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Incidence and risk factors for hepatitis C infection in a cohort of women in rural Egypt

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Summary

A prospective cohort study of the incidence and risk factors for hepatitis C virus (HCV) infection was performed in 2171 pregnant women in three rural Egyptian villages who were HCV antibody (anti-HCV) and RNA (HCV-RNA) negative at baseline. During an average of 2.2 years follow up, 25 incident cases were observed, giving an estimated HCV incidence of 5.2/1000 person-years (PY). The infection rate correlated with community anti-HCV prevalence in pregnant women, while the perinatal incidence rate of 11.2/1000 PY was almost five times that of the non-perinatal rate (2.3/1000 PY). The data suggested iatrogenic perinatal risk factors were associated with infection in one village, while health education reduced infections in another. Among the 25 incident cases, eight were HCV-RNA negative when they were first found to be anti-HCV positive and one-third of the 15 viraemic cases with follow-up data available cleared their HCV-RNA after an average of 1.3 years. None of the 25 incident cases were jaundiced or had symptoms of hepatitis but elevated serum alanine aminotransferase levels confirmed hepatitis in nine. Our data suggest that asymptomatic HCV infections frequently occurred during the perinatal period but often cleared and that educating medical personnel on safe practices possibly reduced HCV transmission.

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Authors' contributions: GTS obtained the funding for the project; GTS, LSM, SKS, MA-H and NM designed the study protocol; DAS, FS, SN, SS, SKS, NM and ME-B contributed to field supervision, data and sample collection and interpretation of the data; MA-H, SE-Kaf and ME-D conducted the laboratory testing and interpretation of data; GTS, DAS, LSM and FS contributed to the statistical analysis and interpretation of results; MH and SE-Kam assisted in assembling the data; GTS, DAS, SKS, MH, SE-Kam, MA-H, NM and LSM drafted the manuscript. All authors read and approved the final manuscript. MA-H, NM and LSM accept responsibility for the reliability of the laboratory results and the data and its analysis, respectively. GTS and DAS are guarantors of the paper.

Keywords

Hepatitis C virus; Incidence; Risk factors; Pregnancy; Rural health; Egypt

1. Introduction

Hepatitis C virus (HCV) infection is possibly the most frequent cause of chronic liver disease in the world (Anonymous, 1999). It has had a major impact on the health of Egyptians due to its high prevalence following well-intended and extensive campaigns 25—40 years ago to control schistosomiasis with intravenous tartar emetic therapy (Frank et al., 2000; Strickland, 2006). Our group and others have reported that the prevalence of HCV infection in different areas and populations increases with age and can be as high as 30—40% in adults in rural areas in the Nile Delta (Abdel-Aziz et al., 2000; Darwish et al., 2001). More important than prevalence (i.e. past and current infections) is the incidence of ongoing transmission. Despite the Egyptian Ministry of Health and Population's (MOHP) efforts at reducing transmission (Talaat et al., 2006), the incidence rate has been relatively high in some groups. These include children with HCV-infected mothers, family members living in rural villages (Mohamed et al., 2005, 2006b) and husbands with HCV-infected spouses (Magder et al., 2005), due to the large reservoir of infection.

We recently reported the prevalence of and risk factors for HCV infection in a large cohort of pregnant women living in three villages in the Nile delta (Stoszek et al., 2006a). Herein, we report the incidence of and risk factors for HCV infection in 2171 of these pregnant women who were initially HCV-naive and had follow-up demographic and health-related information and serum samples. In addition to providing data on the incidence and risk of infection, our study allowed the assessment of increased risks associated with pregnancy and the perinatal period. It also provided the opportunity to evaluate differences in risks between the three communities where these women lived, as healthcare activities have been associated with the prevalence of anti-HCV in one of these villages (Stoszek et al., 2006a).

2. Materials and methods

2.1. Study sites and subjects

A prospective cohort study was conducted over a period of nine years (1997—2006) in three rural villages in Menoufia Governorate in the Nile Delta. Two villages each had 30 000 inhabitants, while the third had a population of 9000 (Stoszek et al., 2006a, 2006b).

