Hepatitis C in a sample of pregnant women in Switzerland: seroprevalence and sociodemographic factors

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Summary

Principles: The aim of this study was to determine the prevalence of hepatitis C (HCV) infection in a sample of pregnant women living in Switzerland in 1990–1991, in order to complement existing data in various populations.

Methods: Blood samples were collected from women from consecutive births in obstetric wards in public hospitals of 23 Swiss cantons over a one-year period. They were tested, among other things, for the presence of hepatitis C virus antibodies (anti-HCV). Statistical analyses were done to explore the association of demographic variables with anti-HCV.

Results: The study included a total of 9,057 women of whom 64 tested positive for anti-HCV, resulting in a crude prevalence of 0.71%. Prevalence varied by age and was highest in the 25–29-year age-group (0.90%). 43/5,685 Swiss women were HCV seropositive (0.76%) compared with 21/3,372 non-Swiss women (0.62%). Stratified analysis showed a significant association between anti-HCV and anti-HBc antibody positivity in Swiss (adjusted OR [aOR] 23, 95% CI 12–43) and non-Swiss nationals (aOR 3.3, 95% CI 1.3–8.3).

Conclusions: The prevalence of anti-HCV antibodies in the early 1990s was <1% in this sample of pregnant women in Switzerland and was associated with age, nationality and the presence of anti-HBc antibodies, a marker of exposure to hepatitis B virus. These results are in accordance with those from other published European studies. If an effective intervention to prevent vertical transmission becomes available, information on the current prevalence of HCV in pregnant women would be needed in order to assess how screening recommendations should be modified.

Key words: Switzerland; hepatitis C infection; pregnant women; cross-sectional study; screening

Introduction

The hepatitis C virus was identified in 1989 and shown to be the aetiologic agent in a substantial part of what was formerly classified as "non-A non-B" viral hepatitis [1]. This blood-borne virus is endemic worldwide, with an estimated 170 million persons chronically infected (approximately 3% of the world population) and an estimated worldwide incidence of 49–66 cases/100,000 persons annually (based on mid-2000 world population estimates) [2]. Its prevalence varies in different parts of the world, ranging from around 1% of the population of Europe (8.9 million) to 5.3% of the population of Africa (31.9 million) [2]. In Switzerland, where hepatitis C is a reportable infectious disease, the annual incidence in the general population is about 7–14 cases/100,000 persons, and the prevalence has been estimated to be between 0.7–1.0% [3]. Prevalences of anti-HCV have been estimated in several high risk groups in Switzerland, including injection drug users (IDUs) and patients undergoing dialysis. Injection drug use is the major risk factor for HCV infection in Switzerland, with reported prevalences varying between 70–82% in specific groups attending rehabilitation clinics [4, 5]. Patients undergoing haemodialysis and peritoneal dialysis had prevalences of 5.7% and 3.1% respectively, according to a nationwide survey conducted in 1999 [6]. Based on a report by the Swiss National Reference Centre for Blood Transfusions, the prevalence in routinely screened new blood donors (19,000–40,000 new donors per year; 1996–2003) was found to be between 0.03–0.16% [7]. Recipients of blood transfusions have been estimated to account for

less than 10% of all persons with HCV in Switzerland, but this varied considerably according to age [3].

As hepatitis C infection is usually chronic and asymptomatic for many years, serological studies are needed to obtain a more accurate estimate of prevalence and to assess the potential public health impact. This study, using sera from a cross-sectional sample of pregnant women, was undertaken to complement existing data on prevalences in other populations in Switzerland.

Methods

From September 1990 to October 1991, serum samples were collected from mothers during consecutive births in obstetric wards of public hospitals in 23 of 26 cantons in Switzerland. This material was originally used for seroprevalence studies of toxoplasma and hepatitis B [8, 9]. Only three cantons did not participate in the study (Appenzell Innerrhoden, Appenzell Ausserrhoden and Basel Landschaft). The toxoplasma study had a target sample size of about 8700 based on an expected seroprevalence of toxoplasma antibodies of 40% in women aged 20–40 years of age, and a target precision expressed as a 95% confidence interval of ±1% [8, 10]. Based on this expected seroprevalence and the number of births by canton in previous years, a target sample size was defined for each participating canton [8]. A single obstetric service was selected in each canton to provide pregnant women for the study until the cantonal target sample size was reached. In the vast majority of participating cantons the obstetric service selected was in the hospital that saw the greatest number of pregnant women, which was usually the public cantonal hospital. The sample represented 10–20% of the women who gave birth in each canton and an overall 11.8% of the total number of deliveries in one year in Switzerland [8]. Data used in this HCV study included information on age, nationality, number of children and whether ever infected with HBV (anti-HBc, a lifetime serological marker of acute, chronic or resolved HBV infection).

