39 (1.09,1.77)	1.28 (0.98,1.66)	0.067
Matam	36 (0.4)	2 (5.6)	0.54 (0.13,2.30)	0.41 (0.09,1.80)	0.24	10 (0.1)	2 (20)	NA	NA	
Socio-economic status										
Illiterate	3765 (46)	410 (11)	1.26 (1.09,1.46)	1.30 (1.11,1.52)	0.001	5494 (74)	518 (9.4)	1.38 (1.13,1.69)	1.43 (1.15,1.78)	0.001
Labourer	1736 (21)	232 (13)	1.59 (1.35,1.88)	1.40 (1.18,1.67)	<0.001	145 (2.0)	25 (17)	2.20 (1.43,3.41)	2.04 (1.29,3.20)	0.002
Healthcare risk										
No. of injections (v. 0)	1536 (19)	130 (8.4)	1	1		1081 (15)	83 (7.8)	1	1	
<5 injections	3649 (44)	362 (9.9)	1.19 (0.97,1.47)	1.71 (1.31,2.24)	<0.001	3275 (44)	244 (7.5)	0.95 (0.73,1.24)	1.22 (0.88,1.69)	0.24
5-10 injections	2280 (28)	221 (9.7)	1.16 (0.93,1.46)	1.67 (1.25,2.24)	<0.001	2222 (30)	224 (10)	1.33 (1.02,1.73)	1.64 (1.16,2.31)	0.005
>10 injections	771 (9.4)	92 (12)	1.47 (1.10,1.95)	2.40 (1.71,3.37)	<0.001	847 (11)	101 (12)	1.60 (1.18,2.19)	1.91 (1.31,2.77)	<0.001
Syringe use (v. none/new)	2532 (31)	290 (11)	1	1		2002 (27)	191 (9.6)	1	1	
Re-used syringe	51784 (63)	475 (9.2)	1.09 (0.89,1.34)	0.54 (0.44,0.66)	<0.001	4937 (66)	415 (8.4)	1.09 (0.85,1.40)	0.64 (0.51,0.81)	<0.001
Unknown syringe type	520 (6.3)	40 (7.7)	0.90 (0.62,1.30)	0.42 (0.29,0.61)	<0.001	486 (6.6)	46 (9.5)	1.24 (0.85,1.81)	0.75 (0.52,1.10)	0.15
Dentist	245 (3.0)	30 (12)	1.30 (0.88,1.92)	1.14 (0.76,1.69)	0.53	270 (3.6)	29 (10.7)	NA	NA	
Family history HCV	296 (3.6)	53 (18)	2.08 (1.53,2.84)	1.91 (1.38,2.64)	<0.001	280 (3.8)	60 (21)	3.01 (2.22,4.08)	2.57 (1.87,3.53)	<0.001
Haemodialysis	12 (0.2)	2 (17)	1.68 (0.37,7.59)	1.75 (0.39,7.86)	0.46	18 (0.2)	6 (33)	5.22 (1.95,13.9)	4.37 (1.61,11.9)	0.004
Blood transfusion	77 (0.9)	12 (16)	1.71 (0.92,3.19)	1.95 (0.95,4.00)	0.069	222 (3.0)	47 (21)	2.92 (2.09,4.08)	2.49 (1.55,3.99)	<0.001
History of surgery	594 (7.2)	56 (9.4)	0.96 (0.72,1.27)	0.83 (0.60,1.15)	0.27	673 (9.1)	86 (13)	1.60 (1.25,2.03)	0.99 (0.70,1.40)	0.95
TOTAL	**8236 (100)**	**805 (9.8)**				7425 (100)	653 (8.8)			

NA – not applicable – no cases of HCV infection

Supplementary Table 2: Prevalence of risk factors/exposures and HCV infection, unadjusted and mutually adjusted odds ratio (95% CI) of HCV infection by sex, with the Baluchistan and North West Frontier provinces omitted.