The subjects were pregnant women who were HCV antibody (anti-HCV) and RNA (HCV-RNA) negative at baseline and followed prospectively for an average of 2.2 years (SD ± 1.8 years). They were among 3409 pregnant women attending community health centres (CHC) in the villages for prenatal care. All gave informed consent to participate in the study. All women who were positive at baseline for both anti-HCV and HCV-RNA (n = 373, 10.9%), anti-HCV only (n = 166, 4.9%) or HCV-RNA only (n = 11, 0.3%) were excluded, as well as those with incomplete follow-up data (n = 688). The 2171 subjects in the cohort were seen during their second or third trimester of pregnancy and asked to return two months post-partum and yearly thereafter until their child was five years old; 365 women had a second pregnancy and 23 had a third pregnancy during follow up. For the first pregnancy, 2073 women were seen at the two-month visit; 1330, 919, 630, 427 and 303 attended the one-, two-, three-, four- and five-year visits, respectively. For the second pregnancy, 278 attended the two-month visit, while 193, 124, 53, 31 and five attended one-, two-, three-, four- and five-year follow up. Fifteen, eight and one woman attended the two-month visit and one-

and two-year visits following their third pregnancy, respectively. This provided a total of 4814 person-years (PY) of follow up.

The women answered a detailed questionnaire at enrolment about socio-demographic characteristics, as well as behavioural and environmental risk factors for acquiring HCV infection. Additional data were gathered at the first post-partum visit about the delivery process and outcome. An 8—10ml blood sample was drawn from the women at the time of enrolment and during each follow-up visit.

2.2. Laboratory testing and criteria

Sera were initially tested for anti-HCV with a second-generation enzyme immunoassay (EIA; Abbott, Wiesbaden, Delkenheim, Germany). During the project this kit was replaced by a third-generation assay from the same manufacturer and all seroconverting paired samples were retested on the same plate with the third-generation assay. Testing for HCV-RNA was performed on sera using RT-PCR without RNA extraction, as previously described (Abdel-Hamid et al., 1997). Sera that were anti-HCV positive and HCV-RNA negative were retested following RNA extraction using QIAamp Viral RNA kit (Qiagen, Santa Clara, CA, USA). Serum alanine aminotransferase (ALT) was tested using standard laboratory methods. The upper limit of normal for the procedure used was 40 IU/l.

Incident HCV cases were defined as individuals who seroconverted from negative to positive for anti-HCV and/or HCV-RNA. Anti-HCV seroconversion in the absence of HCV-RNA conversion was further confirmed by repeat testing the last negative and first positive samples of the same woman in duplicate on the same plate.

2.3. Statistical analysis

Incidence rates were calculated by dividing the total number of HCV infections by the number of PY of follow up. For incident cases, follow-up duration was calculated by measuring the time between study enrolment and the suspected time of infection (assumed to be midway between the last negative and first positive HCV result); otherwise duration of follow up was calculated from study enrolment until the last collected blood sample.

To calculate separate incidence rates in the perinatal and non-perinatal periods, the person-time of follow up that occurred between the time of enrolment during pregnancy and the first postnatal visit was considered to be follow up during the perinatal period; follow up after that was considered to be after the perinatal period. However, if a woman's first postnatal visit occurred more than six months after delivery we modified that approach. In that case, if the woman was HCV negative at the first postnatal visit, the first six months after delivery was assigned to the perinatal period and the remaining time was assigned to the non-perinatal period. If the woman's first postnatal visit occurred more than six months after delivery and she was HCV positive, she was excluded from the analyses that distinguished perinatal from non-perinatal incidence.

Perinatal incidence rate was defined as the number of incident cases detected during the perinatal period divided by the number of perinatal PY of follow up. Non-perinatal incidence rate was defined as the number of incident cases detected during the non-perinatal period divided by the number of non-perinatal PY of follow up. Confidence intervals for incidence rates were calculated using an exact approach based on the Poisson distribution. Confidence intervals for incidence rate ratios were calculated by inverting an exact hypothesis test procedure (Kleinbaum et al., 1982). Non-parametric tests were used to compare ALT levels. Stata version 8 (Stata Corp., College Station, TX, USA) was used to perform the data analyses.

Socioeconomic assessment was based upon responses to questions about household possession of various items, monthly financial expenditures and highest level of education. These were used to create a socioeconomic (SE) index to assess and control for factors associated with the subjects' SE status (Stoszek et al., 2006b). The index had values ranging from 4—12 and was divided into three equal parts: 4—6 being low, 7—9 middle and 10—11 high SE status.