Serology

Serological testing for anti-HCV antibodies (a marker of acute, chronic or resolved infection) was performed with the Ortho 3.0 ELISA (enzyme linked immunosorbent assay) test system (Ortho-Clinical Diagnostics N.V., Beerse, Belgium) by the Central Laboratory of the Swiss Red Cross (Bern, Switzerland). Those who were positive for anti-HCV were confirmed as positive by retesting for anti-HCV using an immunoblot assay. The immunoblot assay used was the Chiron RIBA 3.0 Strip Immunoblot Assay (Chiron Corporation, Emeryville, USA). A positive ELISA test was considered confirmed if two or more bands appeared on the immunoblot assay, undetermined if only one band was detected and negative if no band could be identified.

Statistical analyses

Prevalences were calculated by dividing the number of women with confirmed positive hepatitis C antibody tests by the total number of women included in the study. Age was classified into age-groups (≤24, 25–29, 30–34, and 35 years and over).

To explore the association of demographic characteristics with hepatitis C seropositivity, we calculated crude odds ratios for the association of the odds of positive hepatitis C serology with categorical variables. To account for the cluster-type of sampling of women in just one hospital per canton we then fitted random-effects logistic regression models with separate intercepts for the canton of residence/hospital derived from a Gaussian distribution as implemented in the xtlogit command in STATA 9. With these models we obtained adjusted odds ratios and 95% confidence intervals. For these analyses and for variables with more than one level, e.g. age groups, we consistently defined the group with the most observations as the reference group. Effect modification was explored by including interaction terms in the random-effects logistic regression and calculating the likelihood ratio test statistic. We looked at stratified results for those variables where effect modification was found. All analyses were performed using STATA 9 (StataCorp 2003, College Station, Texas, USA).

Results

The study found an overall prevalence of HCV antibodies of 0.71% (64/9057). The age range of the pregnant women included was 15–58 years (mean 28.3 and median 28 years).

Table 1 shows that the highest seroprevalence of anti-HCV was in the 25–29-year age-group (0.90%), if the women were Swiss (0.76%), or were also anti-HBc seropositive (3.79%). Non-Swiss nationals were less likely to be anti-HCV seropositive (aOR 0.42, 95% CI: 0.24–0.75). Ever having been infected with HBV was strongly associated with being anti-HCV seropositive (aOR 12, 95% CI 6.7–20).

When exploring statistical effect modification, a significant interaction was found between na-tionality and anti-HBc seropositivity (likelihood ratio test p <0.01). Therefore, stratified analyses by nationality (Swiss and non-Swiss) were also done.

Table 2 shows that, in Swiss nationals, the highest seroprevalence of HCV was in the ≤24-year group (1.22%), and that there was a strong association with positive hepatitis B serology (aOR 23, 95% CI 12–43, p <0.01).

In non-Swiss nationals, the highest seroprevalence of HCV was in the 25–29-year age-group (0.88%). There was also a significant association with positive hepatitis B serology, although it was much less pronounced than for Swiss Nationals (aOR 3.3, 95% CI 1.3–8.3; p = 0.019).

Table 1

Factors associated with being HCV seropositive in a sample of pregnant women in Switzerland.

Subject characteristics	Number of women tested (column percent)	No. infected with HCV (percent positive)	Crude odds ratios	Adjusted* odds ratios and 95% CI (p-values from likelihood ratio test)
TOTAL	9,057 (100%)	64 (0.71%)		
Age				
≤24 years	2,035 (22%)	16 (0.79%)	0.87	0.89 (0.48–1.6)
25–29 years	3,665 (40%)	33 (0.90%)	1.0	1.0
30–34 years	2,367 (26%)	12 (0.51%)	0.56	0.57 (0.29–1.1)
35 years and over	990 (11%)	3 (0.30%)	0.33	0.29 (0.09–0.96)
				P = 0.069
Nationality				
Swiss	5,685 (63%)	43 (0.76%)	1.0	1.0
Non-Swiss	3,372 (37%)	21 (0.62%)	0.82	0.42 (0.24–0.75)
				P <0.01
Number of previous children				
None	3,589 (40%)	31 (0.86%)	1.55	1.4 (0.82–2.5)
1 or more	4,126 (46%)	23 (0.56%)	1.0	1.0
Missing	1,342 (15%)	10 (0.75%)	1.34	1.3 (0.63–2.9)
				P = 0.42
Hepatitis B serology				
Negative	8,398 (93%)	39 (0.46%)	1.0	1.0
Positive	659 (7%)	25 (3.79%)	8.45	12 (6.7–20)
				P <0.01

German – AG-Aargau, AI-Appenzell Innerrhoden, AR-Appenzell Ausserrhoden, BE-Bern, BL-Basel-Landschaft, BS-Basel-Stadt, GL-Glarus, GR-Graubunden, LU-Lucerne, NW-Nidwalden, OW-Obwalden, SG-St. Gallen, SH-Schaffhausen, SO-Solothurn, SZ-Schwyz, TG-Thurgau; UR-Uri, ZG-Zug, ZH-Zurich; no women from AI AR BL; French – FR-Fribourg, GE-Geneva, NE-Neuchâtel, JU-Jura, VD-Vaud, VS-Valais, Italian – TI-Ticino
* From random-effects logistic regression model

Table 2

Factors associated with being HCV seropositive in a sample of pregnant women: results stratified for nationality.

