Somatic Growth and Clinical Manifestation in Formula Fed Infants Born to HIV - Infected Mothers During the First Year of Life

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Abstract

This was a comparative study of the growth and clinical manifestation between infected and uninfected HIV infants both of whom were fed with a limited quantity of powder milk from birth until one year of age. HIV-infected pregnant women were enrolled from the second trimester or the beginning of the third trimester. After birth, infants had physical examinations, body weight and height were recorded at 2, 4, 6, 9 and 12 month visits. All mothers were given 7 kilograms of infant formula at each infant visit until the infant was one year old. Diagnosis for HIV infection in these infants was made by two positive concordant results of DNA PCR or RNA PCR or HIV RNA. One hundred and two infants were diagnosed for HIV status and 21.5 per cent were infected. The infected infants showed signs of malnutrition. From 2-4 months of age, the averages of their weights and heights were lower than those of non-infected infants. Abnormal clinical signs were found in most infected infants by the time they were 9-12 months old. In conclusion for the infants born to HIV- infected mothers, monitoring signs and symptoms including their weight and height from birth till 9-12 months old, is predictive of the infectious status of most infected infants. The administration and management of infant formula in a limited quantity to HIV infected mothers in upper northern provinces of Thailand is possible without causing abnormal infant growth.

Key word : Infants Born to HIV-Infected Mothers, Fomula Feeding, Growth and Clinical Manifestation, First Year of Life

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HIV transmission from mother to baby occurs *in utero*, during delivery and after delivery through breast feeding because the virus is transmitted through breast milk. Meta-analysis has shown that the rate of transmission *via* breast milk ranges from 7-22 per cent[1]. In Thailand, at the beginning of the HIV epidemic, it was reported that the rate of infection from mother to infant in the four upper northern provinces of Chiang Mai, Chiang Rai, Phayoa and Lampang was between 37-45 per cent in 1989 to 1991[2-5]. Later reports from Chiangrai, Lampang, in 1996-98 showed the rate of infection to be 23-25 per cent[6,7]. Factors which may have contributed to the decreased rates of perinatal HIV transmission include changes in the following practices; breast feeding, antenatal screening, pre-and post-test counseling, antenatal care, health promotion programs and delivery procedures including avoiding early membrane rupture. So in 1998, the policy of the Ministry of Public Health (MOPH) was to provide infant formula for poor HIV-infected mothers[8]. The main problem in implementation of this policy is the administration of the amount of infant formula which will result in sufficient infant growth without complications caused by non-hygienic and disproportion preparation. The surveillance of signs, symptoms, weight and height can help indicate the status of HIV infection and malnutrition of infants.

MATERIAL AND METHOD

The Departments of Obstetrics and Gynecology and Pediatrics, Lampang Hospital in collaboration with the Research Institute for Health Sciences, (RIHES, Chiang Mai University), the Walter Reed Army Institute of Research (WRAIR) and the Armed Forces Research Institute for Medical Sciences (AFRIMS) were involved in this study. The study enrolled HIV-infected pregnant volunteers in their second or third trimester. They were interviewed about their medical history, physically examined and received medical care as necessary, especially for STDs. All women were counseled to feed their infants with formula. After birth all infants were weighed, measured for length, head circumference and physically examined. They were followed at 2, 4, 6, 9 and 12 months and provided with infant formula specially prepared for infants less than six months of age. On each visit mothers were provided with 7 kg of infant formula. Infant blood samples were collected on filter papers when they were younger than 3 days, 2, 4, and 6 months old for HIV RNA, DNA PCR and RNA PCR. The samples were sent to the RIHES and WRAIR for laboratory examinations. Diagnosis of infection in these infants was done by two positive concordant results of HIV RNA, DNA PCR or RNA PCR at different time points. Signs were categorized according to the guidelines of the Center for Diseases Control and Prevention (CDC), USA[9]. Data analysis for weight and height were performed using the standards of weight, height and nutritional index for Thais from one day to 19 years old, prepared in 1987 by the MOPH. None of the pregnant women received AZT to reduce the rate of perinatal transmission. The infants did not receive sulfamethoxasole/trimethoprim for prevention of Pneumocystic carinii pneumonia.

RESULTS

From April 1996 to September 1998, 102 pregnant women voluntary participated in the study. After delivery, 103 infants were followed and diagnosed for HIV status (there was one pair of twins). One infant died at 48 hours after birth with aspirated meconium pneumonia. A blood sample of this infant was collected and tested HIV negative. This infant was not included in this study. There were two mothers who were not able to come for their delivery at the hospital and who breast fed their baby before receiving the supply of formula from the hospital. The duration of breast feeding was 9 and 49 days, respectively. One baby was intentionally breast fed by her mother for 6 months after many counseling sessions advising her not to do so. This mother was eventually lost to follow-up after the six month visit. It was found that 22 infants were HIV infected (21.5%) and the baby who was breast fed for 49 days was among the infected infants.