3. Results

3.1. Incidence of HCV infection

Twenty-five incident HCV cases were observed during the follow up; 15 cases were both anti-HCV and HCV-RNA positive; eight were anti-HCV positive and HCV-RNA negative; and two women had detectable HCV-RNA in the absence of anti-HCV. Two of the 15 women who had both HCV antibodies and RNA had only HCV-RNA in their first blood sample; anti-HCV was present in a subsequent blood sample. The anti-HCV and/or HCV-RNA incidence rate was 5.19/1000 PY (95% CI 3.26—7.23). The detectable viraemia (HCV-RNA positive) incidence rate for the 17 having HCV-RNA was 3.53/1000 PY (95% CI 1.85—5.21).

Seventeen (68%) of the 25 incident cases were detected at the first sample collection after delivery: 15 women presented during the first six months postpartum, while two were first seen one and two years after childbirth. These two cases were not included in calculating the perinatal incidence rate because HCV transmission may not have occurred during their perinatal period. The estimated perinatal incidence rate (11.24/1000 PY) was 4.9 times higher than the non-perinatal rate (2.3/1000 PY; $P < 0.001$).

Children born to two of the women infected during the perinatal period had anti-HCV in their blood samples collected at the age of two and three months that cleared by the age of one year, suggesting these women were infected during pregnancy.

3.2. Risk factors for HCV infection

Multiple potential risk factors for HCV incidence in the three study villages were analyzed. We observed a positive association between HCV incidence and prevalence among the women in the three villages. HCV incidence and prevalence were 3.0/1000 PY and 13.1%, respectively in village B; 5.1/1000 PY and 16.5%, respectively in village A; and 8.1/1000 PY and 17.3%, respectively in village C. The women in villages A and C were 1.7 and 2.6 times as likely to be infected as those living in village B ($P = 0.075$ for the comparison of rates between villages C and B). Some potential risk factors that had no relationship with being infected were age, level of education, socioeconomic status and occupation (Table 1). A history or presence of schistosomiasis, liver disease, jaundice or hepatitis was not associated with incident HCV infection.

Analysis of perinatal risk factors revealed a trend for greater risk for incident infection in women whose babies were delivered by a physician rather than by a nurse or a traditional birth attendant ($P = 0.14$); in a health facility rather than at their home ($P = 0.12$); and in women having complicated vaginal deliveries ($P = 0.04$), but not by a caesarean section ($P = 1.0$) (Table 2).

No subject had a diagnosed case of hepatitis and the few who had blood transfusions and operations did not sero-convert for HCV. Even though therapeutic injections were received by 86% of the study population, this was not significantly associated with HCV infection during either the perinatal or the non-perinatal period. There was no difference in the rate of

HCV infection, whether injections were given by formal or informal healthcare providers (Table 1).

3.3. Risk factors stratified by communities

To ascertain whether sources of HCV infection differed between villages, stratified sub-analyses were performed. The difference in HCV incidence rates between the villages could be attributed to the perinatal infection rates. The non-perinatal infection rates were much lower and almost the same between villages (Table 3).

Women in the smaller village, A, had a lower socioeco-nomic status than those living in the other two villages. Home deliveries, almost entirely by a single experienced and respected traditional birth attendant, were the rule in this community. Only one-sixth of the women had babies delivered by a physician or nurse in a healthcare facility. If difficulties during labour occurred, the mother was referred to a hospital. Therefore, physician deliveries in this community were in general more complicated and the women in this subgroup more often had invasive procedures than during physician deliveries in the other two villages. The three perinatal incident infections in village A were in women having deliveries assisted by a physician in a health facility; two had a complicated delivery and one had a caesarean section.

The larger two villages, B and C, differed markedly in the risk of HCV seroconversion during the perinatal period. The socioeconomic status of women in these villages was about the same and was better than in village A. Three-quarters of the babies in these two villages were delivered in a health facility by a physician. The overall lower incidence of HCV in village B was due to a lower transmission rate during the perinatal period. None of the mothers in this village who delivered their babies at home assisted by a traditional birth attendant were infected with HCV and the seroconversion rate in mothers who had physician-assisted deliveries in healthcare facilities was lower than in the other two villages.

In village C, the community having the highest incidence rate of HCV, the perinatal risk was high and was almost the same, whether the babies were delivered by physicians in a healthcare facility or by traditional birth attendants at home (Table 3). No significant risk factors were noted during the non-perinatal period. Two incident HCV infections were detected during the first year of follow up. Receiving dental treatment increased the risk of infection (relative risk [RR] =4.86), but was not statistically significant. During the second follow-up year three cases were detected and the risk of infection was non-significantly increased (RR =4.8) in those receiving therapeutic injections.

