Karolinska Institutet

**Department of Microbiology, Tumor and Cell Biology**

# Antiretroviral Drug Resistant HIV-1 in Women and Children Living in Honduras

AKADEMISK AVHANDLING
som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i MTC A302, Theorells väg 1

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av

**Leda Parham**

*Huvudhandledare:*
Docent Annika C Karlsson
Karolinska Institutet
Institutionen för Laboratoriemedicin

*Bihandledare:*
Professor Jan Albert
Karolinska Institutet
Institutionen för Mikrobiologi,
Tumör och Cellbiologi

Professor Ivette Lorenzana de Rivera
Universidad Nacional
Autónoma de Honduras
Escuela de Microbiología

*Betygsnämnd:*
Docent Markus Moll
Karolinska Institutet
Institutionen för Medicin

Docent Sören Andersson
Örebro Universitet
Hälsoakademin

Docent Anna Mia Ekström
Karolinska Institutet
Avdelningen för Global Hälsa

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# ABSTRACT

Antiretroviral therapy (ART) in HIV infected pregnant women contributes to the prevention of HIV transmission to the newborn. However, as ART can also induce HIV drug resistance during suboptimal levels of virological suppression a major concern is the subsequent risk for transmitted drug resistant (TDR) virus to the child. In Honduras and Belize, like in many other countries around the world, mono-therapy was used to prevent mother-to-child transmission of HIV-1 (MTCT) until relatively recently when it was changed to a more effective combination antiretroviral therapy (cART). Prior to this study there was no information about antiretroviral drug resistance in HIV-1 infected women and children in Honduras and Belize, and limited data other from parts of Latin America. The first aim **(Paper I)** was to evaluate the prevalence of drug resistance in HIV-1 infected infants born in Honduras and Belize between 2001 to 2004, before cART was implemented for prevention of MTCT. Genotypic resistance was performed by sequencing of the HIV *pol* region and was successfully in dried blood spots from 66 HIV-1-infected infants (55 from Honduras and 11 from Belize). Mutations associated with antiretroviral drug resistance were detected in sequences from 13% of the Honduran infants and 27% of Belizean infants. Thus the study documented, for first time, the presence of drug resistance in HIV-1 infected Honduran and Belizean infants. Resistance probably was transmitted from the mothers since none of the infants had received antiretroviral drugs as prophylaxis or therapy.

The second aim **(Paper II)** was to evaluate antiretroviral drug resistance in pregnant HIV-1-infected women in Honduras and risk for MTCT subsequent to ART prophylaxis. In addition, we investigated changes in immune activation during pregnancy by evaluating LPS levels. A total of 50 mother-child pairs and 95 HIV-negative pregnant women were enrolled. The presence of antiretroviral drug resistance was monitored in samples drawn during pregnancy and shortly after delivery. Twenty-nine women (58%) were treatment-naïve at study entry and started antiretroviral prophylaxis against MTCT during pregnancy while 21 women were already identified as HIV-1 infected and on ART at study entry. Antiretroviral drug resistance was detected in 20% of the samples obtained from the mothers at baseline; 10% among treatment-naïve patients and 29% among treatment-experienced patients. Furthermore, despite ART prophylaxis 22 of 50 (44%) women were viremic. No MTCT were observed, but still the high prevalence of resistance and viremia indicated that there was a significant risk for MTCT. The LPS levels declined between pregnancy and after delivery in the HIV-1 infected women indicates that pregnancy might influence the LPS levels, a novel finding that merits further investigation. This study demonstrated for the first time a high prevalence of antiretroviral drug resistance and viremia in pregnant Honduran women, which could limit the effectiveness of antiretroviral prophylaxis against MTCT.

Taken together the studies indicate that there is a need for improvements of prevention against MTCT in Belize and Honduras. This includes better access to monitoring of plasma HIV-1 RNA levels and antiretroviral drug resistance testing.


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