Fig. 1 shows the comparisons between the weight of 41 non-HIV infected male infants, 11 HIV infected male infants, 35 non-HIV infected female infants and 8 HIV infected female infants, respectively. Mean average weight of both infant groups was not statistically different at birth (3.05/3.04 P = 0.96, 2.93/2.61 P = 0.05). For male infants the average weight began to statistically differ at 4 and 6 months (7.33/5.93, P = 0.00, 8.31/7.06, P = 0.00). For female infants, the differences were shown at 2, 4 and 6 months (5.11/3.95 P = 0.00, 6.70/4.64 P = 0.00, 7.64/5.83, P = 0.00). At 12

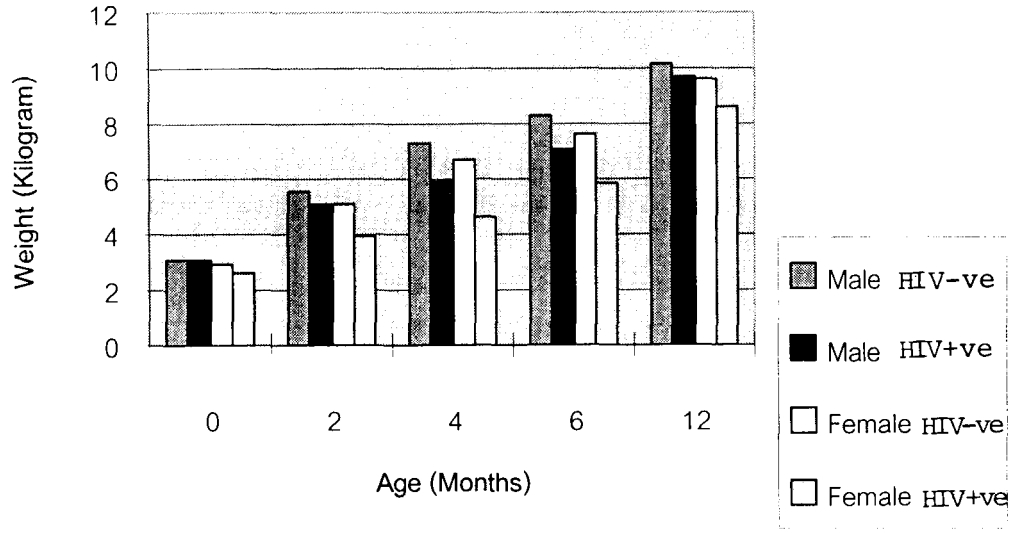

Fig. 1. Weight of infants from birth to 12 months old.

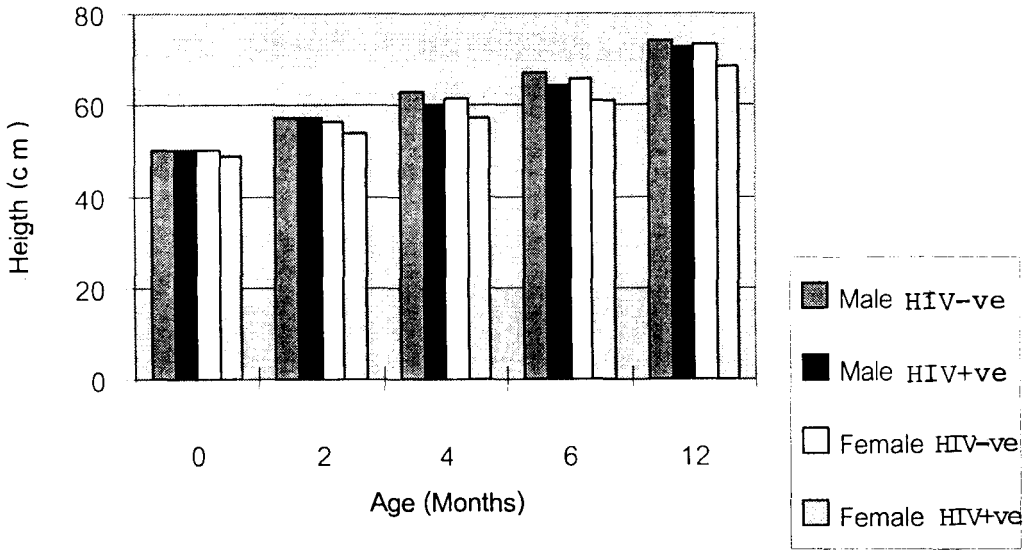

Fig. 2. Height of infants from birth to 12 months old.

months, there were no significant differences in either group for males or females. The number of infants was 26, 7, 19 and 2 respectively.