3.4. Effect of HCV infection on the women's health

None of the incident HCV cases had a history of jaundice, diagnosis of hepatitis or clinical manifestation suggestive of hepatitis during the period of follow up. No significant difference was observed in baseline ALT levels between the 25 incident HCV cases (mean 14.1±3.7 IU/l) and those who did not seroconvert (mean 17.1±11.5 IU/l). However, there was a significant ($P = 0.02$) elevation in ALT in the women who seroconverted vs. those who remained HCV negative (mean 41.0± 43.4 IU/l vs. 18.6± 18.4 IU/l). Twenty HCV incident cases had ALT measured pre- and post-HCV infection. All had normal ALT levels before infection and seven (35%) had ALT levels greater than 40 IU/l afterwards; five of these seven were also HCV-RNA positive and one had a normal ALT level at the first follow up, which became elevated in a subsequent blood sample. Two other women who were HCV-RNA positive had no baseline ALT measured but had elevated ALT during follow up.

3.5. Follow-up of the HCV incidence cases

Seventeen HCV incident cases (two anti-HCV positive, 14 both anti-HCV and HCV-RNA positive, and one HCV-RNA positive) were followed for an average of 1.7±0.9 years (a minimum of 4.4 months and maximum 3.3 years). None lost their anti-HCV during follow-up. Eight (53.3%) of the 15 HCV-RNA positive cases that were followed had persistent viraemia; two (13.3%) had intermittent viraemia, and five (33.3%) cleared their HCV-RNA after an average of 1.3 years, with three persistently negative at their subsequent annual examinations. Four of five who cleared their viraemia had accompanying normal ALT levels during follow up. However, five (62.5%) of eight with persistent viraemia had ALT elevations, at least intermittently, during their annual follow-up examinations.

4. Discussion

Egypt may have the highest prevalence of HCV in the world, averaging 7—25% among adult Egyptian females living in rural areas (Abdel-Aziz et al., 2000; Nafeh et al., 2000). The cohort of pregnant women in the three villages in our study had a 15.8% anti-HCV seroprevalence (Stoszek et al., 2006a). This large reservoir of infectious blood in the inhabitants of these villages appeared to be an important risk factor for infection among women in our cohort, since the village having the lowest anti-HCV prevalence also had the lowest incidence and the village with the highest prevalence had the highest infection rate.

We previously reported risk factors for prevalent or past HCV infection in this cohort of women, when we showed that increasing age, low socioeconomic status, blood transfusion and injection therapy for schistosomiasis were all associated with infection (Stoszek et al., 2006a). When stratified by community, one village had increased risk associated with delivery by a physician in a healthcare facility, while another had increased risk in women whose babies were delivered at home by a traditional birth attendant. Our follow up of the HCV seronegative mothers provided the opportunity to evaluate incident transmission in this cohort.

The overall incidence of HCV seroconversion of more than 0.5% per year among our seronegative women is high. In addition to the large reservoir of HCV viraemia in the community, two other interrelated risks were exceedingly important: the women were five times more likely to sero-convert during their perinatal period than during their subsequent follow up and it appeared that there were specific perinatal iatrogenic risks in two villages. It should be noted that our definition of the perinatal period is broader than the typical definition, extending to the time of the women's first postnatal visit, which was generally two months after delivery. The broader definition was required since we did not have information on their HCV status in the first weeks after delivery.

The risk of HCV infection was particularly high in two of the three communities during the perinatal period. With the exception of two women whose infants were anti-HCV positive at their first visits to the CHC, our data usually did not allow us to determine whether HCV exposures were occurring in these women during the last trimester of pregnancy, during delivery of their baby or post-partum. However, since the seroconversion rate was associated with procedures and complications related to deliveries of the babies, we suspect that many of the infections were occurring at this time. In the smallest of the three villages, village A, in which 84% of the babies were delivered by a traditional birth attendant at home, physician-assisted deliveries in health care facilities were associated with a markedly increased incidence of HCV seroconversion. However, only seven of the incident cases lived in this village, giving an incidence of 5.14/1000 PY. In village C, with the highest incidence, the HCV infection rate was almost eight times greater during the perinatal period than it was outside this period and it did not differ between home deliveries by a birth

attendant or physician-assisted deliveries in a healthcare facility. Since three-quarters of the babies in this village were physician-assisted deliveries in healthcare facilities, nine of the 12 incident cases in women in this village had these risks.

