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HCV Coinfection in a Cohort of HIV Pregnant Women

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Abstract

Objective: To evaluate clinical, epidemiological and mother to child transmission in pregnant women with HIV-HCV coinfection compared to the HIV-positive non-coinfected group.

Subjects and Methods: A retrospective cohort study from 2000 to 2015 involving 61 HIV-HCV coinfected pregnant women versus 743 non-coinfected and were evaluated maternal side effects, pregnancy complications, development of newborns and mother to child transmission of HIV and HCV.

Results: The main route of acquisition of coinfection was sexual intercourse (86.8%). Some opportunistic diseases had a higher frequency in the group. The liver enzyme abnormalities were more pronounced in coinfected group ($P < 0.0001$). The average birth weight of newborns was greater than 2500g in both groups and, likewise, the gestational age is greater than or equal to 37 weeks over 70% of cases. Apgar of 5th minute less than 7 was more frequent in the coinfected group. Mother to child transmission of HIV was 1.8% in coinfected women and 2.7% in those non-coinfected.

Conclusion: In this cohort, the presence of HCV-HIV coinfection was related to worse results in liver enzymes during pregnancy, increased incidence of condylomatosis, pneumonia and active tuberculosis. There was high incidence of prematurity and low birth weight, regardless of the presence of HIV-HCV coinfection.

Keywords: *HIV; Hepatitis C; HCV; Coinfection; Mother to Child Transmission; Pregnancy*

Introduction

HIV infection during pregnancy, despite being well controlled with the use of antiretroviral therapy (ART), still stigmatizes the infected person and causes an incurable disease. The concern becomes even greater in pregnant women due to the possibility of mother to child transmission (MTCT).

Some diseases may occur concomitant to HIV infection and cause serious complications and, if the infected person is a pregnant woman, can cause fetal and neonatal sequel,such as Hepatitis C [1-3]. In the world, there is an estimative that about 130 to 150 million people are infected with hepatitis C virus (HCV) [3]. Some pregnant women can, in addition to HIV infection, be also infected with hepatitis C virus, presenting coinfection, which is the most common condition between drug users. The prevalence of HIV-HCV coinfection varies widely according to the type of population evaluated ranging from 3.8% to 42.6% [4-6].

There are few studies on clinical complications in HCV-infected pregnant women, but there are no evidences that clinical developments of HCV-infected pregnant women differ significantly from those non-pregnant. So far, there is no existence evidence of a mother to child transmission prevention method of this infection [7]. Thus, the American College of Obstetrics and Gynecology does not recommend the tracking of this virus during prenatal care except for patients considered as high-risk (such as drug users, HIV-positive and health

professionals) since there is no prophylactic intervention measures in prenatal care and delivery. Breastfeeding is not also a determining factor for HCV MTCT [5,6,8].

In adults, HIV-HCV coinfection usually accelerates the progression of HIV, aggravating the clinical condition; furthermore, it is known the HCV mother to child transmission probability is increased around 4 times in these patients. HCV infection acquisition through mother to child transmission has become an important source of pediatric HIV infection. Almost all children who remain viremic after several years develop chronic hepatitis. The HCV mother to child transmission rate is critical for HCV-disease prediction in future generations. Conservative estimates suggest that between 10,000 and 60,000 babies can be infected with HCV each year in the world through mother to child transmission [4].

Aim of the Study

This work aims to study the pregnant women who present HIV-HCV coinfection and compare them to the group of pregnant women just HIV-infected, in order to evaluate the effects of this coinfection from the clinical, epidemiological and obstetric point of view and possible repercussions for the mother and newborn.

