MATERNAL AND FETAL DETERMINANTS OF PERINATAL TRANSMISSION OF HIV AMONG HIV POSITIVE MOTHERS ATTENDING ANC AT A NORTHERN NIGERIAN TERTIARY HEALTH INSTITUTION

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ABSTRACT

Objective: To ascertain the major determinants of perinatal transmission of HIV among HIV positive women attending ANC and delivery at the University of Maiduguri Teaching Hospital, Maiduguri.

Patients and methods: A prospective case control study of 52 HIV positive pregnant women who were attending ANC and delivery at university of Maiduguri Teaching Hospital (UMTH) was carried out. Known HIV positive mothers sent from the adult HIV clinic and those found during ANC HIV screening and diagnosis using rapid tests were recruited, while Fetal diagnosis of HIV was done using polymerase chain reaction (PCR) technique at 6 and/or at 12 weeks of birth age. Socio demographic and obstetrics history were obtained and analyzed using SPSS version 11 and test of significance was carried out using chi square tests.

Results: Of the 52 women that were found to be HIV positive, the perinatal transmission rate was 11.5%. Elective caesarean section (ELCS) was offered to 11(21.2%) and all the babies delivered through ELCS were negative for HIV. Advanced maternal age (X^2 =33.53 P <0.001), Low CD4 count (X^2 =15.58 P =0.016), high maternal viral load (X^2=21.85 P =0.005), prematurity ($X2 = 9.872$ P= 0.007), low birth weight ($X^2 = 63.80$ $P <$ 0.001) and birth asphyxia($X^2 = 24.149$ $P <$ 0.001) were the major determinants of perinatal transmission of HIV infection in this study.

Conclusion: The perinatal transmission of HIV is high. Prompt identification of both maternal and fetal risks' factors and Effective interventions aim at minimizing the impact of these factors before or during pregnancy will help to lower some of the preventable determinants of perinatal transmission.

Recommendations: A prenatal and antenatal risks reduction strategy should be advocated. All effort should be geared toward identifying those positive and minimized or modify risks factors through behavior change, prompt initiation of treatment and prophylaxis for those found positive with a view to reduce the incidence of perinatal transmission.

Key Words: perinatal transmission, HIV, maternal, fetal determinants, Maiduguri

INTRODUCTION

Sub-Saharan Africa is hardest hit with 67% of the estimated 33 million HIV infected people. Ninety percent of the 2.0 million children infected with HIV in 2007 were from Sub Saharan Africa. Ninety percent of the children infected were as a result of Mother to Child Transmission (MTCT). The high prevalence of HIV in women of reproductive age and the high fertility rate of African women are factors that contribute to the comparatively high prevalence of transmission of HIV to infants[1].

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The burden of HIV is higher in sub-Saharan Africa than the rest of the world because of the high level of heterosexual transmission, high female to male ratio, high total fertility rate (TFR) and high prevalence of breast feeding[2].

Transmission from Mother to Child of HIV is affected by a number of factors not all of which have been fully elucidated. These can be divided into viral (iral load, viral genotype and phenotype, viral resistance) maternal (maternal immunological status, maternal nutritional status, maternal clinical status, behavioural factors, antiretroviral treatment) Obstetrics (prolonged rupture of membranes > 4hours, mode of delivery, intrapartum haemorrhage, obstetrics procedures, invasive fetal monitoring), fetal (prematurity, genetic, multiple pregnancy) and infants factors (breast feeding, gastrointestinal factors, immature immune system).[3-6]

The objective of this study therefore is to ascertain the determinants of perinatal transmission of HIV and recommend feasible risks reduction measures to minimize the perinatal transmission.

PATIENTS AND METHODS

This was a prospective hospital based study that was carried out at the Department of Obstetrics and Gynaecology of the University of Maiduguri Teaching Hospital. Booking clinics are held every Tuesdays. Voluntary counseling and testing (VCT) were offered at every booking clinic on Tuesdays and subsequent ANC follow up were observed on Wednesdays and Thursdays. 52 HIV positive mothers (37 cases were those found positive during ANC booking, while 15 were patients already of known HIV status referred from the adult HIV clinic of our centre) were recruited for the study.

