

Thiamine responsive Pulmonary Hypertension among exclusively breastfed babies –A Hospital based prospective study from southern India

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Abstract

Pulmonary hypertension remains leading cause of mortality despite many advances in its management. Thiamine deficiency is identified as a reversible cause of pulmonary hypertension in exclusively breastfed infants whose mothers are thiamine deficient. The present study is planned to find out the reversible pulmonary hypertension in association with thiamine deficiency.

Objectives: To study the pattern of pulmonary hypertension and its associated factors due to thiamine deficiency.

Methodology: It is hospital based study in a tertiary care hospital of tumkur. Pretested and pre designed questionnaire was used to collect patients socio demographic data, clinical data and the data regarding investigations and treatment and prognosis.

Results: Total of 300 babies were included in the present study after taking into consideration of all inclusion and exclusion criteria. All the babies, 300 (100) belonged to Hindhu community. 234 (79.3%) belonged to class 3 socio economic status according to modified kuppuswamy classification. Majority 212 (70.6%) had only primary education and 32 (10.6%) were illiterates. 88(29.3%) had come with severe gasping. 287(95.6%) of babies had hepatomegaly and oliguria was present in 144 (48%) of babies. The majority of the infants were presented with shock 256 (85.3%), which was managed. Repeat echo was done serially and the difference in reduction of pulmonary pressure after administration of thiamine was statistically significant (p value <0.005) **Conclusion:** Thiamine responsive pulmonary hypertension presents as an acute condition with severe respiratory distress, vomiting in a previously well and exclusively breast fed baby. Hence clinical suspicion to recognise the symptoms early and diagnose and mere thiamine administration is life saving and which reverses the fatal condition. Health education to mothers and family members about food taboos related to use of polished rice to prevent deficiency of thiamine is also important and supplementation of thiamine as prophylaxis can also be considered in the programmes related to antenatal and postnatal care.

Key words: Pulmonary hypertension, Thiamine, Breastfeeding, food taboos

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Introduction

Pulmonary hypertension remains leading cause of mortality despite many advances in its management. Pulmonary hypertension occurs in an idiopathic form or in association with underlying diseases or conditions. Thiamine deficiency is identified as a reversible cause of pulmonary hypertension in exclusively breastfed infants whose mothers are thiamine deficient. Shoshin beriberi a fulminant form of cardiovascular beriberi characterized by tachycardia, hypotension, severe pulmonary hypertension and lactic acidosis and has been designated as 'a rapidly curable hemodynamic disaster' which is mainly due to thiamine deficiency¹. Thiamine, also called vitamin B1, is an essential micronutrient. The human body's supply of thiamine depends almost entirely on dietary intake; there is no endogenous synthesis, though some forms of bacteria in the intestine can produce a small amount of thiamine².

Although the availability of noninvasive measurement of pulmonary hypertension with echocardiography has made the diagnosis of pulmonary hypertension easier than before³, thiamine deficiency, of which early recognition and accurate diagnosis is imperative, is not assumed to be a cause of pulmonary hypertension⁴. The present study is planned to find out the reversible pulmonary hypertension in association with thiamine deficiency.

Objectives

- To study the pattern of pulmonary hypertension and its associated factors due to thiamine deficiency.
- To study the effect of thiamine administration on the resolution of pulmonary hypertension.

Methodology

It is an hospital based study in a tertiary care hospital of tumkur. Analysis of cases of pulmonary hypertension which were likely to be due to thiamine deficiency admitted to hospital between December 2020 to December 2021. Pretested and pre designed questionnaire was used to collect patients socio demographic data, clinical data and the data regarding investigations and treatment and prognosis.

Inclusion criteria:

All babies admitted to hospital with confirmed pulmonary hypertension by ECHO who are exclusively breastfed.

Exclusion criteria:

Babies admitted with other co- morbid condition

Breastfeeding infants with pulmonary hypertension diagnosed by echocardiography^{4,5} was included in the study. Since quick serial echocardiography was helpful in diagnosis, treatment and follow up of the patients⁶. PH was defined as pulmonary artery systolic pressure (PASP) more than 50mmHg as measured by tricuspid regurgitation (TR) jet with the presence of dilated right atrium and right ventricle^{5,10}. Infants with other related diseases like left to right shunts, pulmonary stenosis were excluded from the study by comprehensive performance of echocardiogram. Thiamine levels were not done as RBC transketolase activity reflective of thiamine status is not easily available. Only clinical response after thiamine supplementation was taken into consideration of thiamine deficiency.

Detailed history of socio demographic status, symptoms, birth and postnatal history was taken. Details regarding development and immunization history was obtained. Maternal dietary patterns, more about type of rice used, cooking patterns, exclusive breastfeeding and use of foods which inhibit thiamine absorption⁷. Food taboos and food fads related to post partum period were elicited. Hemodynamic status, systematic examination were performed. Hemogram, Chest x ray, echo cardiogram was performed as the protocol.

