ORIGINAL ARTICLE

DOES MATERNAL HIV STATUS AFFECT INFANT GROWTH?: A HOSPITAL BASED FOLLOW UP STUDY

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ABSTRACT

Introduction: HIV infection is difficult to diagnose in infants, as most infected babies appear healthy and exhibit no signs and symptoms at birth. The present study was conducted to study the clinical profile & morbidity pattern of infants born to HIV positive mothers, their nutritional status and growth pattern and compare them with HIV non exposed infants.

Methodology: This observational longitudinal study was conducted in Dec 2009 – Dec 2010 where all HIV exposed baby born in the hospital (n=44) were compared with suitable sample of HIV non exposed babies (n=140) in context of clinical profile & morbidity pattern.

Results: In maternal weight <50 Kg category, mean weight, length and head circumference of HIV exposed infants is significantly lower than HIV non exposed infants. However, pattern of weight gain remain similar in both group. Grade 1 and grade 2 malnutrition was more in HIV exposed group at 3 month & 6 month. HIV exposed baby reported higher episodes of diarrhea (28.57%) as compared to non exposed group (15.33%) with statistically significant difference (p value<0.05).

Conclusion: HIV exposure does not adversely affect growth potential of infants but because of their lower baseline values they seem to lag behind. Moreover maternal HIV status does not lead to severe degree of malnutrition if these babies were not themselves affected with HIV.

Keywords: HIV, MTCT, growth, malnutrition, morbidity pattern

INTRODUCTION

HIV prevalence in Antenatal (ANC) population in Gujarat is <0.1%. HIV prevalence in ANC population in Surat is 0.75%.¹ Ninety five percent of paediatric HIV infection occur through parent to child transmission.

It is estimated that about 1,89,000 HIV infected women are delivering every year in India. Only 19% of HIV infected women of child bearing age are reported to have receive Anti Retroviral (ARV) prophylaxis for Prevention of Parent to Child Transmission (PPTCT). Therefore large numbers of children are born every year exposed to maternal HIV infection. Even when the HIV status of the mother is known, only 6% of all infants are followed up at 8 weeks of age.²

HIV infection is difficult to diagnose in infants, as most infected babies appear healthy and exhibit no signs and symptoms at birth. Without effective treatment, an estimated one third of infected infants would have died by one year of age and about half by two years of age.³ Babies exposed to maternal HIV infection during intrauterine life, during process of labour and postnatal time are likely to be affected whether infected or not. Comparative study of their clinical profile as well as morbidity pattern with their non exposed counterparts will be useful in defining routine as well as special care if needed for such infants and may help to predict prognosis of HIV exposed infants. There are very few documentation on the same in India, despite of the huge burden of HIV exposed infants being born every year.

Hence the present study was conducted with objective to study the clinical profile & morbidity pattern of infants born to HIV positive mothers at new civil hospital as well as to follow up these children up to six months for their nutritional status and growth pattern and compare them with HIV non exposed infants.

METHODOLOGY

This is an observational longitudinal study conducted from December,2009 to December, 2010 at New civil hospital, Surat, which is a medical teaching institute catering to health care needs of Surat city as well as neighboring other five districts as tertiary care centre.

All babies born to HIV positive and random sample of babies born to HIV negative mothers at New civil hospital during the study period who could be regularly followed up at birth, 6 week, 3 month and 6 month were included. All infant who are lost to follow up were excluded from study. Both study groups belonged to similar social, economic, ethnic, educational and environmental background.

All the interventions and diagnostic protocols in this study were followed according to National AIDS Control Organization (NACO) and World Health Organization (WHO) guidelines.

For HIV status confirmation all pregnant women attending the antenatal clinic were referred to Integrated Counseling and Testing Center (ICTC) for pretest counseling for voluntary HIV testing. Those who opted for testing were tested for HIV. The results were revealed to patients after post test counseling. HIV testing was carried out by three rapid testing based on different principles as per NACO guidelines.

All confirmed HIV positive pregnant women were referred to ART center and were given antenatal, intranatal and postnatal PPTCT services and care as well as infant feeding counseling according to NACO policy.