Subjects and Methods

Observational and analytical study with a historical cohort, consisting of HIV positive pregnant women receiving care at CAISM/UNICAMP and their exposed newborns evaluated over time. In this study were included allHIV-positive pregnant women assisted in the prenatal clinic specialized in infections in the period between 2000 and 2015. 743 HIV-positive pregnant women and 61 who present HIV-HCV coinfection were evaluated. There was occurrence of 816 pregnancies, 12 of them twins; 10 in the non-coinfected group and 2 in the coinfected group. There were 81 losses to follow-up of children; 14-children information were not found, there were 14 fetal losses and 2 children are still in follow-up (Figure 1).

The list of HIV-positive women was obtained by the clinical records of HIV-positive pregnant women of CAISM/UNICAMP, Hospital Infection Control Committee (CCIH) and Epidemiologic Surveillance Service (SVE). After listing names and hospital record numbers, proceeded to the collection of obstetrical and medical records, as well as consulting the electronic medical records when available (the obstetrical clinics virtual system began to operate in January 2007). The data collection was performed in specific form. As newborns do not have clinical records yet in the first days of their lives (except in cases of severe neonatal complications such as hospitalization in intensive care) and their names are not recorded in the clinical records of mother, a search for the identification of children and their names was necessary, through: 1. Clinical records of own child if there was neonatal hospitalization; 2. Listing of children under follow-up in the Pediatric Immunodeficiency Clinic; 3. Registration of the newborn in Social Work; 4. Registration of the child as a VT case in Epidemiologic surveillance service. All information collected were coded and stored in a database created for this purpose. Each mother-child pair was identified with a number.

Initially, it was performed a descriptive analysis of the variables in the two groups: HIV- HCV-coinfected pregnant women and just HIV-infected pregnant women. To evaluate the association between exposure to HIV and HCV in pregnancy and neonatal periods and maternal and neonatal effects were performed Qui-square test or Fisher's exact test. The unadjusted odds ratio (OR) were estimated with their respective 95% confidence interval (95% CI) for each independent variable. The nonparametric Wilcoxon test was used to evaluate the difference between the means of continuous variables in both groups. The significance was 5%. For statistical analysis was used the SAS software version 9.4.

The maternal quantitative variables analyzed were age, gestational age at delivery, time of membrane rupture prior to delivery. The newborn quantitative variables analyzed were birth weight, gestational age at birth (Capurro), Apgar, head circumference and other variables (route of delivery, marital status, race and formal education) were categorized for statistical analysis. The significance level of 0.05 was used and data was analyzed with the statistical program SAS version 9.4.

Results

From 2000 to 2015, among 816 pregnancies evaluated, 804 HIV-infected pregnant women were analyzed, and the prevalence of HCV-coinfection was 7.59% (n = 61).

Figure 1 shows the excluded cases and the final analysis of the cases.