Interventions:

Babies with the symptoms of pulmonary hypertension were admitted to pediatric ICU. Oxygen and intravenous fluids were given. Babies with severe respiratory distress, poor perfusion were treated with dobutamine. To all the babies thiamine was given IV 100mg diluted in 10ml normal saline every day for 3 days. Echocardiography was done initially and after 24 hrs and everyday till the baby was discharged. Follow up was done after 1month and 6months.

Outcome measures:

Reduction in the pulmonary pressure after thiamine administration [8] detected by echo and resolution of heart failure clinically are the primary outcomes.

Institutional ethical clearance was taken before the study was conducted .

Data analysis:

Mean and SD was used for Quantitative data. Frequency and percentages were calculated for socio demographic data . Paired t test was used to compare before and after treatment with thiamine . P value of <0.01 was considered statistically significant. Epi info 3.5 software was used for statistical analysis.

Results

Total of 300 babies were included in the present study after taking into consideration of all inclusion and exclusion criteria. Among 300 infants, 11(3.6%) babies died and 289 (96.4%) showed complete reversal of pulmonary hypertension after thiamine therapy. The mean age was 3.6 ± 1.5 months. 61% (183) were male babies and female babies were 117(39%).The mean weight was 6.1 ± 1 kg. None of them had developmental delay and all babies were immunized appropriately as per age. All the babies,300 (100) belonged to Hindu community. 234 (79.3%) belonged to class 3 socio economic status according to modified kuppaswamy classification. Maternal education was known to be directly related to maternal nutrition status. Majority 212 (70.6%) had only primary education and 32 (10.6%) were illiterates.

Tachypnea and Tachycardia was present in all the babies. 245 (81.6%) of babies had irritability and poor feeding and all babies had vomiting. None of the babies had symptoms of fever , productive cough. Aphonia was present in majority 216 (71%) of babies which is supposed to be the characteristic feature of thiamine deficiency . 88 (29.3%) had come with severe gasping. 287(95.6%) of babies had hepatomegaly and oliguria was present in 144 (48%) of babies.

Polished rice was consumed by majority of the mothers during their post partum period combined with sambhar with very little dhal , that too for all the 3 major meals. Cooking of rice was seen in the open

vessel with throwing away the excess water which usually contains thiamine,was found in majority of the family.Diagnosing Pulmonary hypertension in babies with the mothers who are have nutritional deficiency was need of the hour [9]. Consumption of coffee, tea and beetal nuts immediately after food was found by coffee, tea ,beetal nuts and cooking soda was found to have anti thiamine activity .

On examination ,fever was absent in all babies. All the babies had Tachycardia and Tachypnea. 95.6% of the babies had hepatomegaly. Auscultation revealed clear breath sounds. Findings on chest X ray was cardiomegaly with right atrial and pulmonary artery dilatation(Fig 1) in almost majority of infants that is 286 (96.4%). Echocardiography showed dilated RA and RV.Severe Tricuspid regurgitation was found in 95% of infants.Mean PASP was 73.2 ± 15.4 (51-116). Right ventricular dysfunction was present in 199 babies but left ventricular function was almost found to be normal in all babies. Severe Lactic Acidosis was found in 11% of the babies with severe PH.

PH completely resolved in 94%of the babies after thiamine administration. Hepatomegaly,Tachypnea ,Tachycardia ,vomiting all reduced within 24hours. PASP at discharge was 20.2 ± 6.2 (9-34) mmhg. The Mean reduction in pulmonary pressure was 53mmHg.

Table 2 presents baseline laboratory features of the infants. Acute metabolic acidosis was a universal feature with a mean PH 7.12 ± 0.2 . All the babies had negative blood culture report with elevated C reactive protein was found in 18% of babies. Median lactate level was 4.6 (6.8). All other lab investigations were within normal limit.

The majority of the infants were presented with shock 256 (85.3%) ,which was managed with normal saline, dopamine, dobutamine and adrenaline perfusion as per the schedule and dosage along with intravenous thiamine. Mechanical ventilation was needed in almost 72% of the babies and the mean duration of stay was 3days. Intravenous thiamine of 100mg / kg was given till the reversal of pulmonary hypertension which was later switched to oral thiamine of 10mg/day. Repeat echo was done serially and the difference in reduction of pulmonary pressure after administration of thiamine was statistically significant (p value <0.005).

Table 1: Study population based on Signs and symptoms:

CVS	N (%)
Tachycardia	300(100%)
Shock	256(85.3%)
Central cyanosis	191(63.6%)
Cardiomegaly	286(95.6%)
TR murmur	285(95%)
Respiratory	
Tachypnea	300(100%)
Gaspings breathing	88(29.3%)
CNS	
Irritability	245(81.6%)
Renal	
Oligurea	144(48%)
Hepatobiliary	
Hepatomegaly	287(95.6%)
Vomiting	300(100)

Table 2: Echocardiographic features:

