Research Article
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Hepatitis C virus (HCV) prevalence and risk of unsafe parenteral practices in Derqui, Argentine

Abstract

Background: Hepatitis C virus (HCV) epidemiology and risk factor (RF) contribution in Argentina can be improved, with prevalence studies addressing unsafe injections in health care settings. Study purpose was: 1) to estimate a defined population prevalence of HCV and 2) to assess RF exposure for HCV, including potential impact of Health Care Unsafe Parenteral Practices (HC-UPP).

Design: A cluster-survey of HCV seroprevalence in Derqui, a representative community of Buenos Aires province, Argentina.

Methods: 1472 all age individuals, selected by probabilistic polyetapic sampling, were surveyed, collecting demographic, socioeconomic status (SES) and risk factor exposure data for HCV. HCV antibodies were determined by MEIA-3 blood assay. HC-UPP was defined as: a) Ever received an injection with a glass syringe or b) Have undergone surgery 3 or more times before 1990 (a period of heavy utilization of re-used equipment in health care facilities). Age-specific prevalence rates were obtained. The association of HC-UPP with HCV adjusted for known HCV risk factors (I.V. illicit drug use [IV DU], health care occupation, any surgery, transfusion history and imprisonment) was tested by logistic regression model (STATA 8.0), and the population attributable fraction (PAF) was calculated.

Results: A young population (43% under 30 years old), of low SES was found. HCV seroprevalence was 0.87%, (95% CI 0.31-1.18), highest among ages 40-49 yrs. (2.51%). Risk factor prevalence for HCV was: 27.3% surgery; 15% reported an injection with a glass syringe; 7.7% were operated on 3 or more times; 7.5% received blood transfusions, 7.37% had worked in healthcare. Only 1.2% of community-based individuals reported IV DU and 1.7% individuals reported history of being in prison. HC-UPP occurred in 19.4% and was associated with HCV (OR 4.34, 95%CI, 1.28-14.78, p=0.024). IV DU showed a trend to increased risk (OR 4.88, 95%CI 0.91-26.20, p=0.06). PAF for HC-UPP was 15.3% (95% CI 8.8%-21.3%).

Conclusion: HCV prevalence was lower than the estimated for LAC. HC-UPP was associated to HCV with high population impact.

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Introduction

The epidemiology of Hepatitis C Virus (HCV) infection is not well known in Argentina or Latin America and the Caribbean (LAC),[1] and improved prevalence estimates and modeling attempts are ongoing.[2] Several estimates suggest that hepatitis C prevalence may range between 0,17% to 5,6%, and in some communities between 2,2 and 7,3%.[3] Another prevalence estimate of 1,23% was suggested for LAC,[4] and a burden of 7.8 million persons affected with Hepatitis C were calculated in year 2010 for LAC.[5]

Frequently prevalence studies lack adequate methodology. The case of Hepatitis C in Argentina shows the same sets of problems. HCV epidemiology and risk factor contribution in Argentina is poorly described, relying on special populations' data, blood bank / laboratory data and potentially biased community based studies about risk factor exposure. To date, most sero-prevalence studies en HCV prevalence resulted from spontaneous demand, due to increases in reported cases[6,7] and focused on small communities or high-risk groups,[8–10] or high-risk populations.[11–13] The gold standard for prevalence studies are community based studies.[10] Some countries, such as Brazil,[15] have well designed prevalence estimates by national surveys.

Injection safety is a worldwide challenge with greater impact on less developed (LDC) and transitional countries (TC).[16] Injections may be appropriate, unnecessary or unsafe.[17] Unsafe injections, defined as syringe or needle reuse without sterilization, are supposed to produce 40% of hepatitis C worldwide, mostly in East Asia.[18,19] A substantial portion of injections is un-necessary. Unnecessary injections are approximately 50% of the total injections (world: 3.4 and Latin América: 1.7 injections/ persons/ year).[20] Reuse proportion is 39.3% (range 1.2-75% in different world regions). A complex series of causes determine the rates of unnecessary and unsafe injections; cultural, economic, technologic and quality /safety combined related problems are related to their prevalence. Cultural beliefs that injections are better include, that they are faster, stronger and more advanced technologies than oral drugs. Unsafe parenteral practices, including unsafe nosocomial control measures, seem to contribute to this problem.