Fig. 2 shows the comparisons of the height between the same infant groups as mentioned in Fig. 1. There were significant differences of infant heights at 4 and 6 months in the male infant groups (62.75/60.07, P=0.01 and 66.79/64.05, P=0.00). For female infants, there were significant differences at birth, 2, 4, 6 and 12 months (50.43/48.75, P=0.03; 56.49/53.93, P=0.00; 65.37/61.03, p=0.00 and 73.00/68.50, P=0.03) respectively.

Eightyone per cent of mothers with infected infants and seventythree per cent of mothers with non-infected infants had a level of education below Grade 6. Furthermore, 97-100 per cent of mothers of both infant groups were not smokers, alcohol drinkers and drug users. There was no statistical difference of maternal background which may affect the growth of an infant *in utero*.

Table 1. Signs and symptoms in 22 HIV-infected infants from 2 to 12 months old.

Infant No.	Characteristics of clinical signs (Clinical category #) 2-3 months	4-6 months	7-12 months
1	C*	-	-
2	A	B	B
3	B	B	B**
4	N	N	N
5	B	B	B
6	A	B	A
7	B	B	B
8	A	A	A**
9	N	B	C*
10	N	N	N
11	N	A	C*
12	B	B	C*
13	B	C*	-
14	N	A	A
15	B	B	B**
16	N	A	A
17	N	A	A
18	B	B*	-
19	B	B	C**
20	A	A	Lost follow-up
21	B	B	B**
22	C*	-	-

Modified from:1994 Revised classification system for human immunodeficiency virus infection in children less than 13 years of age. MMWR 1994 ; 43(no. RR-12): 1-10.
Category N: Asymptomatic, Category A: Mildly Symptomatic, Category B: Moderately Symptomatic,
Category C: Severely Symptomatic.
*Infant died; ** infants received anti-HIV drug

Table 1 shows clinical signs in 22 infected infants from birth until 12 months of age. Seven infants died and the mortality rate was 31.8 per cent. Most deaths were due to severe pneumonia. One infant was confirmed to have PCP by post-mortem lung tissue biopsy. Two infants were diagnosed with PCP by acute and rapid progressive signs, did not respond to board spectrum antibiotics and the result of chest radiographs and levels of LDH higher than 1500 IU/L were taken into account. Other signs in Category C were weight less than 5 percentile on two occcasions and more then 4 weeks apart, including other illnesses. Signs in Category B mainly included pneumonia and anemia or septicemia. Signs in Category A were mainly hepatomegaly and spleenomegaly, lymphadenopathy at more than two sites, dermatitis, middle ear infection and chronic cough.

In 79 non-HIV infected infants during their first year of life, there were 65 episodes of common cold (0.8 episode/infant) and 17 episodes of pneumonia (0.2 episodes /infant) and 17 episodes of diarrhea (0.2 episodes/infants). There were other illnesses such as bronchitis and exanthem subitum. There were only 3 infants who were sick and admitted to the hospital, 2 had septicemia at 1-2 months old and another had pneumonia at 4 months old.

DISCUSSION

This study has shown differences in infant growth between infected and non-infected infants. There were statistical differences in weight at 2, 4 and 6 months of age in females and at 4 and 6 months old in males. At 12 months, there were no significant differences in either infected or non infected infants of either sex. This may be due to the fact that the infected infants had severe illnesses and died before 12 months. For height, there were significant differences from birth, 2, 4, 6 and 12 months in female infants and at 4 and 6 months in male infants. This finding is consistent with the results of Mckinner et al[10]. This group retrospectively studied the growth of 170 infants under 25.5 months old. The comparison between HIV infected and non-HIV infected infants showed that the weight and height of infected infants was lower than the non infected group from 4 months of age.

There were no significant differences between these two groups of mothers for risk factors which may lead to malnutrition status in infants such as socio-economic status, smoking, drug use and maternal education. Hence, malnutrition found in infected infants was likely to be the direct effect of HIV which caused immunodeficiency, the reduction of essential nutrient absorption by the intestine [11] and the increase of resting metabolic rates[12]. In addition, severe illnesses caused by opportunistic diseases and other complications, as shown in Table

1, played a role, i.e. at 4-6 months, 14 infants were ill and had clinical signs classified in category B and C, resulting in a reduction in food intake in these infants.

The mortality rate of infected infants in the first year of life was 31.6 per cent. This was higher than that reported in the U.S. and Europe (25%) during 1990-1994[13-15]. This high mortality rate at Lampang Hospital may be due to the fact that infants were not treated prophylactically for PCP at 4-6 weeks of age. Furthermore, the ability to diagnose and treat opportunistic diseases may have been limited.

