

# Metabolic acidosis and encephalopathy in an HIV-exposed infant on breastfeeding and maternal antiretroviral therapy

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## Abstract

Zidovudine (AZT) treatment during pregnancy, delivery, and the postnatal period is associated with adverse effects in the neonate such as bone marrow suppression, elevation in aspartate aminotransferase activity, and lactic acidosis. With antiretroviral therapy (ART) now being recommended for life in HIV-infected pregnant women, infants born to these mothers and on breastfeeds are going to be exposed to antiretrovirals for a longer duration. We report a rare case of an HIV-exposed infant who received AZT prophylaxis for 6 weeks after birth and was on exclusive breastfeed while the mother was on ART and presented with unexplained severe metabolic acidosis and encephalopathy.

**Key words:** Antiretroviral, breastfeeding, metabolic acidosis

## INTRODUCTION

The introduction of antiretrovirals (ARVs) in HIV-infected pregnant women has drastically decreased vertical transmission of HIV. However, changes in both immunological response and hematological parameters have been detected in HIV-exposed uninfected newborns and attributed to both HIV protein exposure *in utero* and due to exposure to ARVs for a prolonged time.<sup>[1]</sup>

Further, mitochondrial dysfunction in infants exposed to nucleoside reverse transcriptase inhibitors *in utero* has been reported, which could lead to lactic acidosis (LA).<sup>[2,3]</sup> With ARV therapy (ART) now recommended in pregnant women for life for the prevention of vertical transmission of HIV and who still continue breastfeeding,<sup>[4]</sup> infants

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born to HIV-infected mothers will now be exposed to longer duration of ARV through breastfeeds. We report a rare case of an HIV-exposed infant who received zidovudine (AZT) prophylaxis for 6 weeks after birth and was on exclusive breastfeed while the mother was on ART and presented with unexplained severe metabolic acidosis and encephalopathy.

## CASE REPORT

A 4-month-old HIV-exposed female infant presented to the emergency department with multifocal convulsion, dystonic posturing, and altered sensorium. She was born at 35–36 weeks of gestation by emergency cesarean section due to cord prolapse. The mother was diagnosed to be HIV infected before pregnancy and was on ART consisting of AZT, lamivudine (3TC), and nevirapine (NVP), which she continued till date. Her CD4 count was 560 cells/mm<sup>3</sup> at the time of delivery. The baby also received single-dose NPV after birth and then AZT prophylaxis for 6 weeks. The child was exclusively breastfed. At presentation, the child had pallor, altered sensorium, and dystonic posturing. Anterior fontanel was at level and reflexes were brisk though tone was normal, and there was no focal neurological deficit. She had acidotic breathing with hepatomegaly. Other systemic examination was normal. Complete blood count was normal except hypochromic, microcytic anemia (hemoglobin was 9 g/dl). Liver and renal functions were normal, but arterial blood gas analysis showed severe metabolic acidosis (pH: 7.14, bicarbonate: 4.2 mEq/L) with a high anion gap of 30. Serum electrolytes were as follows: sodium: 138 mEq/L and potassium: 4.3 mEq/L. Septic screen in the form of C-reactive protein and blood culture was negative. Plasma sugar was 256 mg/dl, and urine was negative for ketones. The child was treated with intravenous fluids and anticonvulsants. Her sensorium gradually improved. Computed tomography brain revealed bilateral basal ganglia hypodensities suggestive of metabolic encephalopathy [Figure 1]. Serum lactate levels were sent after 24 h of hospitalization and after correction of acidosis which was normal (14 mEq/L [normal: 12–22]). Subsequent blood sugars were normal. Serum ammonia was 70 mmol/L (normal: 30–90 mmol/L), and urinary organic acids screen was normal. Electroencephalogram revealed generalized slowing. Mother was advised to stop breastfeeds and start replacement feeds. Child's HIV polymerase chain reaction was negative. The patient was put on thiamine, biotin, carnitine, and coenzyme Q supplements and regular physiotherapy. She is on regular follow-up.

## DISCUSSION

A mitochondrial toxicity (LA) in infants exposed to long-term regimens of ARV therapy (ART) used for the prevention of mother-to-child transmission of HIV is a

known but rare entity.<sup>[5]</sup> The proposed mechanism for LA is inhibition of mitochondrial DNA (mtDNA) polymerase  $\gamma$  leading to mtDNA depletion. Walker *et al.* showed that AZT and the combination AZT/3TC can produce raised lactate levels and cell death without a reduction in or deletions of mtDNA in an *in vitro* study.<sup>[6]</sup> In large study in France, with 3779 HIV-exposed child, Blanche *et al.* have found that eight children had mitochondrial dysfunction of which two died, three presented with delayed neurological symptoms, and three were symptom free but had severe biological or neurological abnormalities. Four of these children had been exposed to combined AZT and 3TC, and four to AZT alone.<sup>[3]</sup> Noguera *et al.* confirmed the hypothesis that zidovudine-exposed children had a significant risk of transient asymptomatic hyperlactatemia.<sup>[7]</sup> Several cohorts reported that a significant number of exposed but asymptomatic children had increased lactate levels within the 6-week postnatal phase of the ARV prophylaxis exposure. The serum lactate measurement was considered as a surrogate marker of mitochondrial dysfunction and can be used to investigate mitochondrial toxicity.<sup>[8]</sup> Similarly, in our patient, there was prolonged exposure to ARVs through breastfeeds which could have led to severe metabolic acidosis, leading to encephalopathy. Although serum lactate was normal, it was most probably due to sending the sample late for testing. Human studies have shown that ARVs administered to nursing mothers are present in their breast milk, but the extent of ARV transfer from mother to infant via breast milk is variable with lamivudine, and NVP is transferred to infants via breast milk in biologically significant concentrations.<sup>[9]</sup> Administration of essential cofactors such as thiamine, riboflavin, L-carnitine, Vitamin C, and antioxidants have been used as therapy for congenital mitochondrial diseases.<sup>[10]</sup> Similarly, in our patient, we have started coenzyme Q, carnitine, biotin, and riboflavin.

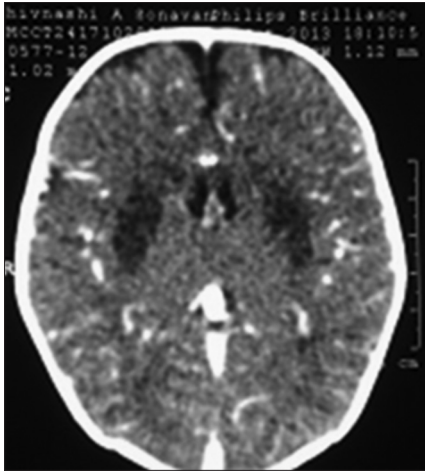
With ART now being recommended for life in HIV-infected pregnant women and continuation of breastfeeding, infants born to these mothers are going to be exposed to ARVs for a longer duration. These children should be monitored very closely to prevent the adverse effect of mitochondrial toxicity of these drugs.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Figure 1: Computed tomography brain showing bilateral basal ganglia hypodensities**

### Conflicts of interest

There are no conflicts of interest.

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