

Clinical Profile and Morbidity Pattern of Infants Born to HIV Infected Mothers in Durban South Africa

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This study describes the clinical characteristics and co-infections in infants born to HIV infected women being followed up in a high risk clinic of South Africa. Sixty three percent (302/476) of mothers attended clinic for varying periods during follow-up. Sixty four per cent of babies had physical clinical signs suggestive of HIV infection. In the majority of babies, persistent signs resolved by 9 months of age. In those with persistent signs, 20% tested positive for HIV infection. Among the HIV exposed infants, co-infections with TB, CMV, syphilis and Herpes zoster were diagnosed which appeared independent of their ultimate seroconversion status.

Key words: HIV, Infants, Parent -to-child Transmission

In the early 1990s the prevalence of HIV-1 infection among women attending the King Edward Hospital Durban South Africa antenatal clinic was 14-18%, which rose to 28% by 1999 and 30% in 2001 (Unpublished data from the Virology Laboratory University of KwaZulu-Natal). Common co-infections seen in the mothers and infants include tuberculosis (TB), cytomegalovirus (CMV) infection, herpes, syphilis, and fungal infections(1). Our initial data revealed that infants having tuberculosis who were also HIV-infected died by three to nine months following a clinical picture of rapid progression(2,3). It was also noted that a number HIV exposed infants who later tested HIV negative experienced physical signs and co-infections similar to the infected babies.

The aims of this study were to describe the

clinical characteristics of infants born to HIV-infected mothers and to compare these with a group of infants born to HIV-uninfected women at the neonatal follow-up clinic (NFC).

Subjects and Methods

Study design and population

This study analyzed records retrospectively of infants attending clinic for follow-up of high-risk neonates (Neonatal Follow-up Clinic, NFC) at King Edward VIII Hospital, Durban. High risk neonates included those admitted to intensive care or suffering from conditions like moderate to severe hypoxic ischemic encephalopathy, severe sepsis, severe jaundice, congenital abnormalities, or if they are born to HIV-infected women.

Only data from infants born to HIV infected mothers and random sample infants of uninfected mothers who attended the NFC between 1999 and 2001 were included in the study. The study was approved by the Research Ethics Committee of the University of KwaZulu-Natal, Durban.

A counselor advised on nutrition and addressed weaning practices(4).

A detailed physical examination of the baby, assessment of feeding practices, and examination for acute illness was done for all infants attending NFC. Babies who were HIV exposed received multivitamins, PCP prophylaxis with cotrimoxazole and were offered testing for HIV-infection using HIV-ELISA at 15-18 months (if not previously tested by polymerase chain reaction).

Definition of transient and persistent signs among HIV-exposed infants at follow-up

Physical signs which could be suggestive of HIV-infection were hepatomegaly (liver size greater than 2 cms below the right costal margin), splenomegaly (palpable spleen below the costal margin), significant lymphadenopathy (nodes >0.5 cm in more than one site), monilial infection of the skin, mouth or perineum, seborrheic dermatitis or pneumonia(5,6). These signs were regarded as 'transient' if they were present for a duration of less than a month; 'persistent' if they were present for a month or more; and recurrent if they recurred after a single 'transient' episode. If the signs were persistent, infants were investigated for the cause of particularly HIV associated infections.

Statistical analysis

Data from the discharge summary and NFC records were extracted and analyzed using EPI Info version 6. Proportions were compared using the Fisher's Exact test for

small samples. P-values of <0.05 were considered significant.

Results

Birth weight categories of babies and HIV exposure are shown in *Table 1*.

The total number of babies admitted to the neonatal unit during the period of study was 11084. Of these, 23% were classified as Low Birth Weight (LBW, birth weight < 2500 g). Thirty-eight percent of infants born to HIV infected mothers were small-for-gestational age (SGA). A total of 476/11084 (4%) of infants born to HIV-infected mothers (HIV-exposed) were requested to attend the NFC. The majority of mothers were tested antenatally (445/476, 93%); 7 (1.5%) were tested while babies were in the newborn period; 14 (3%) in the first three months and 12 (2.5%) at 4 to 6 months of age. The indications for testing mothers postnatally included clinical signs and symptoms which could be suggestive of HIV-infection.

About 50% of mothers had not revealed their HIV status to their partners. Many had more than one partner or had lost a partner by death, separation or abandonment.

Attendance at NFC by HIV-exposed infants

Sixty-three percent (302/476) of mothers attended clinic for varying intervals 82 [17%] attended for 1 to 3 months, 49 [10%] attended

TABLE I—Birth Weight Categories of the HIV-exposed Newborns

| Birth weight (g) | Total for period | Infants born to HIV infected women | Percent (%) |
|------------------|------------------|------------------------------------|-------------|
| <1499 | 508 | 83 | 16 |
| 1500-2499 | 2376 | 165 | 7 |
| >2500 | 8200 | 228 | 3 |
| Total | 11084 | 476 | 4 |

for 4 to 6 months, 35 [7%] attended for 7 to 9 months, 32 [7%] attended for 10 to 12 months) and 104 (22%) mothers attended the follow-up clinic for 13 months or more. Thirty-seven percent of mothers and babies (176/476) never attended the follow-up clinic.

Only 85/302 HIV-infected mothers agreed to re-test their babies for HIV-infection at 15-18 months. The number of babies who tested positive by HIV ELISA and/or PCR (and thus assessed as infected) during these visits were 24 (28%). The rest of the HIV-infected mothers either refused testing or did not present themselves at the visit at which the ELISA tests were scheduled.

