Brief Reports

The HIV-1 Exposed Neonate: Outcome of Intensive Care Management in the First Week of Life

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A prospective study was carried out to determine if the outcome in HIV-exposed neonates requiring intensive care (n=30) is different from that in HIV-unexposed neonates (n=40) requiring intensive care in the first week of postnatal life. It was noted that the outcome in terms of incidence of death and intensive care stay do not differ significantly in these two groups although some hematological parameters may be significantly different. Considering the fact that the outcome is not worse in HIV-exposed babies and that most of these babies ultimately turn out to be HIV-uninfected, these babies should not be deprived of intensive care, whenever necessary.

Key words : *HIV exposed neonates, Intensive care.*

PEDIATRIC HIV infection accounts for a significant mortality and morbidity in childhood(1,2); but the contribution of neonatal HIV infection to neonatal mortality rate has hardly ever been studied. A prospective study in Durban has demonstrated that childhood AIDS patients admitted to pediatric intensive care unit have a worse prognosis as compared to others(3). Since 1996, a group of HIV-infected neonates with opportunistic infections (tuberculosis, syphilis and cytomegalovirus) are shown to have a rapid progressive HIV infection presenting at a mean age of 15 days(4-6) with over 83% of them dying by the age of nine months(6). There is evidence that HIV exposed uninfected infants may have a worse outcome than unexposed infants. The immunological disturbances include lower CD4 counts in HIV exposed but uninfected babies than those who unexposed(7); there is evidence of cell mediated immunity disturbance which may persist over time(8), and, it has been documented that HIV exposed but uninfected babies acquire *Streptococcal pneumoniae* infection more commonly than HIV unexposed babies (9). A study was carried out to determine if these HIV exposed neonates have a short and medium term prognosis that is worse than that in HIV unexposed babies also requiring intensive care.

Subjects and Methods

A prospective study was carried out at the Neonatal unit of the King Edward VIII Hospital, Durban, South Africa after obtaining clearance of the institutional ethics committee. Babies admitted to the neonatal unit during the 12-month period beginning July 2000 were enrolled in the study after obtaining informed

consent. Mothers of all neonates were subjected to HIV testing by HIV-1 ELISA after providing pre-test counseling. Additional tests such as Roche HIV DNA PCR and T cell subset test by flow cytometry were performed in mothers found to be HIV-infected and in their babies after providing post-test counseling. HIV RNA PCR for viral load assessment was performed using Nuclisens Isolation Kit, Organon Teknika, Boxtel, NL. The women who were found to be uninfected and their babies underwent only immuno-logical tests (T cell subset determination by flow cytometry). Maternal details (age, parity, prenatal care received, syphilis serology, mode of delivery, obstetric complications) and clinical details of the neonate (indications for NICU care, outcome, anthropometric para-meters, frequency of infection, neurological complications, haematological and immuno-logical parameters) were noted. Refusal to undertake HIV testing, mothers receiving nevirapine for prevention of perinatal transfer of HIV infection, inability to complete the consent procedure in view of location of the mother in another hospital, maternal death or babies older than seven days postnatal age constituted exclusion criteria. Considering that 30% of mothers would have HIV infection and that the rate of transmission of HIV infection to the fetus is 25%, it was calculated that a sample of 30 HIV-1 exposed babies and 70 HIV-unexposed babies would be required to demonstrate a 35% vs. 70% mortality rate (95% power, OR 4.3). Epi Info version 6 was used for analyzing the data. Non parametric tests were used for statistical analysis. A value less than 0.05 was considered significant.

Results

Ninety nine neonates admitted to the ICU were deemed suitable for inclusion in the study. However, only 70 (71%) mothers consented to participation after pre-test counseling. Thirty mothers (43%) tested HIV positive. Only 14 (47%) of infected mothers consented to their neonates undergoing virological studies (HIV DNA PCR and HIV RNA PCR for viral load assessment). Only eight of these 14 agreed to undergo immunophenotyping in them. Of the 40 HIV uninfected mothers, 17 (42.5%) agreed to undergo immunophenotyping while only 19 (47.5%) consented to subject their neonates to immunophenotyping. As shown in *Table I*, there were no significant differences between HIV-1 infected and HIV-1 uninfected mothers in terms of age, parity, antenatal care, obstetric complications, mode of delivery and medical difference. However, a significant difference was noted in terms of absolute CD4 counts (539 *vs.* 943 cells/mm^3, P = 0.0006), percentage CD4 cells (30% *vs*.42%, P = 0.009) and percentage CD8 cells (49% *vs.* 31%, P = 0.002). As shown in *Table II*, there were no significant difference between the HIV-exposed and HIV-unexposed neonates in terms of birth weight, gestational age, indications for intensive care admission, complications of ventilation, number of positive cultures, incidence of nosocomial pneumonia, findings noted on cranial ultra-sound examination, duration of intensive care, absolute lymphocyte counts, per cent CD4 counts and incidence of death. In contrast, to the above, there was a significant difference between the two groups of neonates in terms of white cell count and decrease of CD4:CD8 ratio. Twenty one of the 30 HIV-unexposed infants and 14 of the 19 surviving HIV-exposed infants were followed up with the neonatal clinic for 12-18 months. One baby who had demonstrated a positive HIV DNA PCR test became symptomatic at 5 months of age, while the other 13 HIV-exposed infants remained asymptomatic and were noted to have a negative HIV DNA PCR test by 6 months of age.