Risk Factor	OR (95% CI) for HCV infection					OR (95% CI) for HCV infection				
	Males					Females				
	Freq.	HCV Prev.	Unadjusted	Adjusted	Adj. p-value	Freq.	HCV Prev.	Unadjusted	Adjusted	Adj. p-value
Never married	11,175	3%	1	1		9,267	3%	1	1	
Ever married	6,651	12%	4.22 (3.70, 4.82)	1.47 (1.17, 1.86)	p=0.001	6,880	10%	3.67 (3.17, 4.25)	1.57 (1.23, 2.01)	p<0.001
Community risks 0	11,858	4%	1	1		5,076	3%	1	1	
Community risks 1	5,138	10%	2.45 (2.15, 2.80)	1.27 (1.10, 1.48)	p=0.002	10,948	7%	2.25 (1.90, 2.67)	1.44 (1.18, 1.75)	p<0.001
Community risks ≥2	830	13%	3.50 (2.80, 4.37)	1.43 (1.13, 1.81)	p=0.003	123	15%	5.15 (3.07, 8.63)	2.22 (1.27, 3.87)	p=0.005
S-ES risks 0	10,206	5%	1	1		8,002	4%	1	1	
S-ES risks ≥1	7,620	8%	1.74 (1.54, 1.97)	1.28 (1.12, 1.46)	p<0.001	8,145	8%	2.21 (1.91, 2.55)	1.52 (1.30, 1.78)	p<0.001
Healthcare risks 0	13,165	6%	1	1		11,409	5%	1	1	
Healthcare risks 1	4,619	8%	1.50 (1.31, 1.72)	1.18 (1.02, 1.36)	p=0.024	4,584	9%	1.82 (1.58, 2.09)	1.39 (1.21, 1.61)	p<0.001
Healthcare risks ≥2	42	26%	5.99 (3.00, 11.96)	3.54 (1.76, 7.14)	p<0.001	154	25%	6.27 (4.28, 9.17)	4.05 (2.71, 6.07)	p<0.001
Punjab (Province)	13,186	7%	1	1		11,926	7%	1	1	
Sindh	4,640	5%	0.73 (0.63, 0.86)	0.70 (0.59, 0.82)	p<0.001	4,221	5%	0.75 (0.64, 0.89)	0.67 (0.56, 0.79)	p<0.001
Age 0-9	3,737	2%	0.40 (0.30, 0.54)	0.53 (0.38, 0.72)	p<0.001	3,587	3%	0.41 (0.32, 0.54)	0.67 (0.49, 0.92)	p=0.012
Age 10-19	4,641	3%	0.61 (0.48, 0.77)	0.79 (0.61, 1.02)	p=0.076	4,175	3%	0.48 (0.38, 0.61)	0.70 (0.53, 0.92)	p=0.010
Age 20-29	3,350	5%	1	1		3,079	6%	1	1	
Age 30-39	2,121	9%	1.98 (1.59, 2.47)	1.55 (1.21, 2.00)	p<0.001	2,055	11%	1.89 (1.54, 2.31)	1.46 (1.17, 1.81)	P=0.001
Age 40-49	1,706	14%	3.38 (2.74, 4.16)	2.45 (1.90, 3.15)	p<0.001	1,477	12%	2.03 (1.64, 2.52)	1.45 (1.15, 1.83)	p=0.002
Age 50-59	1,058	15%	3.40 (2.69, 4.29)	2.48 (1.88, 3.26)	p<0.001	925	13%	2.24 (1.76, 2.86)	1.54 (1.19, 1.99)	P=0.001
Age 60+	1,213	13%	3.03 (2.42, 3.80)	2.09 (1.59, 2.75)	p<0.001	849	11%	1.95 (1.50, 2.52)	1.31 (1.00, 1.73)	p=0.053

S-ES: socio-economic status

Supplementary Table 3: Prevalence of risk factors/exposures and HCV infection, unadjusted and mutually adjusted odds ratio (95% CI) of HCV infection by sex, without adjustment for province.

