

Epidemiology of Pediatric HIV in India

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Welcome, my name is Harjot Kaur Singh, I am one of the Infectious Disease Clinical Fellows at Johns Hopkins University. Today, I am going to present to you the epidemiology of pediatric HIV in India. Before I begin I'd like to say that the epidemiology of pediatric HIV is poorly defined for multiple reasons. One of which is that the definition of pediatrics in India is quite variable among the global and national Indian institutions as well as among physicians themselves.

So, today, I am going to highlight the time line of the Indian epidemic, the scope of the Indian epidemic, touch briefly on molecular epidemiology, spend some time on the modes of HIV transmission, HIV antenatal statistics, also spend some time speaking about clinical manifestations and morbidities in HIV, and then end with HIV mortality.

So, let's get started. The first case of HIV was documented in India in 1986, it was a pregnant woman in Chennai. The first case of perinatal infection with AIDS was documented in 1987. It was several years after that that blood screening for HIV became mandatory. But soon thereafter there were several introductions of prevention of mother to child transmission, and to retroviral therapies, as it became clear that mother to child transmission was responsible for the bulk of pediatric HIV.

So the scope of Indian of pediatric HIV in India is as follows. In the left hand column are the most recent dates of these statistics. So, as you can see pediatric HIV does not make up a large portion of HIV in India, approximately four percent. Although it sounds like a small percentage it results in almost 30,000 newly infected infants each year. The percent of children of all ages who are receiving ART that need to have ART is also approximately four percent. Each year the number of AIDS cases are reported. As of 2006 there was over 5,000 cases of AIDS in India. The current percentage of pregnant women on ART is quite small, it's approximately two percent.

To put some of this in context for you, the number of perinatal cases in the United States in the same time frame was only about 120. And the number of AIDS cases in children under the age of 18 in the U.S. was only about 200. So, as you can see, the Indian epidemic although the numbers sound small, it is still quite large.

Very little is known about the molecular epidemiology of pediatric HIV, but what we do know is it is primarily HIV-1. And that subtype C accounts for the majority of infections. Subtype A and B are reported, but the numbers are quite small. Although HIV-2 has been reported, the numbers are also unknown. This is, again, in contrast to what is the current subtype majority in the United States which is HIV-1 subtype B. And in Africa it's subtype A and C that predominate. And they have slightly higher prevalence of HIV-2.

Most of transmission among children with HIV in India, as you can see here, is primarily mother to child, or vertical transmission. This accounts for approximately 82% of all children in India infected with HIV. Horizontal transmission does occur. The national statistics indicate about 18% of HIV in children is from horizontal transmission. This includes sexual behavior as well as blood transfusions.

If we compare these statistics to those in the United States, you'll find that in some ways they're similar and in some ways they're quite different. So, similar to the high rates of vertical transmission in India. In the United States for children under the age of 13, 92% of them are also infected by mother to child. Horizontal transmission rates are less well known. And this is where the difficulty of defining pediatrics plays a role. Sexual behavior reports an unknown prevalence. But, the United States uses age 13 as a cutoff, and as we would suspect, above the age of 13 sexual behavior probably plays a large role in HIV infections. As far as transfusion goes, there's only one case report in the last year from blood transfusions in the United States, and that is how we get our one percent. The vertical transmission rate in Africa is greater than 95% as well.

The majority of data on horizontal transmission in India is from case series. There are approximately two dozen case series in India on pediatric HIV. And these are the available numbers. So, for sexual behavior there were two cases reported, and of that series it was 30.1%. There are two cases of sexual abuse reported responsible for horizontal transmission. And in both of these cases the percentages were pretty small.

Among medical services, dirty needles are still responsible for HIV transmission in India. In one case series there were four reports accounting for 6.2%. Blood transfusions still play a large role of HIV infection in India. There have been 93 cases in children with percentages ranging anywhere from 5-40%.

If we look specifically at mother to child or vertical transmission in India, and compare that to what is known in the United States because only 1-2% of women in India receive ART therapeutically or prophylactically, the current vertical transmission rate is 25-30%. This is in sharp contrast to the United States rates of less than two percent. Although the exact prevalence of women in the United States on ART is unknown, we suspect that it is pretty high, and that is how the vertical transmission rate in the United States is so low. I do want to point out here that in the United States among women who do not receive ART, that the vertical transmission rate is similar, 25-30%.

