



# Treatment of Transient Hyperammonaemia of Prematurity in a Poor-Resourced Setting during COVID 19 Lockdown: Case Report and Literature Review

Suhair A Osman<sup>1\*</sup>, Leena Babikir A Razig<sup>2</sup> and Alkhansaa M Abdullah<sup>3</sup>

<sup>1</sup>Consultant paediatrician and neonatologist, department of paediatrics, Red Sea University, Sudan

<sup>2</sup>Senior registrar of paediatrics and child health, ministry of health, Sudan

<sup>3</sup>Registrar of paediatrics and child health, ministry of health, Sudan

**\*Corresponding author:** Prof. Suhair A Osman, Department of paediatrics, Consultant paediatrician and neonatologist, Red Sea University, Red Sea State, Sudan, Tel: 00249901920032; Email: Othman\_suhair@outlook.com

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## Abstract

Transient hyperammonaemia of prematurity is one of inborn errors of metabolism that is not very uncommon. Such diseases need specialization in genetics and metabolic errors, with special laboratory resources. It occurs in neonates and its cause is not clearly known. It affects preterm infants more than term ones. The exact incidence is not known as it can be asymptomatic or missed diagnosed as sepsis or respiratory distress, so needs high index of suspicion to be recognized. We want to inform about a preterm infant who was diagnosed on clinical basis only, as a case of transient hyperammonaemia of prematurity and treated successfully with alternative formula made locally by the treating physician, without sodium benzoate, carnitine, of haemodialysis. The aim of this presentation is to reflect brain storming upon facing such cases while working in a peripheral poor- resourced settings or a lockdown situation.

**Keywords:** Preterm Infant; Transient Hyperammonaemia; Poor Resources; Lack of The Specific Treatment

**Abbreviations:** N CPAP: Nasal Continuous Positive Airway Pressure; CRP: C - reactive protein; CRT: Capillary Refill Time; RDS: Respiratory Distress Syndrome; THAP: Transient Hyperammonaemia of Prematurity.

## Introduction

Transient hyperammonemia of prematurity (THAP) can be asymptomatic, or can presents in an overwhelming disease manifested clinically by change of sensorium and unresponsiveness, hypotonia, loss of reflexes, hypertension, seizure, and hyperglycaemia. These symptoms and signs are shared with many neonatal problems, this make the exact incidence unknown, and, in most of the times, missed diagnosis can occur unless a high index of suspicion is

applied to avoid neonatal death. It affects preterm infants more than term ones [1-4]. Although the cause of THAP is not exactly known, hypoxia, immature urea cycle enzymes, and inadequate hepatic blood flow have all been implicated [5-7], but in one study a vascular cause that shunts ammonia-rich intestinal blood away from the liver, directly to the superior vena cava, bypassing liver detoxication of ammonia, is hypothesized [8].

Therefore, in all sick neonates with central nervous system manifestation like seizure, lethargy and weakness, ammonia blood level is deemed necessary [9]. Normal blood ammonia level is 10 - 40 umol/L, but in neonates > 150 umol/L is significant. Genetic causes of hyperammonaemia like urea cycle defects, orotic aciduria and organic aciduria,

should be actively investigated for. THAP needs timely and aggressive therapy with haemo/peritoneal dialysis, systemic hypothermia, and extracorporeal membrane oxygenation, with or without sodium benzoate or carnitine [10,11]. In a resource- poor setting, where ammonia blood level cannot be done due to in availability, and the prementioned treatment modalities are not available, the treating physician should storm his brain and use his clinical common sense to diagnose and treat his patient. We are reflecting this hard experience for our colleagues sharing same situation, to make use of it, if faced with such a case.

