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ORIGINAL ARTICLE

Effectiveness of Early Infant Diagnosis (EID) in Detecting the Serostatus of HIV-Exposed Infants and Children

Khanam Mariam · Goswami Sebanti · Mukhopadhyay Partha

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About the Author

Mariam Khanam is a Post Graduate Trainee in the department of Gynae & Obs at Medical College, Kolkata. She completed MBBS from Burdwan Medical College in 2006. From the very beginning in her post graduate training, she has been immensely interested in HIV in pregnancy and EID (Early Infant Diagnosis), and her thesis was also on "Prevention of Parent to Child Transmission" under the guidance of Dr. Sebanti Goswami (the second author), Associate Professor and Assistant team leader, PPTCT (Prevention of Parent to Child Transmission) unit, Medical College, Kolkata. Dr. Sebanti Goswami is also a master trainer of NACO training program and a Technical Resource Group member of NACO. She also participated in seminars and symposium and presented paper on PPTCT and EID (Early Infant Diagnosis) in various conferences.

Abstract

Background/purpose of the study Although interventions to prevent mother-to-child transmission of HIV infection are being increasingly implemented as a part of national guideline, the prevalence of pediatric HIV remains high. There is remarkable increase in survival if HIV-infected children have access to early infant diagnosis (EID) and treatment.

Methods The study was conducted in the Department of Obstetrics and Gynecology Medical College, Kolkata from July 2011 to February 2014 after obtaining approval from the institutional ethics committee. All the infants of HIV-positive mothers who came for EID between 6 weeks to 18 months of age during the study period were included in the study. A total number of 151 infants were included in the study and divided into Group A and B according to the time of first testing. It was a prospective observational longitudinal study. Data were collected from the EID register of PPTCT unit Medical College Kolkata. EID was done as laid out in the pediatric ART (anti-retroviral therapy) guidelines of the National AIDS Control Organization.

Results Effectiveness of EID is judged by the corroboration of results at 6 week, 6 and 18 months. Comparing the results in group A, we found that 10.26, 8.41, and 7.29 % were positive at 6 weeks, 6 and 18 months, respectively, and with p value of 0.5828 the differences

Khanam M., Post Graduate Trainee, Gynecology and Obstetrics · Goswami S., Associate Professor Gynecology and Obstetrics · Mukhopadhyay P., Professor & Head of the Department, Gynecology and Obstetrics
Medical College Kolkata, Kolkata, India
e-mail: mariamkhanam@ymail.com

Mukhopadhyay P.
e-mail: drpm@gmail.com

Goswami S. (✉), Associate Professor Gynecology and Obstetrics
317 New Raipur, Flat No 1 B, Kolkata 700084, West Bengal, India
e-mail: sebantigoswami@yahoo.co.in

were not statistically significant. In group B, we observed that 47.06 and 45.45 % were positive at 6 and 18 months, respectively. Analysis revealed a p value of 0.9072 indicating no significant statistical difference between the results of testing in different periods. This reflects a good correlation between the 6 weeks, 6 and 18 months value, thus establishing the integrity of the EID.

Conclusion Ultimate integrity of the PPTCT is judged by testing the child. EID is a novel procedure which aims at earlier diagnosis and initiation of treatment in the children.

Keywords Acquired immune deficiency syndrome · Early infant diagnosis · Human immuno deficiency virus · Prevention of parent to child transmission

Introduction

The prevention of parent to child transmission (PPTCT) aims to prevent the perinatal transmission of HIV and reduce the number of infants who are HIV positive. Globally, the number of children younger than 15 years living with AIDS has increased, although the number of newly infected children has been declining, due to increasing PPTCT services.