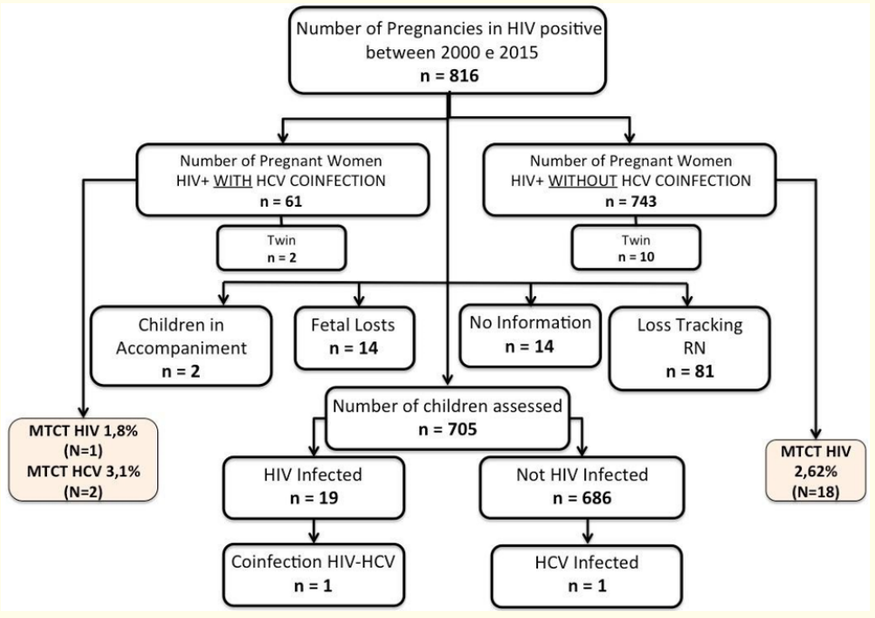

Figure 1: *HCV coinfection in a cohort of HIV pregnant women in CAISM/UNICAMP from 2000 to 2015.*

The mean maternal age was 30 years, with no difference between the groups of HCV-infected and non-infected women. The mean formal education was 9 years and most women were Caucasian in both groups. Just over 10% of women in both groups were drug users; alcohol consumption was shown in about 5% of women in both groups; smoking was more frequent in the coinfected group (20% versus 13.5%). Condylomatosis, pneumonia and active tuberculosis had a higher frequency in the coinfected group; however, other infections have had no significant difference between groups (Table 1).

Key Features	With HCV	Without HCV	p (value)	OR	IC (95%)
Middle School Age (Years of Study)	9	9	0,8257*	0,89	0,38-2,11
Middle Maternal Age (Years)	30,5	28	0,0014		
Caucasian race (%)	67,20	60,80	0,3139*		ref.
Drugs Users (%)	13,50	14,10	0,8922*	0,94	0,41 - 2,17
Smokers (%)	20,00	13,50	0,2349*	1,6	0,76 - 3,35
Alcoholics (%)	5,90	5,60	1,0000**	1,04	0,31 - 3,57
Kind of Delivery (%)					
Vaginal	10,20	6,70			
Forceps	0,00	0,30	0,5625*	1,5	0,62 - 3,67
Cesarean	89,80	93,00			ref.
Twin Pregnancy (%)	3,70	1,50	0,2206**	2,56	0,55- 12,0
Most common infection (%)					
Condylomatosis	23,00	13,60	0,0458*	1,89	1,0 - 3,56
Pneumonia	8,20	3,00	0,0488**	2,89	1,05 - 7,92
Active tuberculosis	8,20	1,10	0,0018**	4,75	1,5 - 15,04
Cervicitis (Gonococo/Clamidia/Tricomonas)	4,90	4,90	1,0000**	1	0,3 - 3,36
Vaginal Candidiasis	29,50	31,50	0,7507*	0,91	0,51 - 1,61
Bacterial vaginosis	36,10	33,40	0,6694*	1,13	0,65 - 1,94
Urinary infection	26,20	35,20	0,1551*	0,65	0,36 - 1,18
Streptococcus B	35,30	33,30	0,8679*	1,09	0,39 - 3,04
Syphilis	4,90	5,20	1,0000**	0,95	0,28 - 3,17
Middle CD4 FINAL (cell/mL)	418,1	555,2	0,0004		
Final Undetectable Viral Load (%)	57,40	59,00	0,8222*	1,07	0,61 - 1,87
Patients on ART Preview (%)	42,60	40,00	0,6910*	1,11	0,66 - 1,89
Patients who stopped ART before pregnancy (%)	3,80	25,10	0,0141*		ref.
Patients who used AZT during delivery (%)	93,20	95,00	0,5328**	1,39	0,48 - 4,06
	n (63)	n (753)			

Table 1: *Epidemiological and clinical characteristics of HIV positive pregnant women with and without HCV.*

** Chi-Square Test; ** Fisher's exact test*

More than half of coinfected women did not use ART before pregnancy (Table 1). The most commonly ART used during pregnancy was of two nucleoside reverse transcriptase inhibitors (NRTI) associated with a PI (Protease Inhibitor) corresponding to more than 50% of the cases in both groups; The most used PI was lopinavir/ritonavir; only a small part of the population of pregnant women used regimen with non-nucleoside reverse transcriptase inhibitor NNRTIs - nevirapine (Table 2).