Pulmonary artery systolic pressure at admission (mean±SD)	73.2±15.4(51-116) mm Hg
Pulmonary artery systolic pressure at discharge (mean±SD)	20.2±6.2 (9-34) mm Hg
Fall in pulmonary arterial systolic pressure after treatment	53.0 (95% CL 49.8-54.8) mm Hg ,p <0.001
Tricuspid regurgitation (n)	Mild 126 Moderate 112 Severe 62
Right ventricular dysfunction(n)	199

Table 3: Baseline laboratory data of study participants:

Parameter	Value
PH(mean +-SD)	7.12±0.20
Hco3(mean+-SD)	11.7±5.23 m Eq/L
Lactate(median IQR)	4.6 (6.8) mmol/L
PCO2(mean +-SD)	29.32±7.46 mm Hg
Total leukocyte count(median IQR)	14600 (7886) c mm
Hemoglobin(mean +-SD)	12.3±1.8 gm/dl
Blood urea(median IQR)	39 (25) mmol/dl
Serum creatinine(median IQR)	0.8 (0.53)mg/dl
Serum aspartate amino transferase	45(69)

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Parameter	Value
Serum sodium(mean +-SD)	137±6.9
Serum potassium(mean +-SD)	4.3±0.75
Negative blood cultures (%)	300 (100)
Positive C reactive protein (%)	6 (18)

Discussion

The global prevalence of thiamine deficiency is poorly documented due to a dearth of population-level biomarker data ^{9 12}. Total of 300 babies was included in the study and mean age in months was 3.6 months as compared to mean age at presentation which was 78.5±30.7 days in a study from northern India ⁵. The mean weight of the baby was 6.1±1 in this study in contrary to mean weight of the study population which was 5.1 kg in a study done by J J bhat et .al ⁴ and it was appropriate for age in all infants. Table 2 shows the clinical features of the study population. The male to female ratio was 183:117 as compared to 155:83 in a prospective study conducted by Sastry et al ¹³. Quite interesting fact was all the babies belonged to Hindhu community. No babies belonged to other community propably due to maternal thiamine levels which might be good in non vegetarians or the etiology is not completely known. Majority 79.3% (234) of them belonged to class 3 socioeconomic status according to modified kuppuswamy classification ,which was similar in a study conducted by Sastry et all., where all the babies had belonged to low socio economic strata ,which probably tells us about the corelation between maternal malnutrition, thiamine defeciency and socio economic status.

70.6% (212) of the babies mother had only completed primary education which indirectly tells us about the unawareness regarding dietary requirement of thiamine in exclusively breast fed babies and practice of food taboos during lactation which might be the cause for thiamine defeciency in lactational mothers. Tachycardia, Tachpnea Hepatomegaly, Vomiting was common in almost all cases which was similar in other studies too ^{14,15}. Other symptoms and signs were Oliguria, edema which was also present in study conducted by JJ Bhat ⁵.

The maternal diet was predominantly of polished rice as rice is the staple diet of south Indians and was consumed for almost for all the 3times a day with use of sambher ,with little amount of dhal. Food fads and food taboos was also present in nursing mothers in south India and which was similar in almost all case studies and studies done so far.

Thiamine defeciency is a reversal cause of severe pulmonary hypertension and acute right heart failure. Response to thiamine administration of 100mg IV with its resolution after it , is the diagnostic criterion of pulmonary hypertension, as estimation of serum thiamine levels, low erythrocyte transketolase activity are expensive and not routinely available and not used in any study for diagnosis of thiamine defeciency.

The reduction in pulmonary pressure was 53.0 (95% cl 49.8-54.8). After infusion with thiamine. There was reversal of all the changes and was found in all cases except for babies with mortality, were reversal happened but the initiation of theraphy was almost very late.

Strength of the study:

Sample size is really huge compared to any other studies done in India .More number of cases were recognized.

Limitations of study:

Thiamine levels was not measured directly because it was difficult to measure ETKA and TPPE. cardiac catheterisation was not performed which would show pulmonary hypertension equivocally, instead ECHO was used to diagnose pulmonary hypertension which was not the gold standard investigation.

Conclusions

Thiamine responsive pulmonary hypertension presents as an acute condition with severe respiratory distress, vomiting in a previously well and exclusively

breast fed baby. Signs of severe tachycardia, tachypnea, hepatomegaly which was diagnosed by echocardiography. Administration of thiamine lead to rapid improvement of cardiac changes. Food fads and taboos during lactation and use of polished rice are the contributing features.

Lack of awareness about the clinical scenario among health care workers leads to late diagnosis of the condition or often mis diagnosis which is leading to high mortality among them. Hence clinical suspicion to recognise the symptoms early and diagnose and mere thiamine administration is life saving and which reverses the fatal condition. Health education to mothers and family members about food taboos related to use of polished rice to prevent deficiency of thiamine is also important and supplementation of thiamine as prophylaxis can also be considered in the programmes related to antenatal and postnatal care.

Recommendation:

Encouragement of thiamine supplements along with iron and folic acid tablets in the various community nutritional programmes leads to reduction of mortality and morbidity among children. Health education and creating awareness among family and community regarding use of unpolished rice which is rich in thiamine.

Source of fundings: self

Ethical clearance: taken

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