Although interventions to prevent mother-to-child transmission of HIV infection are being increasingly implemented as a part of national guideline, the prevalence of pediatric HIV remains high. It is projected that about 1,000 new pediatric cases occur daily worldwide, with 90 % occurring in Sub-Saharan African countries. HIV infection is having an increasing impact on the health of children, threatening to undermine hard-won gains in child survival in countries with high HIV prevalence. Based upon the global estimates, 2.3 million children younger than 15 years of age are living with HIV, the vast majority of whom acquired HIV from vertical transmission [1]. Mortality is high among HIV-infected infants in the first month of life particularly when there is no access to life-saving drugs, including antiretroviral therapy (ART) and Co-trimoxazole prophylaxis (CPT). Thirty percent of HIV-positive children die in their first year of life and approximately half do not survive until their second birthday. Importantly, there is remarkable increase in survival if HIV-infected children have access to early diagnosis and treatment. Early infant diagnosis (EID) is a validated recommendation of the NACO but few studies have been carried out in India so far because EID has been launched only in the past few years. In our institution, it was started only from 2011. The purpose of this study was to find out the serostatus at first contact, and to assess how EID corroborates with diagnosis of HIV at 18 months.

Material and Methods

The study was conducted in the Department of Obstetrics and Gynaecology Medical College, Kolkata from July 2011 to February 2014 after obtaining approval from the institutional ethics committee. All the infants of HIV-positive mothers who were delivered and who subsequently came for EID between 6 weeks to 18 months of age during the study period were included in the study.

Inclusion Criteria

(1) Infants of HIV-positive mothers delivered in the Department of G & O Medical College Kolkata who came back for followup between 6 weeks to 18 months of age. (2) Infants of HIV-positive mothers who were delivered outside but referred for EID to Medical College Kolkata irrespective of whether the mother or baby received antiretroviral prophylaxis.

A total number of 151 infants were included in the study. It was a prospective observational longitudinal study. Data were collected from the EID register of PPTCT unit Medical College Kolkata.

The first test of EID is ideally done when the infant is 6 weeks old as laid out in the pediatric ART guidelines [2]. This 6-week window has been selected because EID testing has greater than 95 % HIV sensitivity at this point. The time point of 6 weeks also coincides with the period of national recommended guideline for first visit of immunization.

Schedule of Data Collection

Infants between Six Weeks to Six Months of Age (Group A)

DNA PCR was performed on DBS (dried blood sample) specimen collected at ICTC (Integrated Counseling and Testing Centre) i.e., PPTCT unit. If DNA PCR shows 'not detected,' infant was followed up at ICTC. If DNA PCR shows 'detected,' infant was referred to ART centre for testing of whole blood specimen. DNA PCR was performed on whole blood specimen at ART centre. If DNA 'detected' on whole blood specimen at ART centre, infant was registered and followed up at the ART centre as per national pediatric ART guidelines. If DNA 'not detected' on the whole blood specimen at ART centre, fresh whole blood specimen was collected and testing repeated. Result of this specimen was used for further management according to national guidelines.

Infants/Children between Six Months to Eighteen Months of Age (Group B)

Antibody testing was performed at ICTC. If antibody test is negative, infant/Child was followed up at ICTC.

If antibody test is positive, DNA PCR was performed on DBS specimen collected at ICTC (Integrated counseling and testing centre) i.e., PPTCT unit. If DNA PCR shows 'not detected,' infant was followed up at ICTC. If DNA PCR shows 'detected,' infant was referred to ART centre for testing on whole blood specimen.

DNA PCR was performed on whole blood specimen at ART centre if antibody test and DBS is positive. If DNA 'detected' on whole blood specimen at ART centre, infant was registered and followed up at the ART centre as per national pediatric ART guidelines. If DNA 'not detected' on the whole blood specimen at ART centre, fresh whole blood specimen was collected and testing repeated.

Result of this specimen was used for further management according to national guidelines. Infants/children showing uninfected must continue to be followed up at the ICTC till 18 months Definitive diagnosis of all infants/children by antibody tests was ensured at 18 months.

Results and Analysis

We divided these 151 infants into two groups according to the age at 1st visit. Group A includes those infants who came between 6 weeks to 6 months of age. Some babies came after completion of 6 months of age and we included them in group B. Table 1 revealed that there were 117 babies in group A and 34 in group B. In Group B, in majority of the cases, the status of the parents was known later (Table 2).