First detailed history and clinical examination of newborns of HIV exposed group as well as HIV non exposed group was carried out soon after birth by a single person which included: History of obstetric details, anthropometry (weight, length, head circumference, and Ponderal Index), general physical and systemic examination for signs and symptoms related to severe HIV disease in newborn.

Weight was measured on electronic weighing machine with sensitivity of 10 kg \pm 5 gm. Length was measured in centimeter with Infantometer. Head, chest & mid arm circumferences: were measured with a non elastic measuring tape, in centimeter. Ponderal index was calculated with formula of weight in gm*100/Height in cm³

Follow up visits were scheduled at 6 week, 3 month and 6 months of age. Detailed history documentation and clinical examination were done at each visit.

HIV exposed babies were provided standard care as per NACO protocol. Relevant investigations and interventions were offered as and when required. Parents were advised to report to our hospital at any time if the child developed any complaints.

Confirmatory test for diagnosis of HIV was done by using nested DNA PCR (DNA Polymerase Chain Reaction) as per NACO 2006 guidelines. Blood samples were collected by trained technician of PPTCT clinic of New civil hospital, Surat and sent to Kashturba hospital, Mumbai as per NACO protocol. Parents were advised to report for antibody Enzyme Linked Immunosorbant Assay (ELISA) for final confirmation.

Data entry followed by analysis was done in Epi info 2007 software. Two groups were compared by using student's t-test for continuous variables and Pearson's chi square and Fisher's exact test for categorical variables. Values are expressed as mean and standard deviation. Whenever the sample size was small, data was checked for normality and when required log transformation was taken to apply the test of significance.

Ethical consideration

Permission for the study was obtained from Human Research Ethical committee of Govt. Medical College & New Civil Hospital. Confidentiality of patients were ensured throughout the study. Informed consent was obtained from parents/guardians of newborns after full explanation (in local language where possible) to them regarding potential benefits and risks.

RESULTS

Neonates of 44 HIV positive mothers were enrolled as a HIV exposed group, while of 140 HIV negative mothers were enrolled as a HIV non exposed group.

Out of 44 HIV positive mothers 14 mothers were eligible for therapeutic ART while rest of the 30 women were offered ART Prophylaxis as per PPTCT guidelines. Also 30 HIV positive mothers, who had delivered at New civil hospital were given intrapartum nevirapine as per NACO guideline. All 44 neonates were given nevirapine and zidovudine according to the WHO guidelines.

Table 1: Baseline profile of infants and mothers

Variables	HIV +ve	HIV -ve	Р
	mothers	mothers	value
	(n=44)(%)	(n=140)(%)	
Gender of baby			
Male	24 (54.55)	81 (57.85)	0.699
Female	20 (45.45)	59 (42.14)	
PROM duration			
\geq 4 hours	11 (25)	32 (22.86)	0.769
< 4 hours	33 (75)	108 (77.14)	
Mode of delivery			
Vaginal delivery	26 (59.09)	89 (63.57)	0.592
LSCS	18 (40.91)	51(36.43)	
Maturity			
Preterm	5 (11.36)	17(12.14)	0.889
Term	39 (88.64)	118 (84.29)	
Post term	0	5 (3.57)	
HIV DNA PCR test		. ,	
+ve at 6 wks($n=42$)	0	-	-
+ve at 6 mnths $(n=39)$	0	-	

PROM=Pre mature rupture of membrane; PCR=Polymerase Chain Reaction; LSCS= Lower Segment Caesarean Section Out of 44 HIV positive mothers who were enrolled in study, 42 mothers came for follow up at 6 week and 39 mothers came at 3 months & 6 months. Out of 140 HIV negative mothers 137 mothers came for follow up at 6 week & 134 mothers came at 3 months and 6 months. Number of infants with HIV DNA PCR positive was zero (Table 1).