The third village, village B, had a lower HCV perinatal incidence rate (5.0/1000 PY) and, thus, had the lowest overall incidence rate (3.0/1000 PY) among the communities. None of the mothers who were delivered at home by a birth attendant seroconverted for HCV and the infection rate for the mothers who had physician-assisted deliveries in healthcare facilities was lower than in the other two villages.

During the nine years of this study our research team supplemented the MOHP's health education efforts on how to reduce exposures to HCV and other parenterally transmitted infections. These health education efforts may have reduced the risk of HCV transmission by needle sticks in all three communities. However, the community and staff of village B's CHC were the most receptive and eager to adopt safe syringe and needle practices. The inhabitants of rural Egyptian villages believe in the therapeutic value of injections over oral medications and receiving injections was reported by 85% of our cohort. None of the incident cases reported reusing syringes and needles and reuse of syringes and needles was rarely reported (0.6% of participants and almost always the woman reused her own syringe). This result indicates that the Egyptian MOHP's campaign for safe injection practices, conducted in governmental hospitals (Talaat et al., 2006) and in the mass media, is effective. Similar strategies have significantly reduced the risk of HCV infection among injection drug users in the USA (Hagan et al., 1995). Less than a third of our subjects were given an injection by informal healthcare providers, e.g. injection-ists, barbers, midwives or family members and this was not a risk for HCV infection. Injections by such persons was associated with anti-HCV seroprevalence in an earlier study we conducted in the Nile Delta (Habib et al., 2001) and this type of exposure was reported to increase the risk of HCV transmission five-fold in India (Marx et al., 2003).

Our finding that only 60% of the women who serocon-verted for anti-HCV had detectable HCV-RNA in the same and subsequent blood samples is in agreement with our publications and others (Abdel-Aziz et al., 2000; Conte et al., 2000; Mohamed et al., 2006a; Nafeh et al., 2000), showing that a higher proportion of healthy adults clear HCV infections than the reports of 80—85% chronicity in hospitalized HCV patients (Mazzeo et al., 2003; Villano et al., 1997). Two of these 15 cases met the strict criteria of being initial infections, in that they had HCV-RNA without detectable anti-HCV in their first blood sample and later seroconverted for HCV antibodies. While two RNA-positive women had intermittent viraemia during follow up, five cleared their viraemia after an average of 1.3 years. This level of clearance is similar to the 45% reported in a cohort of German women who received HCV-contaminated anti-D immunoglobulin (Wiese et al., 2005).

Our incident cases also included two women (2 of 2148, 0.09%) who had HCV-RNA in the absence of anti-HCV. One of these women had a positive RT-PCR test for HCV-RNA during her next annual visit. The other, who had HCV-RNA in retest-ing the same sample, did not have a follow-up blood sample. Data on HCV-RNA status in HCV-antibody negative subjects is uncommon, since the usual practice is to perform RT-PCR only on blood samples from antibody-positive subjects. Investigations conducted in France and the USA report that 0.2—0.9% of anti-HCV negative organ donors were HCV-RNA-positive (Aswad et al., 2005; Challine et al., 2004). Following exposure, a few individuals may have viraemia with intermittently undetectable levels of HCV antibodies (Beld et al., 1999; Mazzeo et al., 2003).

Just as we reported in our cross-sectional study of prevalent infection in this cohort, none of those who had anti-HCV and/or HCV-RNA had symptoms suggestive of, or a diagnosis of hepatitis. In our community-based studies of HCV we seldom detected a presence or history of hepatitis (Abdel-Aziz et al., 2000; Medhat et al., 2002; Stoszek et al., 2006a; Strickland, 2006). However, when we screened for cases of acute hepatitis in communities or in fever hospitals, where patients with suspected hepatitis receive medical care, HCV was a common cause of hepatitis with ALT levels ranging from 100 to 400 IU/l (Meky et al., 2006; Zakaria et al., 2007). Our data suggested these were mostly flare-ups in people with chronic infections rather than incident infections, since most of the patients had both anti-HCV and HCV-RNA. Nevertheless, this could also be initial infection in persons who have been infected long enough for antibodies to be detected. ALT elevations detected in 36% of our incident cases, particularly those who were HCV-RNA positive, support that these were asymptomatic cases of HCV hepatitis.