Subject characteristics	Swiss			Non-Swiss		
	Number of women tested (column percent)	No. infected with HCV (percent positive)	Adjusted* odds ratios and 95% CI (p-values from likelihood ratio test)	Number of women tested (column percent)	No. infected with HCV (percent positive)	Adjusted* odds ratios and 95% CI (p-values from likelihood ratio test)
TOTAL	5,685 (100%)	43 (0.76%)		3,372 (100%)	21 (0.62%)	
Age						
≤24 years	980 (17%)	12 (1.22%)	1.3 (0.63–2.7)	1,055 (31%)	4 (0.38%)	0.42 (0.13 – 1.4)
25–29 years	2,420 (43%)	22 (0.91%)	1.0	1,245 (37%)	11 (0.88%)	1.0
30–34 years	1,638 (29%)	7 (0.43%)	0.52 (0.22–1.2)	729 (22%)	5 (0.69%)	0.73 (0.25-2.1)
35 years and over	647 (11%)	2 (0.31%)	0.30 (0.068–1.3)	343 (10%)	1 (0.29%)	0.30 (0.038 – 2.4)
			P = 0.070			P = 0.35
Number of previous children						
None	2,199 (39%)	22 (1.0%)	1.7 (0.85–3.6)	1,390 (41%)	9 (0.65%)	1.1 (0.44 – 3.0)
1 or more	2,658 (47%)	13 (0.49%)	1.0	1,468 (44%)	10 (0.68%)	1.0
No information	828 (15%)	8 (0.97%)	1.8 (0.74–4.6)	514 (15%)	2 (0.39%)	0.62 (0.13 – 2.9)
			P = 0.23			P = 0.72
Hepatitis B serology						
Negative	5,488 (97%)	25 (0.46%)	1.0	2,910 (86%)	14 (0.48%)	1.0
Positive	197 (3%)	18 (9.14%)	23 (12–43)	462 (14%)	7 (1.52%)	3.3 (1.3 – 8.3)
			P <0.01			P = 0.019

* From random-effects logistic regression model

Discussion

This study found an overall anti-HCV seroprevalence of 0.71% in a large sample of pregnant women in Switzerland between 1990 and 1991. This was within the range of prevalence estimates of 0.1% to 2.4% found in a number of international studies in pregnant women [11]. Specifically within Western Europe, Ward et al. found a prevalence of 0.8% (95% CI 0.55–1.0%) in an inner London multiethnic antenatal population [12]. Also on the basis of a study undertaken in England (North Thames and Bedfordshire), Ades et al. showed a higher seroprevalence of anti-HCV infection according to higher levels of socioeconomic deprivation, with an overall range of 0.02–0.20% [13]. Inner London has areas with high levels of socioeconomic deprivation, and hence the prevalence of 0.8% may reflect that fact. In a cohort of 15,250 pregnant women (age range 20–40 years, mean 30.9 years) studied over 3 years in Northern Italy, Conte et al. found a prevalence of 2.4% [14]. Roudot-Thoraval et al. found a prevalence of 0.99% in a cohort of 2367 pregnant women in France [15].

Our finding of the highest age-specific prevalence in women aged 25–29 years (Swiss and non-Swiss combined) also compares with other studies. One based in Scotland showed the highest seroprevalence of anti-HCV in women aged 25–29 years (0.4%–0.57%) [16]. It is also in agreement with the data from the mandatory reporting system, which indicate that the peak age-specific incidence of HCV infections for women in Switzerland is 20–29 years [17].

The HCV seroprevalence found in pregnant women in the present study was much lower than reported for IDUs and lower than in patients undergoing dialysis, but higher than the estimates in new blood donors [4–7]. Although the women in the present study were not selected according to the presence or absence of known risk factors for HCV acquisition, the prevalence found here cannot be extrapolated to the general population. The prevalence in men, for example, is likely to differ from that in women, as suggested by the data from the mandatory reporting system, with a mean male to female ratio of 1.8 among acute hepatitis C cases reported [17]. Furthermore, the prevalence found here cannot be extrapolated to the general population of women of similar age, since those who become pregnant differ from those who do not as a result of additional characteristics apart from age and nationality. However, in studies performed in France, the prevalences of 1.18% (95% CI 0.9–1.45) and 1.22% (95% CI 0.96–1.48) found in pregnant women in two different regions were very similar to the prevalence found in a representative sample of the general population of men and women aged 20 to 59 years (crude prevalence 1.15%, weighted prevalence 1.05% (95% CI 0.75–1.34) [18, 19]. In a study published by Sag-meister et al., based on a model derived from the estimated annual numbers of HCV-related deaths and transplantations, and from limited information on the natural history of HCV infection, the overall prevalence in Switzerland was estimated to be 1.25–1.75%, although these figures remain debatable given the many assumptions used [20].