ART during Pregnancy (N%)	With HCV	Without HCV	OR	IC (95%)
None	1,7	1,6	1,91	0,23- 5,57
AZT Monotherapy	3,3	3	2,09	0,45 - 9,6
ITRN + ITRN	1,7	1,5	2,09	0,25 - 17,1
ITRN + ITRN + IP (NFV)	28,30	16,10	3,31	1,64 - 6,68
ITRN + ITRN + IP (LPV/R)	28,30	53,10		ref.
ITRN + ITRN + ITRNN (NVP)	26,70	16,60	3,01	1,48 - 6,13
Another scheme with PI	8,30	6,10	2,55	0,9 - 7,24
	n (61)	n (743)		

Table 2: *Antiretroviral therapy regimens most commonly used by HIV-positive pregnant women with and without HCV coinfection.*

The mean viral load at the beginning to the end of prenatal care showed no significant difference between the coinfected and non-coinfected groups. In relation to CD4, non- coinfected pregnant women showed higher values compared to the coinfected group at about 25% ($p < 0.05$) (Table 1). More than half of pregnant women reached undetectable viral load at the end of pregnancy: 57.4% in coinfected group and 59.0% in non-coinfected group.

There was no significant change between the coinfected and non-coinfected groups with respect to changes in blood count. Regarding to liver enzymes evaluated at the beginning of pregnancy, the coinfected group showed a greater change in these enzymes than non-coinfected group. (AST changed in 16.7% versus 2.2%, and ALT changed in 14.6% versus 2.2%) (Table 3). Intra uterine growth restriction (IUGR), Preterm Delivery (PD), hypertension, preeclampsia and diabetes showed no significant differences between the groups; prematurity occurred in 25.9% of coinfected group and in 21.4% of those without coinfection; low birth weight occurred in 29.5% of coinfected and 22.2% without coinfection, with no significant differences between groups (Table 4).

Abnormal maternal laboratory tests (N%)	With HCV	Without HCV	p (value)	OR	IC (95%)
Hemoglobin dosage (anemia)					
1º trimester	30,8	27,1	0,7363*	1,2	0,65 - 2,21
2º Trimester	44,4	46,2	0,5883*	0,93	0,51 - 1,72
3º Trimester	34,30	41,30	0,4771*	0,74	0,36 - 1,53
Platelets dosage (Plateletopenia)					
1º trimester	13,50	9,20	0,3735*	1,53	0,66 - 3,55
2º Trimester	11,10	7,70	0,4608**	1,49	0,56 - 3,99
3º Trimester	8,60	6,40	0,2965**	1,12	0,33 - 3,81
Hepatic enzyme (AST)					
1º trimester	16,7	2,2	< 0,0001**	8,77	3,25 - 23,66
2º Trimester	11,60	2,30	0,0080**	5,51	1,82 - 16,69
3º Trimester	7,4	2,5	0,1962**	3,09	0,62 - 15,34
Hepatic enzyme (ALT)					
1º trimester	14,60	2,20	< 0,0001**	7,5	2,66 - 21,18
2º Trimester	14,00	1,70	0,0005**	9,36	3,09 - 28,42
3º Trimester	3,7	1,6	0,4081**	2,38	0,27 - 21,18
	n (61)	n (743)			

Table 3: *Percentages of abnormal laboratory tests in HIV-positive pregnant women with and without HCV coinfection.*