The purpose of this study was: 1) to estimate a defined population prevalence of HCV and 2) to assess risk factor exposure for HCV, including potential impact of Health Care Unsafe Parenteral Practices (HC-UPP).

Methods

Study design

The study design was a cross-sectional prevalence study, with a cluster-survey of HCV seroprevalence in Derqui, a representative community of a large part of the Buenos Aires province, Argentina.

During November-December 2003, 1472 individuals with age inclusion criteria of 1 to 100 years old, selected by probabilistic polyetapic sampling, were surveyed by previously trained interviewers --audited by a community survey professional team, collecting demographic, socioeconomic (SES) and risk factor exposure data for HCV. HCV antibodies were determined by MEIA-3 blood assay. Surveyors were recruited among community health care workers serving the county.

HC-UPP was defined as: a) ever received an injection with a glass syringe or b) have undergone surgery 3 or more times before 1990 (a period of heavy utilization of re-used equipment in health care facilities). Age-specific prevalence rates were obtained. The association of HC-UPP with HCV, adjusted for known HCV risk factors (I.V. illicit drug use [IV DU], health care occupation, any surgery, transfusion history and imprisonment) was evaluated with a logistic regression model, and the population attributable fraction (PAF) was calculated (Levin´s Formula) [21]. STATA 8.0 was employed using commands for complex sampling.

This is a cross-sectional study, with a complex sample in order to determine the prevalence of antibodies to hepatitis A virus (HAV) (not reported here), and HCV in a defined community representing a significant portion of the inhabitants of the province of Buenos Aires.

Case definition

Cases of chronic hepatitis C are defined as those subjects testing positive for anti-HCV. The controls for risk factors are those that have completed survey with random sample, who tested negative for the same test.

Population sample

Derqui is a suburban county, second rib, of the greater Buenos Aires metropolitan area. Buenos Aires is a megacity, with around 12 million persons; the first rib has a better socioeconomic situation than those of the second rib. The second rib of the greater metropolitan area is very poor and with extremely unequal population. Derqui population was estimated in 252.483 when last surveyed (INDEC 2010).[22]

We proceeded to design a multistage probability sampling and quotas based on age and sex distribution obtained from census data. It was determined that a sample of about 1500 participants offer accuracy for estimating prevalence of 95% and to detect an estimated prevalence of 2% HCV. Since it was expected that the prevalence of HCV below the age of 20 was extremely low, it was decided to stratify the sample into two age groups (older and younger than 20 years) and take the sample with a 3:1 ratio, so as to have adequate age groups with the largest size in 20 years. The work of selecting households and participants was conducted by members Derqui primary care health teams, which have a high degree of community integration and experience working with this population. These teams were trained prior to the study techniques both in community outreach, probabilistic selection of households and other study procedures, by a professional surveyor who supervised the process and defined the manual of procedures in the field for sample detection. In many instances, direct members of the community assisted in the study. The study was conducted between October and December 2003.

Questionnaire

A questionnaire was developed based on the survey questions used in NHANES III and to evaluate the presence of risk factors not considered in this study and more appropriate for our setting. The questionnaire was assessed by interviewers and was tested by selected members of the target population to assess clarity and understandability, problem correction of questions or data collected. Socio-demographic data, drinking water quality, and risk factors for transmission or parenteral contact with human blood information was collected, and risk factors for sexually transmitted diseases were assesed. HC-UPP was defined as: a) ever received an injection syringe with a glass or b) Have underwent surgery 3 or more times before 1990 (a period of heavy utilization of re-used equipment in health care facilities). An informed consent form was applied to all adults or children´s caregivers, before applying the questionnaire and before obtaining the blood sample. The study was approved by the Institutional Review Board of the Academic Health Center (Hospital Universitario Austral) and by Public Health authorities of Derqui County, Buenos Aires Province, Argentine.