Emphasis was placed on confidentiality, benefit of knowing their status and the fact that their participation will not in any way harm them or their babies. They were also free to opt out or withdraw from the study at any point if they so wish. These women were followed up through delivery and the first 12 weeks post - partum to ascertain the status of their babies and possible risks factors for those found positive.

This study was carried out from 12th August 2009 – 21st February 2010 after approval was granted by the research and ethical committee of the hospital.

For those that consented, an initial interview was conducted to obtain the socio demographic and Obstetrics data. The diagnosis of HIV infection was made in two stages i.e. the initial screening using Determine[@]Rapid tests (revised serial method), the rapid test detects antibodies to HIV using latex agglutination. Those found positive with initial screening were further tested with another rapid tests Stak – Pak[@] for diagnosis. Where these two test were found to be discordant a 'tie breaker (third rapid test) using Unigold[@] was done. The rapid tests were all carried out in the ANC clinic within 30 minutes.

Those found positive at the initial screening were confirmed with 'Western Blot' technique. This was done in the main immunology laboratory of the Hospital. Patients who tested positive by western blot were offered post test counseling and enrolled in to the PMTCT programme to continue their ANC follow up according to the national protocol[1], while negative mothers were offered post test counseling and appropriately counseled on how to remain negative. And subsequent relevant ANC follow up events through to delivery and first 12 weeks post partum in HIV positive mothers.

According to the Nigerian national guideline 2010[1], in addition to the normal criteria for initiation of ART in adults infected with HIV, pregnancy constitutes another indication for ART or prophylaxis. Treatment is offered as per the WHO clinical staging and eligibility criteria.[2] according to the Nigerian PMTCT 2010 guideline irrespective of the CD4 count all HIV positive mothers are to received

HAART while the infants received single dose nevirapine suspension 2mg/kg within 72 hours of birth and Zidovudine 4mg/Kg twice daily for six weeks. Our centre (UMTH) as one of the national PMTCT centre were offering HAART to all our HIV positive pregnant irrespective of their gestational age and CD4 count even before the formal released of the Guideline and mothers have the option to either breast feed or formula feed their babies whichever one is feasible.

The information obtained were entered into a questionnaires already designed for the study. The infants of the HIV positive mothers were followed up to first 12 weeks of age to determine their HIV sero status using polymerase chain reaction (PCR) after separation amplification and reading using the PCR machine. This technique detects viral nucleic acid either RNA PCR (cell free virus in the body fluid) or DNA PCR (cell associated virus.[2] An infant is considered HIV positive if the PCR is reactive for viral DNA at 6 and/or 12 weeks of age.

Data were analyzed using SPSS version 11 statistical package .Test of significance was done using Chi square test. A P value of <0.05 was accepted as significant.

Inclusion criteria

1. All HIV positive pregnant women that were diagnosed at booking 1st time and consented to participate in the study.
2. All those pregnant women of known HIV status that were referred from the Adult ART clinic that consented to participate.

Exclusion criteria

1. Those that refuse to consent to participate in the study.

2. Those that withdrew or opted out of the study.

RESULTS

Out of the 52 mothers that were found to be HIV positive. Six (6) of the babies were confirmed HIV positive by 12 weeks of age. Observed maternal determinants of Perinatal transmission found in this study were maternal age (P <0.001), maternal CD4 (P =0.016) and maternal viral load at delivery (P =0.005) as illustrated on table I. Specifically maternal age group 30-39years, maternal CD4 count less than 350cells/mm3, and maternal viral load > 750 cells/mm3 are important determinants in mother to child transmission of HIV in pregnancy as observed in this study.

Table II explained the relationship between maternal factors and fetal outcome as seen earlier. Maternal CD4 less than 350 was found to influenced low birth weight and perinatal transmission of HIV p= 0.034 and p= 0.016 respectively. Also maternal viral load at delivery was equally observed to have significant Influence on perinatal transmission (p = 0.005), but however not found to significantly affect fetal weight.

Mode of delivery was found to have strong association with fetal age at delivery, fetal weight and perinatal transmission of HIV (P = 0.010, 0.015 and 0.046 respectively).