So moving on briefly to some antenatal statistics - as you know, India is a country with 35 states and six of those have been documented to have HIV antenatal prevalence of greater than 1%. There is some report that the rate has been constant over the last years and we hope that would have an impact soon on the number of perinatal cases. The six states that have such a high prevalence are Andhra Pradesh, Tamil Nadu, Maharashtra, Karnataka, Manipur, and Nagaland.

The next slide shows a map of India with these antenatal statistics from 2005. And you can see in the southern part of India and the eastern part of India are the areas with the highest prevalence. And these correspond to the states that I listed.

So moving on briefly to the clinical manifestations and morbidity in HIV. In general pediatric HIV is not equivalent to adult HIV. And in other sessions you will hear more about what these manifestations are, but briefly children tend to suffer from primary infections - both opportunistic and other. Where as adults tend to suffer reactivation infections due to waning immunity as their HIV progresses. In general, the overall progression of HIV in children is more rapid and it tends to occur with more immature immune systems, although the CD4 counts are still high. For this reason, in children under the age of six, CD4 absolute counts are unreliable. And the recommendations currently are to use CD4 percentages.

In addition, because children can acquire this infection at such an early age there tend to be prominent effects on growth and neurodevelopment. Most infants do not have abnormal findings at birth. And for those infants who are not routinely screened, the mean age of presentation is 17 months. Children are divided into three basic categories based on their presentation. This includes rapid progressors, intermediate progressors, and slow progressors. Rapid progressors tend to show symptoms in the first months of life. These include opportunistic infections as well as neurological manifestations. Intermediate progressors tend to show symptoms after the first year of life. This includes failure to thrive or current bacterial infections and Lymphocytic Interstitial Pneumonitis. Slow progressors are those children that show minor manifestations and these tend to appear later in childhood.

The next two slides are quite busy. They're basically a summary of some of the literature published on the clinical profile of children with HIV in India. The columns across the top basically indicate 13 different case series. And the rows down the side list the different manifestations that are seen in HIV infection. The very first row are the number of cases of HIV, so if you scan across with me, you can see that the range of children included in these studies is anywhere from 10 up to 317. And when the studies indicated which patients were symptomatic, these were numbers that tended to be greater than 50%. The point of this slide is to show you that the range of these findings, in children, is quite variable. For example, fever ranges from 10% of patients up to 95% of patients. In general however, these numbers reflect numbers that are found in Sub-Saharan Africa. And overall tend to be much higher than the ranges found in the United States.

The next slide, which is laid out the same way, representing 13 different studies across the top and opportunistic infections are listed on the left-hand side. Here, the point is the same, the ranges are variable, although somewhat more consistent among studies for opportunistic infections. And again, when you compare these to what is known, these rates are similar to what is found in Sub-Saharan Africa - where there is also a high epidemic of HIV. But, much higher than what is found in the United States. For example, if you look at the tuberculosis range, it's reported to

be anywhere from 19-68%, where as in the United States, the rate is less than 1%. I would suspect that some of these estimates are actually underestimates, given the limited diagnostic availability.

Moving on to our final topic, which is mortality. So baseline mortality for children in India, who are not HIV infected, according to the WHO is approximately 8.5% annually. This is for children under the age of five. For HIV infected children the data is limited to the published studies that I have shown you. And these studies do not distinguish mortality rates among ages or by the year. So the overall mortality rate in these studies is anywhere from 10-34%, which is quite high. So, if you are a child in India, you have not only a higher baseline rate of mortality, but you also have a high HIV specific mortality, and these would be combined resulting in a pretty high mortality for all children, especially those HIV infected.

If we put these numbers in perspective in the next slide, comparing them to both United States and worldwide estimates, you will see that the estimates in India are quite similar to those reported for the worldwide estimate -- very high baseline mortality rates by the age of five, and very high HIV specific mortality rates. But again these are somewhat variable according to their age range. If you look at the United States, you will see a stark contrast where the baseline mortality rate is one-tenth of what it is in India and in the U.S., and also, quite small, among the HIV positive children as well. So, in summary, the epidemiology of pediatric HIV is not well defined. One of the reasons for this is the definition of pediatric AIDS varies quite considerably. The majority of molecular sub typing in India is HIV1 subtype C. And the majority of transmission is mother to child are vertical. All children with HIV tend to have high morbidity and high mortality.

I would like to acknowledge a few people for their help with this presentation, and thanks very much.