Serology

Samples were obtained by field crews and transported refrigerated to the laboratory on the day of the HUA. There, after being centrifuged and separated plasma were determined following serology and laboratory analysis: anti HCV: - Methodology MEIA, HAV IgG - Methodology MEIA, alanine transaminase - Methodology UV.

Statistical analysis

Averages were calculated for continuous variables and percentages for dichotomous / ordinal. We calculated 95% CI based on normal approximation using standard errors for means and proportions by calculating the degree of additional variability caused by the type of design used (multistage sampling). For this individual weights were constructed selection probability ($p = n / N$) and defined as primary sampling unit radius census. To assess the independent contribution of risk factors for HCV infection probability, multivariate models were developed using a logistic regression technique adapted to the type of sampling. For all statistical calculations were used commands for complex sampling estimate provided in STATA 8.

Results

Population characteristics

The final sample of 1472 participants was achieved (98% predicted). Population is a “young”, and that 43% of the population is 30 years or less, 8,9% where aged <18 yrs. old and 11,6% were aged >65 yrs. old; with 47% of male participants (Table 1). The 20.8% reported not having a job at the time of the survey, and 86% were under 12 years of education. The 89.7% of the population is the main source of drinking water a well, 4.5% water and 5.3% drink bottled water. No data are available for 0.5% of the participants. The average number of years that the participants reported having been resident in Derqui was 17.4 years. Regarding the prevalence of risk factors for HCV infection, 26% underwent an operation, 7.5% underwent at least one transfusion, 15% received a glass syringe injection, and 12.2% reported having one or more tattoos. The 3.6% has had work related hospital activity. Only 1.2% EV acknowledges having used drugs in the last year and 1.7% reported having been in prison.

Seroprevalence of HCV

The absolute number of defined positive participants was 23 individuals (1.5% of the sample) (Table 1). The weighted prevalence in the population structure was 0.87%, (95% CI 0.31-1.18). Considering the group older than 30 years as cut-off value for age, the prevalence was 1.8%, (95% CI 0.74-2.57) among the aged. Females

showed a slightly higher prevalence but not statistically significant (0.77% vs. men. Female 0.95%). Table 2 shows the prevalence by age, highlighting that the peak prevalence is between 40-49 years, with a second in participants 70 or more years.

Conventional risk factors

Table 3 presents the results of multivariate analysis to determine the independent contribution of risk factors studied to determine the status of HCV infection. The history of surgery or at least report having used intravenous recreational drugs were the only factors independently associated with the risk of HCV positive serology.

Unconventional risk factors

The HC-UPP occurred in 19.4% and was associated with HCV (OR 4.34, 95% CI, 1.28-14.78, p = 0.024). Intravenous illicit drug use (IV DU) showed a tendency to increased risk (OR 4.88, 95% CI 0.91-26.20, p = 0.06). Both associations were demonstrated after conducting probability sampling and multivariate analysis for complex samples. The population attributable fraction (PAF) for HC-UPP was 15.3% (95% CI 8.8% -21.3%).

Table 1 Results: Baseline Demographics, prevalence of positive serology for hepatitis C and age specific prevalence

	HCV+	HCV-	P
	N(Weighted proportion*)	N (Weighted proportion*)	
N	23 (0.87%)	1449	
Males	12 (39.35%)	668 (54.01%)	NS
Partner	14 (60.13%)	919 (51.25%)	NS
Age	44.18±17.4	49.15±16.4	NS
<18	1 (0.69%, 0.68-0.70)	130	
19-45	7 (0.69%, 0.67-0.70)	540	
45-65	12 (1.98%, 1.97-1.99)	616	
65+	3 (2.06%, 2.03-2.09)	168	

*Population weight estimated as N/n

Table 2 Risk Factors for HCVI

	HCV+	**HCV-N (Weighted proportion*)**	**OR (Unadjusted) (95%CI)**	**Pearson c2**
	N (Weighted proportion*)			
Transfusion	5(31.96%)	177(7.28%)	7.22, (1.27-40.89)	0.01
Surgery >3	5 (61.17%)	144(23.21%)	5.21, (1.26-21.45)	0.01
Glass syringe	13(28.09%)	492(15.31%)	2.16, (0.64-7.28)	NS
Tattoos	1(19.38%)	21(12.17%)	0.14, (0.01-1.35)	NS
IV DU	2(4.30%)	18(1.18)	4.93, (0.80-30.16)	NS
Hospital Work	5 (26.68%)	16(3.26%)	9.72, (1.89-49.72)	0.01
Imprisonment	2(4.32%)	18(1.57%)	2.80, (0.49-15.85)	NS