Risk Factor	OR (95% CI) for HCV infection					OR (95% CI) for HCV infection				
	Males					Females				
	Freq.	HCV Prev.	Unadjusted	Adjusted	Adj. p-value	Freq.	HCV Prev.	Unadjusted	Adjusted	Adj. p-value
Never married	15,293	2%	1	1		12,707	2%	1	1	
Ever married	9,032	9%	4.14 (3.65, 4.70)	1.34 (1.07, 1.67)	p=0.010	9,811	8%	3.53 (3.07, 4.06)	1.46 (1.17, 1.83)	p<0.001
Community risks 0	17,306	3%	1	1		6,796	3%	1	1	
Community risks 1	6,105	9%	2.73 (2.41, 3.10)	1.63 (1.42, 1.87)	P<0.001	15,492	6%	2.18 (1.85, 2.58)	1.45 (1.21, 1.73)	p<0.001
Community risks ≥2	914	12%	4.10 (3.30, 5.10)	1.89 (1.50, 2.38)	P<0.001	230	10%	3.82 (2.41, 6.07)	1.62 (0.99, 2.63)	p=0.052
S-ES risks 0	14,166	4%	1	1		10,389	3%	1	1	
S-ES risks ≥1	10,159	7%	1.84 (1.64, 2.07)	1.35 (1.19, 1.53)	p<0.001	12,129	6%	2.00 (1.75, 2.30)	1.35 (1.16, 1.57)	p<0.001
Healthcare risks 0	17,570	4%	1	1		15,660	4%	1	1	
Healthcare risks 1	6,701	6%	1.45 (1.28, 1.65)	1.02 (0.89, 1.17)	p=0.75	6,675	7%	1.75 (1.54, 1.99)	1.26 (1.10, 1.44)	p<0.001
Healthcare risks ≥2	54	20%	5.57 (2.86, 10.83)	2.69 (1.37, 5.28)	P=0.004	183	22%	7.16 (5.00, 10.26)	3.96 (2.72, 5.76)	p<0.001
Age 0-9	5,309	2%	0.36 (0.27, 0.49)	0.50 (0.37, 0.69)	p<0.001	5,013	2%	0.39 (0.30, 0.50)	0.60 (0.45, 0.82)	p<0.001
Age 10-19	6,360	2%	0.59 (0.47, 0.74)	0.80 (0.63, 1.03)	p=0.087	5,808	2%	0.48 (0.38, 0.60)	0.65 (0.51, 0.85)	p<0.001
Age 20-29	4,420	4%	1	1		4,272	5%	1	1	
Age 30-39	2,831	7%	1.90 (1.54, 2.34)	1.54 (1.21, 1.95)	p<0.001	2,910	8%	1.84 (1.52, 2.23)	1.51 (1.23, 1.85)	p<0.001
Age 40-49	2,292	11%	3.17 (2.60, 3.88)	2.41 (1.90, 3.07)	p<0.001	2,109	9%	1.88 (1.54, 2.31)	1.46 (1.17, 1.81)	P<0.001
Age 50-59	1,479	11%	3.04 (2.43, 3.80)	2.35 (1.81, 3.06)	p<0.001	1,289	10%	2.20 (1.75, 2.76)	1.66 (1.31, 2.11)	p<0.001
Age 60+	1,634	11%	3.06 (2.47, 3.79)	2.28 (1.76, 2.95)	p<0.001	1,117	9%	1.90 (1.48, 2.43)	1.44 (1.11, 1.87)	p=0.006

S-ES: socio-economic status

Supplementary Table 4: Prevalence of individual risk factors/exposures and HCV infection, unadjusted and mutually adjusted odds ratio (95% CI) of HCV infection by sex.