Apparently male predominance was seen in both seropositive and seronegative mothers contributing to 24 (54.55%) and 18 (57.85%) babies respectively though the association was not significant (P=0.699) (Table 1). History of PROM of \geq 4 hours duration was present in 25% seropositive and 22.86% seronegative mothers (P=0.769) (Table 1). None, out of all 25%

HIV positive mothers who had more than 4 hour duration of rupture of membrane had transmitted HIV to their infants, which was confirmed by DNA PCR subsequently. On comparing with HIV nonexposed group of babies born to seronegative mothers there is no significant difference in the rate of Lower Segment Caesarean Section (LSCS) due to the HIV status of mothers. On comparison of rate of prematurity between the babies of normal and People Living With HIV/AIDS (PLWH) mothers there is no significant difference (Table 1). Total 42 infants were tested for HIV DNA PCR at 6 week and 39 at 6 months and all reports were negative which means that zero transmission of HIV from mother to baby was found in our study (Table 1).

Table 2: Baseline anthropometry of babies in HIV	V exposed and non exposed group
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Variables	HIV exposed group (n=44) (%)	HIV non exposed group (n=140) (%)	P value
Birth weight			
<1.5 kg	1 (2.27)	2 (1.43)	0.57
1.5-2.5 kg	23 (52.27)	62 (44.29)	
>2.5 kg	20 (45.46)	76 (54.29)	
Low birth weight			
Present	18 (40.90)	55 (39.29)	0.85
Absent	26 (59.10)	85 (60.71)	
Mean birth weight of baby (kg) (Mean ±	SD)		
Total	2.42 ± 0.45	2.57 ± 0.40	0.04
Maternal weight <50 kg	2.29 ± 0.35	2.60 ± 0.33	0.01
Maternal weight 50-60 kg	2.37 ± 0.44	2.53 ± 0.40	0.09
Maternal weight >60 kg	2.73 ± 0.49	2.50 ± 0.46	0.23
Mean length of baby at birth (cm)			
Total	47.09 ± 2.20	47.91 ± 1.97	0.02
Maternal weight <50 kg	46.44 ± 1.88	48.07 ± 1.68	0.01
Maternal weight 50-60 kg	46.83 ± 2.18	47.86 ± 2.04	0.04
Maternal weight >60 kg	48.69 ± 2.09	47.82 ± 2.23	0.33
Mean head circumference of baby at birt	h (cm)		
Total	33.03 ± 1.35	33.78 ± 1.44	0.003
Maternal weight <50 kg	32.61 ± 1.37	33.77 ± 1.41	0.03
Maternal weight 50-60 kg	33.02 ± 1.29	33.78 ± 1.47	0.02
Maternal weight >60 kg	33.56 ± 1.57	33.81 ± 1.45	0.68
Mean Ponderal Index of baby at birth			
Total	2.28 ± 0.23	2.30 ± 0.25	0.72
Maternal weight <50 kg	2.27 ± 0.25	2.33 ± 0.21	0.40
Maternal weight 50-60 kg	2.28 ± 0.22	2.30 ± 0.28	0.73
Maternal weight >60 kg	2.33 ± 0.26	2.26 ± 0.23	0.44

As seen from table 2, mean weight, length and head circumference of infants born to HIV positive mothers whose weight <50 kg is significantly lower than infants born to HIV negative mothers with weight <50 kg. Weight, length and head circumference of neonates of HIV positive mothers is significantly lower than neonates of HIV negative mothers whereas Ponderal Index is not affected by HIV status of mothers. Even on comparing the distribution of babies on various weight groups no significant difference was found between babies of HIV positive mothers and HIV negative mothers. Among PLWH mothers maximum numbers of babies belong to weight group of 1.5-2.5kg (52.27%), while very low birth weight is seen in 2.27% (Table 2).

There was a statistically significant difference in weight of infants of HIV seropositive and seronegative mothers at all follow up, but pattern of weight gain remain similar in both HIV exposed and non exposed groups (Table 3). Low birth weight babies of PLWH mothers have statistically significant lower values of weight at all intervals compared to HIV non exposed group. But trend of weight gain shows similar pattern. Head circumference of babies of HIV positive mothers is significantly lower than babies of HIV negative mothers at birth, but on follow up difference in Head circumference is not statistically significant (Table 3). Comparison of length at birth in two groups shows significantly lower mean length in HIV exposed group which suggests HIV status does affect length of baby but on follow up they seem to have catch up (Table 3).