**Teste Qui Quadrado; ** Teste Exato de Fisher.*

Gestational complications (N%)	With HCV	Without HCV	p (value)	OR	IC (95%)
Premature Labor	11,7	14,3	0,5724*	0,79	0,35 - 1,79
Arterial hypertension	8,3	5,9	0,3988**	1,46	0,56 - 3,84
Pre-eclampsia	3,40	1,10	0,1675**	3,17	0,66 - 15,31
Diabetes	9,10	5,90	0,3736**	1,59	0,6 - 4,21
Oligoamnios	10,00	5,60	0,1558**	1,89	0,77 - 4,64
Intrauterine growth restriction	5,00	4,30	0,7417**	1,16	0,34 - 3,9
Hypothyroidism	1,7	3,3	1,0000**	0,5	0,07 - 3,78
Subclinical uterine rupture	0,0	0,8	1,0000**		
Uterine hemorrhage	1,60	1,90	1,000**	0,86	0,11 - 6,65
Another complication	28,3	13,5	0,2349*	1,6	0,76 - 3,35
	n (61)	n (743)			

Table 4: *Pregnancy complications in HIV-positive women with and without HCV co infection.*

**Chi-Square Test; ** Fisher's exact test*

The mother to child transmission rate of HIV was 1.58% in coinfected group and 2.39% in non-coinfected. The Apgar score of 5 minutes < 7 occurred in 4.9% of coinfected and 0.7% in coinfected. Regarding to hematological disorders of newborns, there were no significant differences between groups. Liver abnormalities were present in 66.7% of newborns of coinfected group while in the non-coinfected group these changes did not reach 40%. Congenital malformations occurred in nearly 10% of all pregnancies, being the major defects: the cutaneous changes and hemangioma, aggressions to the central nervous system, cardiac and genitourinary malformations (Table 5).

Neonatal changes (N%)	With HCV	Without HCV	p (value)	OR	IC (95%)
RN weight					
< 2500g	29,5	22,2	0,1913*	1,47	0,82 - 2,61
>= 2500g	70,5	77,8			ref.
Apgar 5º minute					
< 7	4,90	0,70	0,0185*	7,5	1,75-32,17
>= 7	95,1	99,3			ref.
Capurro					
< 37 sem	25,90	21,4	0,4268*	1,28	0,69 - 2,37
>= 37 sem	74,10	78,60			ref.
Hepatic birth dysfunction	66,7	35,1	0,0331**	3,7	1,09 - 12,54
Neonatal pathology	34,50	26,7	0,2007*	1,44	0,82 - 2,54
Congenital malformation	10,3	10,0	0,9329*	1,04	0,43 - 2,51
Skin changes/hemangioma	4,90	1,10			ref.
Heart disease	0,00	2,40			
Gastrointestinal	0,00	0,30	0,0991**		
Genitourinary	0,00	2,30			
Genetics	0,00	0,30			
Musculoskeletal	1,60	1,10		0,33	0,03 - 3,93
Central Nervous System	3,30	2,30		0,31	0,04 - 2,26
No information	n = 7	n = 84			
HIV infection	1,6	2,4	0,0818**	0,69	0,09 - 5,29
	n (61)	n (743)			

Table 5: *Changes in children of HIV positive women with and without HCV co-infection.*

**Chi-Square Test; **Fisher's exact test.*

Table 6 described 19 cases of newborns who became infected with HIV. Poor adherence to treatment and the presence of infectious comorbidities were factors observed in these cases.