Clinical course

Infants born to HIV positive women (HIV exposed)

During the period of follow-up, 192/302 (64%) babies had physical signs which could be suggestive of HIV infection. Of these, 56 (29%) had signs occurring in the newborn period, 91 (47%) under 3 months of age, 35 (18%) at 4-6 months and 10 (5%) after 7 months. Among the infants with physical signs, 73 (38%) had transient signs and 119 (62%) had persistent signs. Signs persisted for varying period of time in these 119 babies. Twenty-nine percent (35) resolved within 3 months, 29% (35) resolved in 6 months and a further 23% (27) resolved by 12 months. In infants whose signs did not resolve by 12 months, all 22 (19%) tested positive for HIV-infection. (Table II)

Of the 61 ELISA negative babies (sero-reverters), 27 (44%) had physical signs suggestive of HIV infection during period of follow-up. The physical signs developed between the newborn period and 7 months of age and resolved within a period of 2 to 12 months. Fourteen of these 27 (52%) were

growth retarded at birth. Sixteen had persistent physical signs (2 hepatosplenomegaly due to tuberculosis, 8 lower respiratory tract infections, 3 generalised lymphadenopathy, 2 oral monilia and 1 perineal monilia).

Among the HIV-exposed infants with persistent signs co-infections were diagnosed in 69 (59%), 57 babies were diagnosed to be having tuberculosis of whom 6 were culture positive, 8 had CMV culture positive infection, 2 had syphilis and 3 herpes zoster. The co-infections in relation to HIV status of the babies are presented in Table III. The most common co-infection was tuberculosis and of those who had the HIV ELISA (26 infants) the majority of 18 tested HIV ELISA negative.

Discussion

The limitations of the study include that the study was of retrospective nature and the

TABLE II—Onset and Duration of Clinical Signs which could be Suggestive of HIV-infection* among Infants Born to HIV Infected Women (N = 192)

| Onset of clinical signs | N (%) |
|-------------------------------------|----------|
| Newborn | 56 (29) |
| <3months | 91 (47) |
| 4-6months | 35 (18) |
| 7-12months | 10 (5) |
| Transient signs (present ≤1 month) | 73 (38) |
| Persistent signs (present >1 month) | 119 (62) |
| 1-3 months | 35 (29) |
| 4-6 months | 35 (29) |
| 7-12 months | 27 (23%) |
| >12 months | 22 (19%) |

* Clinical signs suggestive of HIV infection included: hepatomegaly, splenomegaly, significant lymphadenopathy, monilial infection of the skin, mouth or perineum, seborrheic dermatitis and pneumonia.

TABLE III—*Co-infections in Infants Born to HIV +ve Mothers in Relation to their HIV Status at 15-18 months.*

| Co-infection | HIV status at 15-18 months of age | | |
|--------------------------|-----------------------------------|---------------------|------------------|
| | Infected n (%) | Uninfected n (%) | Unknown n (%) |
| Tuberculosis n = 57 | 8 (14) | 18 (32) | 31 (54) |
| Cytomegalovirus n = 8 | 4 (50) | 2 (25) | 2 (25) |
| Syphilis n = 2 | — | 1* (50) | 1 (50) |
| Herpes zoster n = 2 | — | 1* (50) | 1 (50) |

* Baby exposed to both syphilis and herpes zoster.

poor follow-up of infants born to HIV-infected infants. High loss to follow-up, despite a great deal of counseling is a common issue and a challenge to many programs and studies in the third world setting. Also, the infant feeding practices could not be adequately evaluated in the current study. Despite these limitations, this study attempted to generate important information regarding follow-up of HIV exposed infants who leave neonatal facilities in poorly resourced countries. Fear of the stigma of HIV, a fear of a positive result, the reactions of the partners and community have a negative influence on clinic attendance(7).

Out of those babies who developed physical signs which could indicate HIV infection, over a third had transient signs. These probably reflected the common viral illnesses of this age group as in the majority all tests for HIV co-infections were negative. In many of the babies having even persistent signs most eventually resolved without a definite diagnosis of co-infection. The infections that were diagnosed amongst others included TB and CMV.

Why so many HIV exposed but infection negative babies express signs of infection is not clear. It is possible that some immunological factors are passed to the baby from the mother influencing the response to infection. Uninfected infants lose the passively transferred maternal HIV-1 antibodies between 6-12 months of age. However, in 2% of cases it has been documented that the maternal antibody may persist up to 18 months of age(8,9). There is evidence that the CD4 counts in HIV exposed but uninfected babies are lower than those who are unexposed(10); there is also evidence of cell mediated immunity disturbance which may persist over time(9,11). The reticuloendothelial responses may possibly be exaggerated in these babies. In addition, it has been documented that the seroconversion rates in HIV exposed but uninfected infants is slower than those who are unexposed(12).

It is important to note that the early onset of the signs do not predict an infected infant since babies exhibited signs which are thought to be suggestive of HIV-1 infection from as early as the neonatal period. LBW infants and those with growth restriction at birth are at higher risk of and associated co-infections(3). Further, health care professionals should be cautious not to label these babies as infected as this may be erroneous clinical findings.

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Contributors: SK and AM were involved in the conceptualization of the protocol, design of the study, clinical and laboratory data collection. SK verified data and undertook the statistical analysis. MA finalized the manuscript and will be the guarantor.

Key Message

- The clinical features and infection profile of HIV exposed infants are similar irrespective of their ultimate seroconversion status.

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