Risk Factor	OR (95% CI) for HCV infection					OR (95% CI) for HCV infection				
	Males					Females				
	Freq.	HCV Prev.	Unadjusted	Adjusted	Adj. p-value	Freq.	HCV Prev.	Unadjusted	Adjusted	Adj. p-value
Never married	15,293	2%	1	1		12,707	2%	1	1	
Ever married	9,032	9%	4.14 (3.65, 4.70)	1.42 (1.14, 1.78)	p=0.002	9,811	8%	3.53 (3.07, 4.06)	1.52 (1.21, 1.92)	p<0.001
Barber	6,014	9%	2.78 (2.46, 3.13)	1.18 (1.03, 1.35)	P=0.020	97	7%	1.54 (0.71, 3.33)	1.46 (0.66, 3.24)	p=0.36
Ear or nose piercing	539	6%	1.35 (0.93, 1.95)	1.58 (1.07, 2.33)	p=0.022	15,603	6%	2.18 (1.85, 2.56)	1.49 (1.23, 1.79)	p<0.001
Tattoo/acupuncture	149	7%	1.54 (0.83, 2.85)	1.04 (0.56, 1.94)	p=0.91	81	10%	2.17 (1.07, 4.38)	2.42 (1.12, 5.25)	p=0.025
Sharing smoking eqpt.	1,257	12%	2.72 (2.26, 3.27)	1.13 (0.93, 1.38)	P=0.22	178	8%	1.69 (0.97, 2.95)	1.00 (0.57, 1.75)	p=0.99
Illiterate	8,744	6%	1.46 (1.29, 1.64)	1.15 (1.01, 1.31)	p=0.038	12,029	6%	2.01 (1.75, 2.30)	1.57 (1.35, 1.83)	p<0.001
Labourer	3,128	10%	2.48 (2.16, 2.85)	1.25 (1.07, 1.46)	p=0.004	408	8%	1.70 (1.19, 2.42)	1.30 (0.90, 1.88)	p=0.16
>4 Medical Injections	6,678	6%	1.48 (1.30, 1.68)	1.24 (1.08, 1.42)	p=0.002	6,708	7%	1.77 (1.55, 2.01)	1.37 (1.19, 1.57)	p<0.001
Haemodialysis	29	10%	2.22 (0.67, 7.36)	2.01 (0.59, 6.80)	P=0.26	37	19%	4.62 (2.06, 10.4)	3.20 (1.38, 7.39)	p=0.007
Blood transfusion	102	12%	2.58 (1.41, 4.73)	1.52 (0.82, 2.82)	P=0.18	297	19%	4.88 (3.61, 6.60)	2.90 (2.10, 4.00)	p<0.001
Punjab (Province)	13,186	7%	1	1		11,926	7%	1	1	
Sindh	4,640	5%	0.73 (0.63, 0.86)	0.69 (0.58, 0.81)	p<0.001	4,221	5%	0.75 (0.64, 0.89)	0.65 (0.55, 0.77)	p<0.001
Baluchistan	3,831	1%	0.15 (0.11, 0.22)	0.16 (0.11, 0.23)	p<0.001	3,766	1%	0.16 (0.11, 0.22)	0.14 (0.10, 0.19)	p<0.001
North West Frontier	2,668	1%	0.18 (0.13, 0.27)	0.20 (0.14, 0.28)	p<0.001	2,605	2%	0.24 (0.17, 0.33)	0.20 (0.14, 0.28)	p<0.001
Age 0-9	5,309	2%	0.36 (0.27, 0.49)	0.49 (0.36, 0.67)	p<0.001	5,013	2%	0.39 (0.30, 0.50)	0.63 (0.46, 0.85)	p=0.003
Age 10-19	6,360	2%	0.59 (0.47, 0.74)	0.76 (0.59, 0.97)	p=0.028	5,808	2%	0.48 (0.38, 0.60)	0.69 (0.53, 0.89)	p=0.004
Age 20-29	4,420	4%	1	1		4,272	5%	1	1	
Age 30-39	2,831	7%	1.90 (1.54, 2.34)	1.55 (1.22, 1.97)	p<0.001	2,910	8%	1.84 (1.52, 2.23)	1.47 (1.19, 1.81)	p=0.003
Age 40-49	2,292	11%	3.17 (2.60, 3.88)	2.45 (1.92, 3.12)	p<0.001	2,109	9%	1.88 (1.54, 2.31)	1.39 (1.11, 1.74)	p=0.004
Age 50-59	1,479	11%	3.04 (2.43, 3.80)	2.45 (1.88, 3.18)	p<0.001	1,289	10%	2.20 (1.75, 2.76)	1.55 (1.21, 1.98)	p<0.001
Age 60+	1,634	11%	3.06 (2.47, 3.79)	2.29 (1.76, 2.98)	p<0.001	1,117	9%	1.90 (1.48, 2.43)	1.25 (0.96, 1.63)	p=0.10

Supplementary material 1: Survey questionnaire, household.

Supplementary material 2: Survey questionnaire, individual.