Case	Year	PN Visits	Initial CD4	Final CD4	Final VL	ARV	Time on ARV	Adhesion	IV AZT	AZT newborn	Ruptured membrane	Labor	Capurro	Birth Weight	Maternal Pathology	Neonatal Pathology	Death
1	00	10	<100	-	85	AZT	112	Yes	Yes	No	0	No	41	3370	No	PCP, IVAS	No
2	00	9	-	-	14000	AZT	49	Yes	Yes	Yes	2h	Yes	36	2530	NIC	Toxo, pneumocystis	No
3	00	2	517	-	17000	AZT	40	No	Yes	No	0	No	40	3110	Sífilis, TB	Rubella	No
4	01	8	289	-	-	AZT	14	Yes	Yes	Yes	0	No	38	3230	No	No	No
5	01	3	-	-	-	HAART	21	Yes	Yes	No	0	No	34	2635	No	No	No
6	01	9	30	5	47000	HAART	260	No	Yes	Yes	1h	Yes	37	1985	Candid, condilomatosis, NIC, Toxo	Toxo	No
7	02	6	315	-	420	AZT	10	No	Yes	Yes	240h	Yes	33	1320	Stevens-Johnson, Hep C	No	No
8	02	3	110	-	17000	HAART	255	No	Yes	Yes	0	No	40	3000	Neurotox	Toxo	No
9	03	5	344	-	< 50	HAART	140	Yes	Yes	Yes	0	Yes	40	3695	No	No	No
10	04	6	424	630	1410	HAART	84	No	Yes	Yes	0	No	35	1340	No	Oral Candid	No
11	04	5	233	-	-	AZT	135	No	Yes	No	0	No	33	1705	No	CMV	No
12	04	0	-	-	-	-	-	-	No	No	0	Yes	-	-	No	Yes	No
13	05	0	-	-	-	-	0	-	No	No	63h	Yes	32	3125	No	No	No
14	06	2	160	-	-	HAART	21	No	Yes	Yes	0	Yes	39	2790	No	No	No
15	06	1	135	120	38380	HAART	-	No	Yes	Yes	7h	Yes	37	2015	No	1º twin	No
16	08	3	86	146	63	HAART	70	Yes	Yes	Yes	0	Yes	37	2100	Oral Candid	Neurotoxo, CMV, TB	No
17	11	5	332	336	3834	HAART	-	No	Yes	Yes	0	Yes	38	1845	Vaginosis, Pneumonia	No	No
18	11	13	84	110	64	HAART	273	No	Yes	Yes	0	No	39	2335	Vaginosis, Candid	Congenital cataract, Ascites, Splenomegaly	No
19	15	-	236	236	514	HAART	238	No	Yes	Yes	0	Yes	34	2190	Herpes, chancroid, condyloma, ITU, candid.	No	No

Table 6: *Characteristics of infected newborns with HIV. CAISM/UNICAMP 2000 - 2015.*

Discussion

More than eight hundred pregnant women infected with HIV were analyzed and, within this group, another one, particularly poorly studied, can be highlighted: the group ofcoinfected with hepatitis C. In the evaluated period, from 2000 to 2015, was found an incidence of HIV- HCV coinfection in 7.59% in this cohort of women; rate according to what is described in literature, despite the great variability of its occurrence according to the type of studied population [5]. In this cohort, the presence of HCV-HIV coinfection was associated with a higher incidence of maternal and neonatal liver changes. In the group of patients under analysis there was a high incidence of prematurity and low birth weight, regardless to the presence of HIV-HCV coinfection, but the occurrence of low Apgar score was higher in coinfected patients.

Although the study capacity to detect significant differences in qualitative results have been limited, because this sample size was adequate to detect some significant associations between pregnancy results and HIV-HCV coinfection. The small number of cases with information about the HCV transmission decreased the accurate estimate of this risk beyond the lack

of quantitative viral load. Larger series or aggregate data analysis may be needed to explore these issues. Finally, this study did not have a group of HIV-negative and HCV-positive women who might have still allowed a greater number of comparisons.

The literature data reinforce HIV-HCV coinfection has strong relationship with drug addiction [1,3,9]; in the present study, over 20% had drug use report, around 10% had alcohol consumption and more than 20% used tobacco. Sexual intercourse was the major route of infection for these women but this result can be affected by HIV infection. The hepatitis C virus (HCV) sexually acquired remains a public health problem, especially in HIV-positive men who have sex with men or even in heterosexual couples with increased sexual risk behavior, including "serosorting" and sexual practices with intense mucosal trauma, which rises the acquisition and transmission of HCV [5,10].

Most of the coinfected women were Caucasian. This ratio was not surprising, since studies have shown a greater incidence of HCV infection in Caucasian; however, racial minorities are disproportionately affected and often under-treated because of social differences [11].