Follow up	low up HIV Exposed		HIV non Exp	oosed group	P value	Weight gai	n (gm/day)	P value
	Mean ± SD	No. of	Mean ± SD	No. of	_	HIV exposed	HIV non	
		Infants		Infants		group	exposed gr	
Weight (kg	g) (All babies)							
Birth	2.42 ± 0.45	44	2.57 ± 0.40	140	0.04	_	_	_
6 weeks	3.48 ± 0.53	42	3.72 ± 0.46	137	0.004	22.92 ± 6.46	26.24 ± 5.57	0.001
3 months	4.56 ± 0.58	39	5.10 ± 0.52	134	0.00	23.07 ± 5.33	30.41 ± 7.70	< 0.001
6 months	6.05 ± 0.55	39	6.29 ± 0.48	134	0.006	16.73 ± 3.45	13.32 ± 2.93	< 0.001
Weight (kg	g) (Only low bir	rth weight bal	bies)					
Birth	1.99 ± 0.29	18	2.16 ± 0.30	55	0.04	_	_	_
6 weeks	3.01 ± 0.32	16	3.38 ± 0.43	53	0.002	21.97 ± 5.44	27.23 ± 5.16	0.001
3 months	4.05 ± 0.23	14	4.74 ± 0.54	51	0.00	22.41 ± 4.96	30.28 ± 7.87	0.001
6 months	5.61 ± 0.35	14	5.98 ± 0.54	51	0.02	16.82 ± 3.35	13.83 ± 3.36	0.005
Head circ	umference (cm)							
Birth	33.03 ± 1.35	44	33.78 ± 1.44	140	0.003	-	-	-
6 weeks	35.98 ± 1.26	42	36.40 ± 1.36	137	0.07	-	-	-
3 months	38.9 ± 1.34	39	39.13 ± 1.51	134	0.38	-	-	-
6 months	41.91 ± 1.16	39	42.52 ± 1.96	134	0.07	-	-	-
Length (cr	n)							
Birth	47.09 ± 2.20	44	47.91 ± 1.97	140	0.02	-	-	-
6 weeks	52.96 ± 2.34	42	53.44 ± 1.93	137	0.19	-	-	-
3 months	58.12 ± 2.59	39	58.64 ± 2.08	134	0.19	-	-	-
6 months	63.62 ± 2.08	39	63.97 ± 1.68	134	0.27	-	-	-

Table 3: Trend in	anthropometric parameters	s of babies in HIV expo	sed and non exposed group

 Table 4: Distribution of malnourished babies according to Indian Academy of Paediatrics classification of Protein Energy Malnutrition

Protein Energy Malnutrition	Babies a	at 3 months (%)	Babies at 6 months (%)		
(PEM) classification	HIV exposed group (n=39)	HIV non exposed group (n=134)	HIV exposed group (n=39)	HIV non exposed group (n=134)	
Grade 1	12 (30.77)	22 (16.42)	18 (46.15)	26 (17.16)	
Grade 2	12 (30.77)	8 (5.97)	3 (7.69)	6 (4.48)	
Grade 3	1 (2.56)	2 (1.49)	0	0	
Grade 4	0	0	0	0	
P value	< 0.001		0.002		
Total malnutrition cases	25 (64.1)	32 (23.88)	21 (53.85)	32 (23.88)	
Total normal	14 (35.9)	102 (76.12)	18 (46.15)	102 (86.12)	
P value	< 0.001		< 0.001	. ,	

It was observed that grade 1 and grade 2 malnutrition was more in HIV exposed group than HIV non exposed group at 3 month & 6 month (Table 4). Grade 2 Protein Energy Malnutrition (PEM) is seen maximum at 3 month of age 30.77% which declined to 7.69% at 6 month that documented positive impact of intervention in form of good nutritional counseling offered to mother at the follow up visits. Grade 3 PEM was only 2.56% at 3 months.