Discussion

TABLE I– *Maternal Obstetric and Hematological Data : HIV-1 Infected and HIV-1 Uninfected Mothers.*

		HIV positive n = 30	HIV negative n = 40	P value*
Maternal Data				
Age (yrs) <18	3	2		
18-35	23	34		0.33
>35	4	4		
Parity 0	10	11		0.59
1-4	20	25		0.01
>5	0	4		
Antenatal care	22	33		0.59
Obstetric complications	16	22		0.91
Delivery vaginal	14	10		0.1
Cesarean section	3	25		0.17
Laboratory Testing		n = 8	n = 17	P value
Hemoglobin		10.3 (±1.2)	11.3 (±1.5)	0.118
White cell count ($\times 10^9$/L)		8.1 (±3.2)	9.1(±3.4)	0.49
Absolute lymph ($\times 10^9$/L)		1933 (±796)	2285 (±678)	0.558
Platelet ($\times 10^9$/L)		395 (±86)	327(±97)	0.074
Abs CD4 (μL)		539 (±239)	943 (±272)	0.0006
CD4%		30.1 (±10.7)	41.7(±7)	0.009
Abs CD8		935.8 (±555)	721.8 (±378)	0.299
CD8%		49 (±12.9)	30.88 (±8.7)	0.002
CD4:CD8 ratio		0.72 (±0.5)	1.48 (±0.59)	0.004

This study demonstrates that the outcome in HIV-exposed babies is not significantly different from that in HIV-unexposed babies, although some of the hematological parameters may show a significant difference in these two groups of babies. It is also worth recording that most of the HIV-unexposed babies ultimately turn out to be uninfected when tested by virological tests at 6 months of age. A thought is often put forward that with the shortage of resources and paucity of ICU beds, ICU care in resource poor situations should be offered to only those babies in whom it would be worthwhile(10). There is a risk that HIV-exposed babies would be categorized as "not worthwhile". Our study has demonstrated that this is not true and hence withholding ICU care is unjustified not only on ethical grounds but also on hard scientific facts brought out in the study.

Factors that influenced early termination of the study included the reluctance of mothers to consent to HIV testing in order to participate in the study. Fear of a positive result is well known, however, little is written around the topic. Two recent reports one from the

TABLE II– *Comparison of Various Neonatal Parameters Among HIV-1 Exposed and HIV-1 Un-exposed Infants.*

	HIV exposed (n=30)	HIV unexposed (n=40)	P value
Birth weight			
>2.5 kg	3	5	
< 1.5kg	19	18	0.30
>1.5kg	8	17	0.17
Small gestational age	14	20	0.97
Indications for ICU			
HMD*	17	22	0.59
Pneumonia	8	7	0.18
Mec aspir†	2	2	
Other	3	9	
ICU‡ complications	20	25	0.9
Clinical problems	9	13	0.97
Positive blood cult	7	5	0.38
Postive ETT§ cult	14	15	0.59
Antibiotics 2nd line	10	11	0.79
Nosocomial pneumonia	10	14	0.88
ICU stay			
<7 days	15	27	0.02
8-14 days	10	7	0.21
>15 days	5	6	1.00
Deaths	11	10	0.42
Laboratory Testing n=14	n=19	p value	
Haemoglobin 12.0(±2.4)	12.5(±2.8)	0.572	
White cell count (x109/L)15.04(±13.1)	10.5(±4.3)	0.002	
Absolute lymph (x109/L)4461(±3778)	3069(±1518)	0.383	
Platelet (x109/L)238 (±143)	212(±165)	0.633	
Abs CD4 (µL)1573 (±1213)	1718 (±953)	0.173	
CD4%	48(±14.3)	54 (±13.4)	0.198
Abs CD8 1045 (±1187)	1047 (±1394)	0.996	
CD8% 22.9 (±8.08)	17.2 (±6.3)	0.04	
CD4:CD8 ratio	2.36 (±1.10)	3.73 (±2.4)	0.013

*HMD hyaline membrane disease†Mec asp meconium aspiration‡ ICU Intensive care unit §ETT endotracheal tube.

Zimbabwe and the other from the Latino countries stress the fear, and stigma associated with the epidemic(11,12). The introduction of the antiretroviral, nevaripine, as standard of care to reduce perinatal transmission of the HI virus in this setting clearly influenced the recruitment of cases into to the study(13)

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Contributors: MA, PJ, TP conceptualized the protocol; collected clinical and laboratory data; AM helped in data collection; PK and SC were involved in virological working.

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