In Brazil, there is still a stigma and prejudice about people of low income, low formal education, black skin and HIV-positive. If the same woman is also HCV positive will soon imagine that is a drug user. In many societies, HIV and HCV are stigmatized because of their association with deviant behavior, as sex between men and drug injection [5,10,12,13]. Stigma and discrimination can contribute indirectly but significantly to the growth of HIV-HCV epidemic. Strong evidence showed that stigma and discrimination could discourage accessibility to guidance messages and to health services [14,15]. In this study, however, breaking this paradigm, most of coinfected women were not drug users. The profile of most HIV-HCV coinfected patients presented in this study is of Caucasian women aged around 30 years, mid- level formal education, without drug, drinking or smoking use history prior to pregnancy. In the service offered to the patients, they had full access to prenatal care, delivery, postpartum and their newborns but, unfortunately, this situation does not occur in the rest of thecountry.

During prenatal care, control laboratory tests showed no significant change in hemoglobin and platelets levels in both coinfected and non-coinfected groups. Regarding to liver enzymes (AST/ALT), they showed changes in the most of coinfected pregnant women maintaining this pattern in the course of the pregnancy, which was expected by the potential liver damage derived from hepatitis C virus, which was also observed in other locations [17]. Condylomatosis, pneumonia and active TB had a higher frequency in coinfected group; however, other opportunistic infections did not differ significantly between the groups.

Most pregnant women did not use antiretroviral therapy before pregnancy and, despite of multidisciplinary approach to prenatal care, the vast majority had substantial problems in treatment adhesion and regular use of prescribed antiretroviral therapy during pregnancy [16]. The most used ART during pregnancy was the combination of two NRTIs (nucleoside reverse transcriptase inhibitors) and protease inhibitor (more than 50% of pregnancies in both groups), the majority with the use of lopinavir until 2005; at CAISM-UNICAMP, the main PI used was nelfinavir. The preference for the protease inhibitor regimen is in accordance with literature, and in Brazil, the preference was for the use of lopinavir-ritonavir combination [18].

Currently, Brazilian guidelines from the end 2015 suggest a single-dose tenofovir- lamivudine-efavirenz regimen combined with the initial treatment for therapy in pregnant women facilitating adherence to treatment [16,18]. In this study, there were not patients using this regimen, since this recommendation was taken from the end of 2015.

Data collected showed more than 20% of prematurity and low birth weight, factors that interfere in the risk of mother to child transmission. The reasons for this difference in the population studied are not well understood yet, but it has also been observed in other studies in the literature [19,20]. Only the PI therapy (protease inhibitor) was associated with prematurity, and this factor justifies the findings in the cohort under analysis, given the fact the majority of pregnant women used PI regimen. In general, is known that prematurity and low birth weight were observed as ART use complications during pregnancy, which differs from the findings of the present study [18,21-26]. Thus, the literature data confirm the safety of antiretroviral drugs during pregnancy. In this context, pregnant women, even when HIV-HCV coinfected, if treated with highly active antiretroviral therapy (HAART) will significantly reduce the risk of mother to child transmission of both infections [27,28]. In this cohort of HIV-positive women, however, there was a significant incidence of prematurity and low birth weight, regardless of the presence of HCV-coinfection.

There were no differences in the occurrence of hypertension or diabetes among coinfected and non-coinfected women, which is in agreement with other studies [29-31].

Apgar less than 7 was more frequently observed in coinfected population, suggesting an increase in neonatal risk in this women population, which has also been observed in other studies [32,33]. The most widely used route of delivery was elective cesarean section because that was the main recommendation of the Brazilian guidelines to women with unknown viral load or higher than 1,000 copies/mL after 34 weeks of gestation. Elective cesarean section in the 38th week of pregnancy was the national recommendation for reducing the risk of mother to child transmission. For pregnant women using antiretroviral drugs and suppression of sustained viral load, if there is no cesarean section indication for other reasons, the vaginal delivery route is indicated and this, from 2015, is also the recommendation at CAISM-UNICAMP [33]. Thus, the massive majority of patients under study had cesarean section because was the clinical protocol recommendation by 2015.