In our study, majority of the women (89 out of 151) adopted formula feeding. 57 women preferred to breast fed their babies exclusively and five women went for mixed feeding (in spite of counseling). Transmission rate is more in breast fed infants (21.05) than formula fed infants (13.48 %). Effects of different feeding options are depicted in Table 3, and it shows that among 57 breast fed infants 12 are positive and 45 are negative. So the transmission rate among breast fed infants is 21.05 %, whereas transmission rate among formula fed infants is 13.48 %.

Table 1 Age at which the infant came for 1st time for EID

Age at 1st visit	Number	%
6 weeks–6 months (Group A)	117	77.48
>6 months–18 months (Group B)	34	22.52
Total (A + B)	151	

From Table 4, we see that in Group A among 117 babies twelve (10.26 %) were found to be positive and 105 (89.74 %) negative at 6 weeks. Three babies expired (two positive and one negative), and seven were lost to followup (six negative and one positive) between 6 weeks to 6 months of age. So we had 107 babies for testing at 6 months out of which nine (8.41 %) were positive and 98 (91.59 %) were negative. Between 6 to 18 months, three babies expired (two positive and one negative) and eight (all negative) were lost to followup. So at the end of 18 months, we had 96 babies for confirmatory testing out of which seven (7.29 %) were found to be positive and 89 (92.71 %) negative.

Table 5 shows among 34 babies who came for first time after 6 months of age 16 (47.06 %) were positive and 18 (52.94 %) were negative. Between 6 to 18 months, two babies (both positive) expired and 10 (six negative and four positive) were lost to followup. At the end of 18 months, we had 22 babies for confirmatory testing out of which 10 (45.45 %) were positive and 12 (54.55 %) were negative.

Discussion

Despite the fact that the children are vulnerable to HIV/AIDS, the diagnostic facilities of HIV in children were limited in the yesteryears. Late diagnosis accounts for the gloomy outlook of HIV in the pediatric population. EID of the HIV status of the babies born to HIV +ve mothers has initiated a new frontier in the management of pediatric HIV. The various indirect tests such as ELISA, which assess antibodies, are not reliable in children. This is because the maternal antibodies continue to circulate in the child for up to 1 year of age and sometimes beyond [3]. The direct tests that assay the antigen or the antigenic component of the virus are more reliable and preferred in infants and children. Such direct tests include PCR, western blot, and viral culture [4]. Viral culture are often time consuming, require a biosecurity secluded laboratory, and sometimes results in low sensitivity [5].

In our study, 77.48 % of the babies (Group A) came between 6 weeks–6 months and 22.52 % between 6–18 months (Group B). In a study by Torpey K et al. conducted in North Carolina, USA, majority of the children (58.6 %) had a PCR test between 6 weeks to 6 months [6]. It is a welcome sign to find the greater share of the babies coming earlier.

Majority of the babies hailed from lower socio-economic status (84 %). When HIV intruded into the human population, it mainly was a disease of the lower socio-economic strata. But gradually it has started engulfing the middle and the higher strata too. We encounter the majority in the low income group as ours being a Government hospital gives more privilege to the poor.

Table 2 Type of ARV prophylaxis to mother/or baby

Type of prophylaxis	Number	Percentage of total	Group A	Group B
Mother ART + SdNVP to baby	13	8.6	13	0
Mother ART + no drug to baby	2	1.3	0	2
No prophylaxis to both	41	27.2	15	26
SdNVP to baby only	23	15.2	20	3
SdNVP to both mother + baby	21	13.9	21	0
sdNVP to baby only	51	33.8	48	3
Total	151			

Table 3 Effect of different feeding options

Result	Number	Percentage (%)
Breast fed		
Positive	12	21.05
Negative	45	78.95
Total	57	100
Formula fed		
Positive	12	13.48
Negative	77	86.52
Total	89	100