All the babies delivered through elective caesarean section were observed to have reached term, of normal weight and HIV negative, while emergency c/s was offered to 1 of the mothers whose baby was found to be preterm, low birth weight and HIV positive.

Time of maternal diagnosis of HIV infection, and type of intervention or treatment offered were not shown to statistically influence fetal out come in this study.

Table III illustrated the fetal factors influencing perinatal transmission of HIV infection. Preterm delivery, birth asphyxia and low birth weight were observed to have strong association with perinatal HIV infection with P= 0.007, *P*< 0.001 and *P*<0.001 respectively

DISCUSSION

The HIV Seroprevalence rate found among the study population is 10.4%, which is similar to 11.8% and 10.5% reported from the same institution in 2003[7] and 2004[8] respectively, while the perinatal transmission rate is 11.5%. Our findings though within the range of 1.2% - 12% reported in most states of Nigeria[2], is however higher than the national Seroprevalence rate of 4.4% reported in 2005[2.] Other Hospital based studies from Nigeria have equally reported much lower prevalence rates[9, 10] compared to our finding. The higher prevalence rate from our studies might have been influence by the fact that the study centre is a HIV designated treatment centre and some of our ANC clients were enrolled into the PMTCT programmed from the adult clinic.

Elective caesarean section though not a popular method of preventing perinatal transmission of HIV in developing countries[11], was offered to 21.2% of our patients, this is similar to reported in Makurdi[12] (21.7%), but much higher than 10.3% reported from Kano[9], Nigeria. The justification for the high elective caesarean section rate in this study was informed by the recommendation that this option of delivery should be offered to HIV positive mothers in our environment to prevent mother to child transmission of HIV[13]. All the babies delivered through elective caesarean section were found to be HIV negative, hence the choice of this mode of delivery by their mothers was a wise decision aim at preventing transmission of HIV to their neonates. A much larger trial have also advocated elective caesarean section as an effective way to minimize perinatal transmission of HIV particularly for those on prophylaxis and those on HAART with detectable viral load.[14,15]

Several studies have previously established that HIV-1 infection in pregnancy is associated with prematurity and low birth weight.[10,16 -21.] Though the difference in birth weight was not statistically significant between the two study groups, babies born to HIV positive mothers were found to weigh less than those of HIV negative mothers with mean of 2.87kg and 3.43kg respectively.

The high prevalence of mild birth asphyxia found in this study is in agreement with earlier reports in some parts of Nigeria.[10, 20, 22,]. This may be attributed to general reservation to avoid unnecessary intrapartum interventions and fetal manipulations that are presumed to increase the risks of perinatal transmission of HIV.

Several reports have confirmed the effectiveness and stressed the use of antiretroviral drugs in preventing mother to child transmission of HIV.[8,14,22 -26] , in line with this 100% of our patients were on HAART. The high perinatal transmission rate observed among the HIV positive mothers can be partly explained by the late gestational age at booking, the diagnosis of HIV infection was only known during the ANC hence, the expected timely interventions in majority of the mothers that could have averted fetal transmission were done lately.

The role of high maternal viral load, low CD4 count, advanced HIV disease state, prematurity and obstetrics and breastfeeding practices have been shown to significantly increase the risk of Mother to child transmission of HIV[27 -31]. Significant maternal and fetal determinants of perinatal transmission identified in this study were high maternal viral load >750cell/mL, CD4 count <350 cells/mm^3, delivery less than 37 weeks, birth asphyxia, and low birth weight. Six of the HIV positive babies were delivered by mothers with low CD4 count (<350 cells/mm^3 and high viral load >500 cells/mL, while 3 and 4 of the HIV positive babies were found to be premature and of low birth weight. Maternal age 30-39 years was also found to have strong association with perinatal transmission of HIV infection. This is in agreement with a study from Congo Brazzaville.[32]

All the mothers in the study group choose to formula feed their babies; this is surprising because breastfeeding has a very strong cultural tie particularly in this environment. Effective counseling, the relatively high level of education of the HIV positive mothers, and about 30% of them were enrolled in to the PMTCT programme from the adult ART clinic might have been responsible for the increase uptake of breast milk substitute as an alternative mode of feeding. The advantage of formula feeding over breast milk for the prevention of postnatal transmission of HIV had been reported by many researchers.[8,33-35]

CONCLUSION

The perinatal transmission of HIV is high. Prompt identification of both maternal and fetal risks' factors and Effective interventions aim at minimizing the impact of these factors before or during pregnancy will help to lower some of the preventable determinants of perinatal transmission.