*Population weight estimated as N/n

Table 3 Association between HCUP and HCVI

	OR (Crude)	**OR (Adjusted*)**
HC-UPP	3.06, (95%CI, 1.29-7.28), p<0.01	4.34, (95%CI, 1.28-14.78), p<0.01
IV DU	4.93, (95%CI, 0.80-30.16, p=NS	4.88, (95%CI 0.91-26.20), p=0.06
		Population Attributable Fraction (PAF)
HC-UPP		15.3% (95% CI 8.8%-21.3%).

Conclusion

This paper makes two main points: an estimate of hepatitis prevalence and provides some observations regarding risk factors of hepatitis C transmission in Argentina. Hepatitis C sero-prevalence of anti

-HCV (+) results, adjusted for age and sex, as measured by serum antibodies is 0.87% (95% CI, 0.31-1.18), while the value for those older than 30 years is 1.80% (95% CI, 0.74-2.57). Health Care Unsafe Parenteral Practices (HCUPP) are among the most significant contributors to its causation. Age stratification shows an increasing age related prevalence as frequently found in many countries.[23]

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Our study emphasizes that health care unsafe parenteral practices may be a major contributor to hepatitis C prevalence in LAC. The study shows remarkably similar results to the main LAC study on hepatitis prevalence, the Brazilian National Prevalence Study,[24] which shows lower than usually reported prevalence, wide regional heterogeneity, injected and sniffed drug abuse, and a major role for hospitalizations and glass syringe injections, among other risk factors related to social circumstances (such as lack of sewage disposal). Brazil national study concludes that known risk factors explain only 50% of hepatitis C cases. Hepatitis C virus transmission in Latin America may be much more complex than usually assumed.[25]

The prevalence estimate found also compares to that of other community populations.[26] Our study suggests an age related increase in prevalence, with a similar pattern to that of Italy and Japan; the prevalence curve overlaps over that of other LAC countries. Prevalence studies display three predominant patterns according to age: countries with current high risk of transmission have a peak of prevalence at middle age (Australia, USA), indicating high risk in recent periods (10-30 years), specially mediated through drug addiction and related behaviors (HIV transmission co-infection). Other countries with high and increasing prevalence according to age, peaking in the elderly (Japan, Italy) indicate old exposures (>30 years). Finally, increasing prevalence in all ages and increased values among the elderly, indicate increased risk through a continuous exposure due to a high-risk situation in the past, mostly through unsafe parenteral practices (Egypt), and a continuous pattern of infection after that exposure. These effects of age in increasing prevalence are required for modeling, which can predict the progression to cirrhosis, cancer and transplantation. [27]The classic case of unsafe injections was the HC epidemic due to vaccination against schistostomiasis.28 According to this data Argentina follows a pattern similar to that of Italy and Japan. Our peak age prevalence rate is similar to that of Brazil. An historical review of these patterns is available.

Risk factors for HCV infection are well known.[29] Behavioral risks factors relate to IVDU are predominant in more developed countries (MDC), but its importance in other countries is less well known.[30] Meta-analysis about the burden of HCV among IV DU, estimates that midpoint prevalence was 60-80% of IV DUs had anti-HCV (25 countries) and more than 80% of IV DUs (in 12 countries).[31] In this study IV DU was short of significance, most probably due to voluntary denial, recall bias, or true low prevalence of IV DU in Argentina. Other patterns of drug abuse are more predominant than those of IV DU, as the Brazilian national study shows.