Table 4 Result of EID in group A

	6 weeks–6 months		6–18 months		18 months	
	No	%	No	%	No	%
Positive	12	10.26	9	8.41	7	7.29
Negative	105	89.74	98	91.59	89	92.71
	117		107		96	

χ^2 for trend: 0.3017, p value = 0.5828. Correlation coefficient (Spearman rank correlation) = 0.142, p value = 0.129

Table 5 Results of EID in group B

	6–18 months		18 months	
	No	%	No	%
Positive	16	47.06	10	45.45
Negative	18	52.94	12	54.55
Total	34		22	

χ^2 for trend: 0.0136, p value = 0.9072. Correlation coefficient (Spearman rank correlation) = 0.301, p value = 0.074

Antiretroviral prophylaxis/therapy is one of the arms of PPTCT. Table 2 shows the type of anti-retroviral prophylaxis or therapy that was received by either the mother or the baby or both. In some cases, the mother did not get Tab Nevirapine because sometimes it was missed unfortunately, and sometimes delivery took place in emergency/taxi and the mother missed the opportunity to get Tab Nevirapine. It was also not possible to provide this prophylaxis to the mother in cases of home deliveries or when the baby was brought later to health facility or in unbooked cases where the serostatus of the mother was detected later after delivery. It was very unfortunate that in 41 (27.2 %) cases, neither mother nor baby received any type of prophylaxis. Majority of them were due to later diagnosis. Other reasons include home deliveries and missed cases.

One of the challenges of the entire PPTCT program is losing the infants during the followup period. Many of the parents change their residence and telephone number after delivery in fear of stigma and discrimination. This leads to our inability to trace them even after sending outreach workers (ORW). This was more so earlier when EID was not initiated, and many infants got lost in the long period of 18 months. In spite of introduction of EID, we found 25 babies (16.55 %) getting lost to followup. The entire purpose of preventing transmission to babies goes into vain when we cannot trace all the babies. Anoje C et al. in Nigeria found that 67 % of positive babies could not be traced and presumed to be lost to followup [7].

Effectiveness of EID is judged by the corroboration of results at 6 weeks, 6 and 18 months. Comparing the results in group A, we found that 10.26, 8.41, and 7.29 % were positive at 6 weeks, 6 and 18 months, respectively, and with p value of 0.5828 the differences were not statistically significant. In group B, we observed that 47.06 and 45.45 % were positive at 6 and 18 months, respectively. Analysis revealed a p value of 0.9072 indicating no significant statistical difference between the results of testing in different periods. This reflects a good correlation between the 6 weeks, 6 and 18 months value, thus establishing the integrity of the EID.

Lukong et al. [8] conducted a study on 174 infants in Nigeria where blood samples were sent for PCR at 6 weeks of age and again 6 weeks after that. They concluded that all infants who were −ve in the first sample were found to be negative in the second sampling as well. They concluded that PCR has a role as a direct test in EID particularly where other direct tests are not readily available.

Out of the 151 babies under our study, eight babies expired before 18 months of their life so that we could not take them up to the point of confirmatory test. This projects the extent of vulnerability of the babies to the infection, thus demanding more stringent and targeted approach to the care of HIV-exposed children.

Conclusion

The ultimate aim of PPTCT is to gift the world a HIV-free generation. Recent advances in technology have given birth to newer and more effective regimens aiming at near zero transmission. Success of the PPTCT is judged by testing the child. For that, we need a testing method which can be performed as early as possible and at the same time should be accurate enough to guide us in early management. EID is a novel procedure which aims at earlier diagnosis and initiation of ART in the children at the same time it allays anxiety among the parents of the positive children who can concentrate on the other aspects of upbringing of the child.

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Compliance with ethical requirements and Conflict of interest All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5). Informed consent was obtained from all patients for being included in the study. Mariam Khanam, Sebanti Goswami & Partha Mukhopadhyay declare that they have no conflict of interest.

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