RECOMMENDATIONS

A prenatal and antenatal risks reduction strategy should be advocated. All effort should be geared toward identifying those positive and minimized or modify risks factors through behavior change, prompt initiation of treatment and prophylaxis for those found positive with a view to reduce the incidence of perinatal transmission.

Table I: Maternal determinants of perinatal transmission of HIV *(N=51) = live birth

Age	HIV negative babies	HIV positive babies	Total
<20	0	1	1
20-24	10	0	10
25-29	19	1	20
30-34	9	2	1
35-39	6	2	8
=40	1	0	1
Total	**45**	**6**	***51**
	X^2 =33.53	P =0.000	
Parity			
Primigravida	3	1	4
2-4	25	1	26
5-7	16	4	20
=8	1	0	1
Total	**45**	**6**	***51**
	X^2 =4.64	P =0.590	
Education			
Nil	7	2	9
Primary	11	1	12
Secondary	17	1	18
Post-secondary	6	0	6
Tertiary	4	2	6
To tal	**45**	**6**	***51**
	X^2 =8.39	P =0.396	
Booking CD4(cells/mm^3			
<250	5	4	10
250-349	21	2	23
350-499	13	0	13
=500	6	0	6
Total	**45**	**6**	***51**
	X^2 =15.58	P =0.016	
Viral load(cells/mm^3 at delivery			
Undetected	10	0	10
201-500	16	0	16
501-750	12	2	14
751-1000	7	2	9
>1000	0	2	2
Total	**45**	**6**	***51**
	X^2 =21.85	P =0.005	

Table II: Relationship between maternal immunologic, virologic, treatment status and fetal outcome.

Variables	*Fetal age*		*Fetal weight*		*HIV status (N=51)*	
Mat. CD4	term	preterm	normal	low	+ ve	- ve
<250	8	2	6	4	2	5
250-349	22	1	22	1	4	21
350-499	10	3	11	2	0	13
=500	6	0	6	0	0	6
Total	**45**	**7**	**45**	**7**	**6**	**45**
	P = 0.227		*P = 0.034*		*P = 0.016*	
Viral load						
Undetected	10	0	10	0	0	10
201-500	15	2	15	2	0	16
501-750	12	2	12	2	2	12
751-1000	7	2	7	2	2	7
>1000	2	0	1	1	2	0
Total	**45**	**7**	**45**	**7**	**6**	**45**
	P = 0.613		*P = 0.344*		*P = 0.005*	
Time diagnosed						
Pre conception	15	1	14	2	3	13
Antenatal	31	5	31	5	3	32
Total	**45**	**7**	**45**	**7**	**6**	**45**
	P = 0.462		*P = 0.892*		*P = 0.458*	
Treatment offered						
HAART	45	7	45	7	6	45
Total	**45**	**7**	**45**	**7**	**6**	**45**
	P = 0.170		*P = 0 .870*		*P = 0.673*	
Mode of delivery						
SVD	35	5	33	6	5	33
Elective C/S	11	0	12	0	0	12
Emergency C/S	0	1	0	1	1	0
Total	**46**	**6**	**45**	**7**	**6**	**45**
	P = 0.010		*P = 0.015*		*P = 0.046*	

Table III: Fetal factors influencing perinatal transmission of HIV infection (N = 51)

Fetal age	**HIV negative**	**HIV positive**	**total**
Preterm	3	3	6
Term	42	3	45
Total	**45**	**6**	**51**
	$X^2 = 9.872$ *P = 0.007*		
Fetal weight			
Normal	43	2	45
Low birth weight	2	4	6
Total	**45**	**6**	**51**
	$X^2 = 24.149$ *P< 0.0001*		
Fetal Apgar score			
Normal	30	1	31
Mild asphyxia	14	3	1 7
Moderate asphyxia	1	2	3
Total	**45**	**6**	**51**
	$X^2 = 63.80$ *P< 0.0001*		

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