The observed association of anti-HCV and anti-HBV seropositivity is consistent with other studies and was expected since the modes of transmission of the two viruses are similar, and therefore risk factors for anti-HCV positivity, such as IDU, are also risk factors for HBV infection [21, 22]. In Swiss nationals we found a stronger association of anti-HCV with anti-HBV seropositivity than in non-Swiss nationals (aOR 23 versus aOR 3.3). This wide difference in aORs was an unexpected finding and probably reflected particular characteristics of the population subgroup in Switzerland with the highest HCV seroprevalence – IDUs, who are also more likely to have a higher lifetime risk of HBV infection. In non-Swiss nationals HBV seroprevalence probably reflected the endemic level of HBV in the country of origin, with a range of risk factors including but not predominantly consisting of injection drug use.

This study had limitations since it was a secondary analysis of a study originally designed for toxoplasmosis infection, and thus only very basic sociodemographic information could be analysed in relation to the HCV infection marker. There was no information on known risk factors such as IDU or history of blood transfusion, and hence, for example, it was not possible to draw any direct inference about why Swiss women had higher odds for being anti-HCV positive. In addition, because the study design meant that women were recruited from a single hospital ward in each canton (usually the largest public hospital), this might have led to biased results if certain sociodemographic and unmeasured behavioural risk factors for HCV were associated with admission to those wards. For example, women of lower socioeconomic class might have been both more likely to give birth in a public hospital than women of higher socioeconomic class, and have had a higher seroprevalence of hepatitis C infection markers. However, we were unable to explore this further as we had no further information on recruiting hospitals [9]. Furthermore, the percentage of women of foreign nationality giving birth in this study was, at 37%, substantially higher than the national percentage of 22% of births attributed to women of foreign nationality in 1991, as reported by the Swiss Statistical Office (http://www.bfs.admin.ch/). This overrepresentation of foreign women may be a consequence of recruiting in public hospitals and could have lowered the overall prevalence found. The prevalence observed in this study might thus be considered to reflect the situation for women giv-

ing birth in public hospitals in Switzerland, but not necessarily for the approximately 20% who gave birth in private hospitals [9]. The strengths of this study were the large nationwide recruitment of consecutively delivering women across 23 cantons and the large sample size achieved, which allowed us to describe sociodemographic associations even when the outcome of interest was rare.

How do these results contribute to the debate on screening for HCV in pregnant women?

Universal screening for HCV in pregnancy is currently not recommended because no changes in care would reduce the risk of vertical transmission, which is thought to be low (5–6%) in the absence of HIV; antivirals are contraindicated in pregnancy and no post-exposure prophylaxis has been shown to be effective [23–25]. However, identifying HCV in pregnancy could have some advantages. Pregnant women are seen regularly throughout pregnancy and already have routine blood tests for various conditions including HBV (HBsAg). If found to be positive for HCV, they could also be counselled to allow a more informed choice concerning lifestyle factors, e.g. avoidance of excessive alcohol intake, as well as prevention of further disease spread. The baby could also be tested to see whether transmission has occurred and could be regularly followed up, as appropriate. This study identified some factors, such as being positive for HBV, which could be used for targeted screening for HCV in pregnancy. However, more than 50% (39/64) could be missed if the screening depended only on positive HBV serology. The current screening recommendations for Switzerland are targeted at those with individual risk factors such as IDUs, persons who had a blood transfusion be-fore 1992, persons who received blood products before 1987, dialysis patients, children of HCV positive mothers, healthcare personnel who have been exposed to blood and persons with elevated liver transaminases [3]. These recommendations already include pregnant women who fall into any of these risk categories. However, up to 40% of pregnant women with HCV have no identifiable risk factor and a further percentage will deny risk factors, even if present, and will not be tested [11, 12].

Whilst routine antenatal testing for HCV is not currently recommended in view of its low prevalence and for other reasons discussed above, the case for universal antenatal screening for HCV will need to be reconsidered if an effective intervention to prevent vertical transmission becomes available. In the meantime, more recent information on the prevalence of HCV and its determinants in pregnant women in Switzerland would be helpful in order to decide how the screening recommendations should be updated.

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