Table 5: Frequencies of morbidit	conditions in infants of both groups
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Morbidity	Episodes	(up to 6 week	p to 6 weeks) (%) Episode (6 wks to 3 mnths) (%) Episode (3 mnths to 6 mnths) (Episode (6 wks to 3 mnths) (%) Episode (3 mnths to			ths) (%)	
	HIV exposed (n=42)	HIV non exposed (n=137)	P value	HIV exposed (n=39)	HIV non exposed (n=134)	P value	HIV exposed (n=39)	HIV non exposed (n=134)	P value
Diarrhea	12 (28.57)	21 (15.33)	0.05	6 (15.38)	10 (7.46)	0.23	5 (12.82)	12 (8.96)	0.68
Fever	5 (11.90)	14 (10.22)	0.98	2 (5.13)	13 (9.7)	0.57	3 (7.69)	13 (9.7)	0.95
URTI	2 (4.76)	8 (5.84)	0.90	5 (12.82)	21 (15.67)	0.66	7 (17.95)	20 (14.93)	0.65
Asymptomatic	7 (16.67)	15 (10.95)	0.32	6 (15.38)	15 (11.19)	0.67	5 (12.82)	9 (6.72)	0.37
Hepatomegaly	. ,	. ,		. ,	. ,		. ,		
LRTI	2 (4.76)	0	-	3 (7.69)	6 (4.48)	0.70	1 (2.56)	0	-
Otitis media	1 (2.38)	2 (1.46)	-	3 (7.69)	8 (5.97)	0.99	2 (5.13)	5 (3.73)	0.94
Lymphade- nopathy	2 (4.76)	0	-	1 (2.56)	0	-	0	1 (0.75)	-
Skin lesion	1 (2.38)	0	-	2 (5.13)	5 (3.73)	0.94	1 (2.56)	0	-
Oral thrush	2(4.76%)	0	-	2 (5.13)	Ò	-	`О́	0	-
Jaundice	0	0	-	1 (2.56)	0	-	0	0	-
Pyomeningitis	0	0	-	1 (2.56)	0	-	0	0	-
Severe pallor	0	0	-	Ò Í	0	-	0	0	-

URTI: Upper Respiratory Tract Infections; LRTI: Lower Respiratory Tract Infections

None of the babies had grade 4 PEM. There was statistically significant difference in rate of malnourishment in various grade of PEM according to Indian Academy of Pediatrics (IAP) classification between HIV exposed and HIV non exposed groups. Severe degree of malnutrition was not found in babies of PLWH mothers. Overall HIV status of mother seems to have a significant effect on the nutrition of their infants since the rate of malnutrition is significantly higher than HIV non exposed group both at 3 month and 6 month (Table 4).

On analyzing data as per table 5, 28.57% of babies from exposed group were reported to episodes of diarrhea as compared to 15.33% of non exposed group. The difference between both the groups was statistically significant (p value<0.05). Number of diarrheal episodes seems to reduce with increasing age of the infant during follow up. Fever, Lower Respiratory Tract Infections (LRTI), and jaundice did not show significant difference in both the groups and one patient from exposed group had severe sepsis (Table 5).

DISCUSSION

Male predominance (54.55%) in our study in HIV exposed group correlates with the similar observation in the non exposed group which means that HIV positive status of the mother does not affect gender of newborn delivered and thus it probably reflects on the sex ratio of the institutional deliveries and the community as a whole. Another studies by Ssu Weng et al⁵ and Taha E et al⁶ had a male predominance, 55.0% and 51.6% respectively, in babies born to HIV positive mothers.

In our study rate of Premature Rupture of Membrane (PROM) of more than 4 hrs was 25% which was similar to study of Taha et al (19.3%).⁷ Though PROM more than 4 hrs in HIV positive mothers is one of the risk factor for transmission of HIV⁸ in their babies, this aspect of disease transmission could not be studied in current study as there were no HIV positive infants in this study. The rate of PROM is having very heterogeneous distribution in all the studies so no definitive inference can be made.

In our study majority (59.09%) of babies were born by normal vaginal delivery, while in Taha et al study 98.8% were normal deliveries.⁷

In our study we found no significant effect of HIV status of mothers on the maturity of their babies. Other study Ssu Weng et al also did not show any such correlation of maturity of babies with PLWH status of mothers.⁵

In our study, mothers weighing >50 kg in both HIV exposed and HIV non exposed group did not show statistically significant difference in all anthropometry parameters of neonates, whereas in mothers weighing <50 kg HIV exposed group had significantly lower value in anthropometry parameters of their neonates. This observation suggests that coexisting maternal malnutrition & HIV infection have more adverse impact on nutritional status of newborns. Study by K Castetbon et al⁸ documented similar finding conforming more adverse effect of coexisting maternal malnutrition & HIV status of mother on mean birth weight of their neonates. However study K Castetbon et al does not define cut off value of maternal weight whereas in present study we documented cut off value of maternal weight as less than 50 kg.