Shortly after birth, there was a higher incidence of liver changes in the group of newborns from HIV-HCV coinfected, with more than 60% showing liver enzyme abnormalities in the neonatal period. Chronic infection has a different clinical course in children compared to adults.

Each study highlights the progression of HCV is minimal or slight in children, although severe liver damage can develop and liver transplant may be necessary [35,36]. Children grow regularly with variations in height and normal weight [37], but a quarter will develop hepatomegaly in the first decade of life, and they may also have slight variations in peripheral lymphocytes and neutrophils [38]. Also, in many studies worldwide, a wide range of ALT concentrations was observed in vertically infected children: the majority shows modest changes; ALT levels are higher in the first two years of life and then begin to decrease [39-41]; from a practical point of view, is not a reliable prognostic marker. Data, in the present study, demonstrated a higher occurrence of changes in liver enzymes in newborns, but not as high values, showing results in accordance with literature.

Regarding to congenital malformations, there was no significant difference between the groups of coinfected and non-coinfected ($p = 0.0991$). However, the malformation rateseen in studied cohort was 10%, the great part skin changes and hemangiomas, more prevalent in the coinfected group with occurrence almost five times higher. A wide variety of extrahepatic manifestations have been associated with chronic HCV infection, but most occur in adults, not being seen in children [42,43]. Best evaluations should be made to explain the higher malformations incidence in the analyzed cohort, but in general, most were minor malformations.

The mother to child transmission of HCV is favored by HIV-HCV coinfection around four times more than in case of infection only for hepatitis C [27,34].

This study found no higher HIV transmission among coinfected, which has also been described in the literature; however, the majority of studies point a significantly increased risk of HCV mother to child transmission in HIV-positive women. Nonetheless, this may be due to the small number of coinfected women analyzed. Several studies suggest a risk four times higher to acquire HIV in pregnant women who are also infected by HCV [44].

HCV infection affects a large number of women in childbearing age worldwide, and the transmission of the virus from mother-to-child remains a serious public health problem. Several mother to child transmission reports were identified; however, no specific measure has been placed as determinant to reduce the transmission risk, with the exception of antiretroviral therapy in women with HIV-HCV coinfection, which seems to help reduce this event [45].

The data collection of large clinical trial demonstrated that successful treatment of HCV infection is associated with incidence reduction in liver disease progression, including liver failure, cirrhosis and hepatocellular carcinoma [46,47]. However, it is important to note that virologic cure does not necessarily reflect the cure of risk of liver disease. Persistent hepatic inflammation and/or progression to cirrhosis have been reported in a small subset of patients after viral elimination [17,48,49]. The present study could not evaluate the situation, since the quantitative HCV viral load was performed on a small portion of pregnant women and, in the majority, was carried out only the qualitative test. However, there is no specific therapy recommendation for the C virus in pregnant women, due to the high risk of toxicity [45].

The study also showed that HIV-HCV coinfection may impact the course of pregnancy, triggering a major change in liver pregnant women in addition to also be associated with a higher incidence of low Apgar score and neonatal liver abnormalities; there was, however, an increased risk of mother to child transmission of HIV. A limitation of this study is the small number of women with coinfection in the cohort analyzed. Future studies with larger samples are needed to better evaluate these possibilities in a population of Brazilian pregnant women.

Conclusion

In this cohort, the presence of HCV-HIV coinfection was related to worse results in liver enzymes during pregnancy, increased incidence of condylomatosis, pneumonia and active tuberculosis. There was high incidence of prematurity and low birth weight, regardless of the presence of HIV-HCV coinfection.

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