Our results indicate that HCV transmission was occurring in this cohort of women at annual rates of 1.1% during the perinatal and 0.23% during the post-perinatal period. Risk correlated with the community reservoir of infection, i.e. HCV antibody and RNA prevalence in pregnant women. The absence of increased perinatal and total risk of HCV infection in women living in the village that was most receptive to health education on the control of blood-borne infections suggests that educating medical personnel on the use of safe practices during the perinatal period may reduce HCV transmission in Egypt and other lesser-developed countries, just as it has in the USA (Fischer et al., 2000).

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Table 1

Sociodemographic risk factors for incident hepatitis C virus infection

Variable	Incident cases/person-years	Incidence rate/1000 person-years	Relative risk (95% CI)		*P*-value
Overall incidence rate	25/4814	5.19			
Village					
A	7/1362	5.14			
B	6/1966	3.05	0.59	(0.2—2.1)	0.50
C	12/1485	8.08	1.57	(0.6—4.7)	0.47
Age (years)					
<22	8/1460	5.48			
22—30	13/2878	4.52	0.82	(0.3—2.3)	0.82
>30	4/474	8.44	1.54	(0.3—5.8)	0.67
Socioeconomic status[a]					
Low	9/1579	5.70			
Middle	13/2585	5.03	0.88	(0.3—2.3)	0.93
High	3/646	4.64	0.82	(0.1—3.3)	1.0
Housewife					
No	4/826	4.84			
Yes	21/3987	5.27	1.09	(0.36—5)	1.0
Reuse syringes					
No	11/2886	3.81			
Yes	0/18	0	0	(0—63.9)	1.0
Received injection by					
Physician/nurse	17/3041	5.59			
Others	7/1556	4.5	0.80	(0.3—2.1)	1.0

[a]Socioeconomic index created from lifestyle questionnaire. Score: 4—6 = low; 7—9 = middle; 10—12 = high.

Table 2

Perinatal risk factors for incident hepatitis C virus infection

Perinatal risk factors	Perinatal incident cases/perinatal person-years	Perinatal incidence rate/1000 person-years	Relative risk (95% CI)		*P*-value
Perinatal incidence rate	15/1335	11.24			
Attendant at delivery					
Nurse/birth attendant	3/551	5.44			
Physician	12/766	15.67	2.88	(0.8—16.0)	0.14
Place of delivery					
Home	3/569	5.27			
Health facility	12/757	15.85	3.01	(0.8—16.6)	0.12
Mode of delivery					
Vaginal	11/1103	9.97			
Ventouse suction extraction	2/19	105.26	10.6	(1.1—50.6)	0.04
Caesarean section	2/199	10.05	1.01	(0.1—4.7)	1.0
Hospitalization					
No	3/556	5.40			
Yes	12/770	15.58	2.89	(0.8—16.0)	0.14
Therapeutic injections					
No	6/284	21.13			
Yes	9/1016	8.86	0.42	(0.1—1.5)	0.18

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Table 3

Incidence rates and perinatal risk factors stratified by village

Variable	Village A		Village B		Village C	
	Incident cases/person-years (IR/1000 PY)	*P*-value	Incident cases/person-years (IR/1000 PY)	*P*-value	Incident cases/person-years (IR/1000-PY)	*P*-value
Overall incidence	7/1362 (5.14)		6/1966 (3.05)		12/1485 (8.08)	
Perinatal incidence	3/359 (8.36)		2/402 (4.97)		10/574 (17.42)	
Post-natal incidence	2/1002 (2.0)	0.24	4/1564 (2.56)	0.71	2/911 (2.20)	0.004
Attendant at delivery						
Nurse/traditional birth attendant	0/297 (0)		0/110 (0)		3/144 (20.83)	
Physician	3/59 (50.85)	0.009	2/290 (6.90)	1.0	7/417 (16.79)	0.99
Place of delivery						
Home	0/302 (0)		0/120 (0)		3/147 (20.41)	
Health facility	3/55 (54.55)	0.007	2/281 (7.11)	1.0	7/421 (16.63)	1.0
Mode of delivery						
Vaginal	0/328 (0)		2/325 (6.15)		9/449 (20.04)	
Vacuum suction	2/4 (50.0)	<0.001	0/11 (0)	1.0	0/4 (0)	1.0
Caesarean section	1/22 (45.45)	0.13	0/66 (0)	1.0	1/112 (8.93)	1.0
Perinatal hospitalization						
No	0/292 (0)		0/120 (0)		3/145 (20.69)	
Yes	3/65 (46.15)	0.012	2/282 (7.09)	0.98	7/423 (16.55)	0.98

IR: incidence rate; PY: person-years.