For 79 non-infected infants, mean weight and height from birth until 12 months were at 50-75 percentile of the standards of weight, height and nutritional index for Thais from one day to 19 years old. The amount of infant formula provided, 7 kg at each visit, should be sufficient for the first 2 months of life. When the baby grew older, the mother was counseled to give one meal of supplementary food daily at 3 months of age, 2 meals at 6 months and 3 meals at 9-10 months. There were two reasons for this. Firstly, formula milk could not be provided over the limit set by the provider. Secondly, when the baby was one year old, the mother could give 3 meals of solid food. This would reduce infant formula use and control costs for mothers and health centers with limited budgets. With regard to complications which may be caused by non-hygienic and disproportion milk preparation, diarrhea was found to occur at a rate of 0.2 episodes/infant. This figure was less than that found in children under 5 years old (1.34 episode/person/year) reported by General Communicable disease control in 1993 as a nationwide rate[16].

In conclusion, for the infants born to HIV-infected mothers, if the pediatricians follow their signs and symptoms including their weight and height from birth until 9-12 months old, they are predictive of the infectious status of most infected infants. The administration and management of infant formula supplied in a limited quantity to HIV infected mothers in poor rural areas in Northern Thailand is feasible without causing abnormal infant growth.

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การเจริญเติบโตและอาการแสดงของทารกคลอดจากมารดาซึ่งติดเชื้อเอ็ชไอวี และได้รับการเลี้ยงดูด้วยนมผสม จากแรกคลอดจนอายุหนึ่งปี

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คณะผู้วิจัยได้ทำการศึกษาและเปรียบเทียบการเจริญเติบโต อาการแสดงของทารก 2 กลุ่มที่ติดเชื้อ และไม่ติดเชื้อเอ็ชไอวี โดยทารกได้รับการสนับสนุนอย่างต่อเนื่องให้สามารถเลี้ยงดูด้วยนมผสมในปริมาณที่จำกัดตั้งแต่แรกคลอดจนถึงอายุ 1 ปี หญิงตั้งครรภ์ที่ติดเชื้อเอ็ช ไอ วี จะถูกรับเข้าศึกษาตั้งแต่ไตรมาศที่ 2 หรือช่วงแรกของไตรมาศที่ 3 โดยติดตามซักประวัติตรวจร่างกายทุกครั้งที่นัด หลังคลอดทารกจะได้รับการตรวจร่างกาย ชั่งน้ำหนักและวัดส่วนสูง และนัดมาตรวจเมื่ออายุ 2, 4, 6, 9 และ 12 เดือน มารดาทุกคนจะได้รับนมผสมสำหรับเลี้ยงดูบุตรครั้งละ 7 กิโลกรัม จนกระทั่งทารกอายุ 1 ปี การวินิจฉัยว่ามีการติดเชื้อในเด็ก จะต้องมีผล DNA PCR หรือ RNA PCR หรือ HIV RNA เป็นบวก 2 ครั้ง. ทารกที่สามารถติดตามตรวจร่างกาย และตรวจวินิจฉัยสภาวะการติดเชื้อเอ็ชไอวี ทั้งหมด 102 คน พบอัตราการติดเชื้อร้อยละ 21.5 ทารกกลุ่มที่มีการติดเชื้อจะมีภาวะทุโภชนาการ ค่าเฉลี่ยของน้ำหนัก และส่วนสูงน้อยกว่ากลุ่มที่ไม่มีการติดเชื้อตั้งแต่อายุ 2–4 เดือน และจะพบอาการแสดงทางคลินิกที่ผิดปกติในทารกที่ติดเชื้อเกือบทั้งหมดเมื่ออายุ 9–12 เดือน. โดยสรุป ทารกที่คลอดจากมารดาที่ติดเชื้อเอ็ชไอวี ถ้าแพทย์ผู้ดูแลได้ติดตามดูอาการ อาการแสดง และชั่งน้ำหนักวัดส่วนสูงตั้งแต่แรกคลอด จนกระทั่งอายุประมาณ 9–12 เดือน จะสามารถพยากรณ์ถึงสภาวะการติดเชื้อของทารกได้เป็นส่วนใหญ่และการบริหารจัดการสนับสนุนนมผสมในปริมาณที่จำกัดสำหรับมารดาที่ติดเชื้อ และยากจนในแถบชนบทจังหวัดภาคเหนือตอนบนของประเทศไทยสามารถทำได้ โดยไม่ทำให้การเจริญเติบโตของทารกผิดปกติ

คำสำคัญ : ทารกคลอดจากมารดาติดเชื้อเอ็ชไอวี, นมผสม, การเจริญเติบโตและอาการแสดง, อายุ 1 ปี

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