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Birth parameters	Our study (mother	In Ssu Weng et al study	HIV non exposed group	In Ssu Weng et al	In Ssu Weng et al
1	positive/ infant	mother positive/ infant	of our study (mother	study mother negative	study mother
	negative) (n=44)	negative5 (n=206)	negative /infant negative)	/infant negative5	positive /infant
		(1998) Rwanda	(n=140)	(n=276) (1998)	positive ⁵ (n=48)
				Rwanda	(1998) Rwanda
Mean weight (kg)	$2.42 \pm 0.45^{*}$	$2.77 \pm 0.429^{\#}$	2.57 ± 0.40	2.824 ± 0.408	2.53 ± 0.431
Mean length (cm)	$47.09 \pm 2.20*$	$47.7 \pm 2.1^{\#}$	47.91 ± 1.97	47.9 ± 2	47.2 ± 2.5
Mean HC (c.m)	$33.03 \pm 1.35^*$	$34.2 \pm 1.5^{\#}$	33.78 ± 1.44	34.4 ± 1.4	33.5 ± 1.6
Mean Ponderal Index	2.28 ± 0.23	$2.25 \pm 0.28^{\#}$	2.30 ± 0.25	2.57 ± 0.29	2.42 ± 0.28

*p value <0.05; #p value <0.01; HC: Head circumference; all value in Mean±SD

As seen from table 6, in both the studies (Surat based and Rwanda based) there is a significant effect of HIV status of mother on the anthropometric parameters of their neonates which means that even if the neonates have not been infected their growth and nutrition in intrauterine period is significantly affected by the maternal HIV status.

Study from Kigali, Rwanda⁸ documented that mean birth weight in infants born to HIV+ women as 2947 gm (SD = 429) and 3104 gm (SD = 461) in infants born to HIV negative women (p = 0.001). It also showed that frequencies of Low Birth Weight (LBW), prematurity and intrauterine growth retardation were higher in infants born to HIV positive women than to HIV negative women (p = 0.009, 0.01, and 0.053, respectively). We observed no significant difference in LBW rate among babies of HIV positive mothers and HIV negative mothers. LBW in infants born to HIV positive women could be partly attributable to impaired maternal weight. These results underline the need for nutritional surveillance and dietary counseling, hoping to improve the prognosis of pregnancy in HIV positive women, regardless of other therapeutic interventions. Ganger J et al, (2008) in India,⁹ showed that the incidence of malnutrition in babies born to HIV infected mothers was 36%, 82%, 20%, using birth weight, Head Circumference, Ponderal Index, respectively, compared to 10%, 56%, 8% incidence in babies born to HIV seronegative mothers, respectively. This is similar to our study.

Up to 6 weeks diarrhea was the major morbidity condition encountered in current study. Significant difference in frequency of diarrhea between HIV exposed and HIV non exposed group can be explained by influence of feeding pattern. Replacement feeding was found to be more with episode of diarrhea. Number of diarrheal episodes decreases with increase in age of child which may be due to improving nutrition and immunity of the child with age.

Limitation of study

As the study's sample size is small, study on the larger sample is desired to extrapolate the observation for large community level. Larger follow up period is required to document the growth pattern and velocity throughout infancy and early childhood.

CONCLUSION

Pattern of weight gain, growth of brain and linear growth velocity in HIV exposed and non exposed group is similar though the baseline values were lower in exposed group. Thus, HIV exposure does not adversely affect growth potential of infants but because of their lower baseline values they seem to lag behind. Therefore if efforts are focused on increasing birth weight, HIV exposed infants can have as normal growth as their non exposed counterparts. Moreover maternal HIV status does not lead to severe degree of malnutrition if these babies were not themselves affected with HIV. As such, HIV exposure also does not make the infant more vulnerable to infectious illnesses.

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