Health care exposures in Argentina may be more relevant than expected in the international literature. Our construct of HC-UPP correlated, after adjustment to well known risk factors, with HCV prevalence (OR 4.34, 95%CI, 1.28-14.78, p=0.024). This may occur through unsafe injections, hospitalizations, surgery, health care work or other unknown mechanisms. Although unsafe injections represent 12% of the Global Burden of Disease (GBD), evidence about epidemiology and relative importance of unsafe and unnecessary injections in Argentina is scarce, both for the community and in the health care sector. In a study similar to ours,[32] in a random sample aged 18-40 years of a community in slums of Chennai, India, reported a prevalence of 2.4% Hepatitis C among non-drug addicts males, associated with use of informal health care providers ("Quacks") (OR: 5.83 (IC 95% 1.57-21.6). A case control in Pakistan study found increased risk of hepatitis C infection among those reporting more than 5 injections per year.[33] This pattern of exposures to unsafe and unnecessary injections is repeated in several communities in India, and the median population attributable fraction for hepatitis C infection due to unsafe medical injections is 38%, ranging from 18 to 62%.[34] The concordance of this study with findings in other far remote populations like those in India and Pakistan, is a strength to remark possible mechanisms of unsafe parenteral practices.

Glass syringe use reported as a risk factor may be a proxy marker of unsafe injections or other unsafe parenteral practices. The proportion of glass syringes observed in this study is 15% among HC (-) and 28% among HC (+) patients. Other studies suggest the same risk factor for blood borne viruses.[35] In Egypt, national campaigns against schystostomiasis between 1920 y 1980, with several injections in several week periods and syringe reuse without adequate sterilization, disseminated the virus C and led to a high population prevalence (18%).[36] It may also be a proxy of secular changes in injection practices, the elderly being more prone to injections with glass syringes. The cumulative number of injections per year and over years increases the risk of transmission of HC in Taiwan[37] and Pakistan community based[33] or clinic based studies.[38] Brazil national prevalence study found glass syringes to be a problem, as it happens in our study. The unsafe handling of disposable syringes may be related to the question asking for glass syringes in this study.

Transfusion is a significant established risk factor in this study as in other main studies. However, worldwide improvements in blood bank and transfusion safety occurred over time and places. Unsafe parenteral practices in the health care setting may overlap with unsafe and unnecessary injections in the community, and the relationship to health care occupation suggests this relation. This study suggests that nosocomial transmission is an important risk as well. Unsafe injections increase 10-100 times among hospitalized children and adults. In more developed countries unsafe injections in health care settings is almost nonexistent, while is an important although poorly quantified problem among Less Developed Countries (LDC).

In Argentina, the association of prior surgery and even health care occupation, may well be related to multiple unsafe health care associated infections, such as re-sterilization of devices or material, like hemodialysis filters, or poor nosocomial infection control practices and surgical infection rates.[39] Surgical infections need to be associated to other nosocomial infection rates.[40] (Argentina has very poor record of surgical infections estimated in 19%; vs. Chile 0.9-3.3%; Brazil 0.2-6.3%;[41] while USA has less than 5% for low risk surgery and 12% for high risk[42]). The issue of potential occupational exposure among health care workers also emerges from this study. Estimates of this problem are well known and recognized as important ones.[43]

Several limitations are obvious this study. Firstly, the lack of viral confirmation is a weakness of this sample; HC virus was confirmed with different strengths various studies, usually 80% are PCR positive among serologically positive patients. Secondly, we developed, adapted and tested the questionnaire in the field. As the study was almost unfunded, no trans-cultural validation of the instrument was possible. However, questions are very direct and fact based to induce complex interpretations, different international studies used very similar questions and provided valuable information. Thirdly, the study addressed, but was not designed to study, the risk factors of unsafe, unnecessary or nosocomial infections as the focus of the study, but to define the prevalence of hepatitis C. New studies addressing this problem as such are required, and should address the unsafe injections in a more detailed way, perhaps combining qualitative and quantitative methods.

Parenteral exposure through health care sources is less well known than IVIDU as a risk factor, and may be one to address in future HCV epidemiology studies in Latin America. Hepatitis C is more related to health care exposures than expected in LDC. Health care should not be a vehicle of hepatitis C virus transmission. The population attributable fraction found in this study is of concern in a LAC country.

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Conflicts of interest

Authors declare that there is no conflict of interest.

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