## Case Presentation

A Sudanese female preterm was born at 31 weeks of gestation via normal vaginal delivery after an uneventful pregnancy, to nonconsanguineous parents who have a previous 3 years old healthy male child. She was vigorous at birth and needed no resuscitation, with birth weight of 1.6 kg. Shortly after birth she became distressed due to respiratory distress syndrome (RDS) needed nasal continuous positive pressure (n CPAP) of 6 cm H<sub>2</sub>O for 5 days and then weaned to O<sub>2</sub> per nasal cannula till it discontinued over another 4 days, and started gradual trophic feeding with her mother expressed breast milk (EBM). when the feeds reached built up to 6 ml per feed, she started to be lazy, less active, and gradually developed severe hypotonia, elevated blood pressure at the 99<sup>th</sup> centile for her age, hyperglycaemia of more than 260 mg/dl, and became unresponsive. Pulses were of good volume at 140 beat / min, capillary refill time (CRT) at 2 seconds, anterior fontanelle was full but not tense. At this stage we ruled sepsis out on clinical basis due to good circulatory and perfusion (pulses and CRT) and hypertension, confirmed by laboratory normal levels of platelets, C - reactive protein (CRP), and negative blood culture. Brain ultra sound scan showed no evidence of intraventricular haemorrhage (IVH), and her renal function tests were all normal, along with blood gases.

## Management

We put her on nothing per oral (NPO), with maintenance fluid dextrose 5 % with a 1/5 normal saline, due to her persisted hyperglycaemia, and amlodipine 5mg / day for the hypertension. Over 4-7 days she improved and regained her full activity, with hypertension and hyperglycaemia all normalized, and amlodipine discontinued. At this stage we thought she might have an inborn error of metabolism (IEM). Since hyperglycinaemia can present as same, but absence of myoclonic jerks and response to elimination of protein, makes it a remote possibility. Second possibility we thought of, was transient hyperammonaemia of prematurity (THAP), augmented by the presence of hypertension, and marked improvement with protein elimination, but we cannot confirm this laboratory wise. During these days she

became emaciated and was not growing, as we have no available intralipid and amino acid solutions in our territory these days during Coved - 19 epidemic. Same time we have no arginine, or sodium benzoate. We primed her with breast milk , again she went into same condition, so we went to same previous plan, but her failure to thrive was a challenge as isomil milk formula (soya- based protein) is not available in our territory and we couldn't bring from any were due to Corona virus lockdown.

We consulted some clinical pharmacists for alternative therapy, but with no sound result, so we did brain storming, and conclude to a formula made of: rice water, corn oil 0.5 ml with each feed of rice water, an adult tab containing L arginine (neurozan), no milk at all, and we supply her with zinc, probiotics, vitamin D drops, and iron plus folic acid. She tolerated this mixture very well and gained weight. Then after three weeks, we gradually introduce breast milk with gradual withdrawal of our innovative formula. At the time of reporting, she was two month old, on full breast milk, her weight 3.1 kg, and doing normally. On follow up at the three and 6 months postnatally, she demonstrated a satisfactorily growth and appropriate development, with no neurological sequel, and weight of 4 kg and 5.8 kg respectively.

## Discussion

In a limited- resourced setting with no good laboratory services and drug in availability, aggravated by Coved- 19 lockdown, facing such cases is challenging and stressful to the treating doctor and his staff. Such situation needs application of vigilance, a high common clinical sense, and innovation. Clinical signs like normal circulatory evidence, along with hypertension could help differentiate sepsis from other causes of neonatal weakness or encephalopathy. Knowing some characteristics of the common metabolic disorders can help a neonatologist differentiate between different metabolic problems when metabolic specialist is not available. In our case, we confirmed that her encephalopathy is related to protein intake, by rechallenging with refeeding with breast milk. Reported cases in the literature seemed to be more severe as most of them needed mechanical ventilation, haemodialysis, hypothermia, or even ECMO [5,7-11]. This can be attributed to late presentation/ diagnosis, or use of total parenteral nutrition, or large amount of milk. Our case needed nasal CPAP and then elimination of milk to revert to normal.

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with us.

### Conflict

We report no conflict of interest concerning this case.

### Consent

The consent to report on this case is taken from both parents with purpose to raise the awareness of our colleagues on the presence of THAP, and to reflect our innovative formula in poor setting.

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