GLIMPSES of NEOCON 2016

held between 8th to 11th December, 2016 at Indore, MP
Editorial

Review Article 6  Targeted Neonatal Echocardiography  
Anchala Singh

16  Skin Care in Dermatological Conditions in Newborns  
Vibhu Mendiratta, Shiwangi Rana

Original Article 22  Birth Weight in Relations to Maternal Weight Gain During Gestational Period and Birth Order in a Tertiary Care Hospital in Bhubaneswar, Odisha  
Mishra Jayanti, Panda Jyochnamayi, Mishra Jyotiprakash

25  Neonatal Candida infection: Risk factors and sensitivity pattern  
Rajesh Kumar, Pankaj Kumar, Manoj Kumar Singh, Sachin Singh, Ankur Goyal  
Gyan Prakash, Vineet Kumar Singh

29  Central Lines in Newborn Infants in a Tertiary Hospital: A retrospective analysis  
Babu B, Mallaiah R, Ahuja A

32  Prediction of Nutritive Sucking in Preterm Babies (<34 weeks); an Essential Tool for Optimal Care of LBW Babies  
Nisha Kumari, Ashish Jain, Siddarth Ramji

39  Quality Improvement Initiative to Prevent Hypothermia at Admission in Neonatal Intensive Care Unit Among Preterm Neonates < 32 Weeks' Gestation  
Sindhu Sivanandan, M Jeeva Sankar, Ashok Deorari

Case Report 50  Different Spectrum of Manifestation Neonatal Lupus Erythematosus in Dizygotic Twins: A case report  
Rameshwar Prasad

53  Olmesartan Intake During Pregnancy Leading to Reversible Renal Failure and Skull Hypoplasia in a Preterm Newborn  
Lata Bhat, Supriya Bisht, Kavita Khanijo
NNF Office Bearers 2015-16

Dr Ajay Gambhir  
President NNF

Dr Sunil Mehendiratta  
Secretary NNF

Dr Alok Bhandari  
Joint Secretary  
cum Treasurer NNF

Dr B. D. Bhatia  
President Elect NNF

New Office Bearers 2017-18

Dr B. D. Bhatia  
President NNF

Dr Ajay Gambhir  
Immediate Past President NNF

Dr Alok Bhandari  
Secretary NNF

Dr Lalan K Bharti  
Joint Secretary  
cum Treasurer NNF
Dear Members

Greetings from NNF

Happy New Year

Experience over the last 25 years has shown that point-of-care ultrasound is a very useful tool when used by non-radiologists. Its value will be optimized by understanding its limitations and by adopting a focused binary decision making approach to answer specific questions without going into detailed radiological studies. Point-of-care ultrasound became an extension of the clinical examination. There are extensive efforts trying to design low-cost portable ultrasound systems by changing the transducer design, the transmission and reception circuitry needs, or the beam forming algorithms which may lead to horizontal expansion of the use of reliable non-expensive portable ultrasound machines. The successful story of using ultrasound by non-radiologists, the advanced technology, and the refinement of the educational methods will encourage future clinicians to use ultrasound in their domains. Role of echocardiography in neonatal intensive care unit (NICU) has changed over last few years. Earlier all echocardiography assessments were done by cardiologists but recently neonatologists have become interested in the echocardiographic assessment of hemodynamic instability of newborn. The terms Targeted Neonatal Echocardiography (TNE) or Functional Echocardiography has been introduced to describe the use of echocardiography as an adjunct in the clinical assessment of the hemodynamic status in neonate.

The major functions of the human skin are maintenance of water and electrolyte homeostasis, thermoregulation, antimicrobial defense, protection from trauma, environmental toxins and ultraviolet radiation, synthesis of vitamin, immune surveillance and cosmetic function. It also serves as a sensory organ and facilitates mother-child attachment. The birth of the baby represents a sudden transition from the intrauterine life to the external environment. Although the skin of the newborn has similar structural components as that of an adult, it differs in some characteristics from adult skin. As compared to adult skin it has thinner cells, compressed fewer Stratum corneum, low melanin content, highly permeable to fat soluble substances and increased absorption due to higher surface area to body weight ratio. Care of the skin in newborn as discussed in the January issue, in this we are going to discuss common dermatological conditions seen in neonates and their treatment.

Regards

Dr Sunil Mehendiratta
Editor in Chief
Targeted Neonatal Echocardiography

Anchala Singh
Department of Neonatology, Lady Hardinge Medical College & Associated Kalawati Saran Children Hospital, New Delhi, India

Introduction
When echocardiography is necessary in the newborn period, it often is needed urgently\(^1\). However, staffing, organizational, and geographic limitations make it unlikely for pediatric cardiologists to provide 24 hour coverage for echocardiographic assessment of sick newborns in most centers\(^2\). Pediatric cardiology services also could be overwhelmed with requests for assessments of ductal shunting in preterm infants who have yet to develop clinical signs\(^3\).

In many parts of the world, literature on the value of early hemodynamic assessment and increased access to ultrasonography equipment with improving image quality has motivated neonatologists to develop echocardiographic skills. As a result, echocardiography is increasingly considered an integral component of the assessment of the critically ill newborn\(^2,4,5\). An increasing number of neonatologists are undertaking assessments of functional hemodynamic status by echocardiography, with particular interest in volume of ductal shunt\(^3\), severity of persistent pulmonary hypertension\(^6\), and detection of low systemic blood flow\(^7\). Moss et al found 82% complete concordance rate between the scans performed by trained neonatologists and a pediatric cardiologist assessment\(^8\). Lee et al showed that the echocardiography by a neonatologist can identify a PDA with a sensitivity of 87% and a specificity of 71%\(^9\).

The **Functional echocardiography** and **Point of care Echocardiography** terms are being used to describe this use of echocardiography as an adjunct to clinical assessment\(^10,11\). Functional Echocardiography is different from echocardiography done by a pediatric cardiologist, where the main focus is to provide an opinion regarding structural heart disease and an assessment of cardiac function at the time of the measurement. Functional Echocardiography evolved from the need for sequential or more continuous monitoring of the hemodynamic condition of critically ill newborns.

**Targeted neonatal Echocardiography (TNE)** is proposed to “describe the bedside use of echocardiography to longitudinally assess myocardial function, systemic and pulmonary blood flow, intracardiac and extracardiac shunts, organ blood flow and tissue perfusion\(^12\).”

There are two types of TNE :-

1- **Standard or Full TNE**\(^12\) - refers to study of following components of heart
   a- Evaluation of LV systolic function
   b- Evaluation of LV diastolic function
   c- Evaluation of RV function
   d- Assessment of atrial-level shunt
   e- Assessment of PDA
   f- Evaluation of RV systolic pressure (RVSP) and PA pressure
   g- Assessment of systemic blood flow
   h- Assessment of pericardial fluid-

**Indications**\(^12\)
1- Clinically suspected PDA
2- Assessment of infants with perinatal asphyxia
3- Abnormal cardiovascular adaptation presenting with hypotension, lactic acidosis or oliguria during the first 24 postnatal hours and beyond in VLBW infants to diagnose low systemic blood flow state
4- Suspected PPHN
5- Congenital Diaphragmatic Hernia

2- **TNE with Focused imaging or Focused TNE**

**Indications**\(^12\)
1- Suspected pericardial effusion
2- ECMO cannulation
3- For putting Central line

Outside of these limited indications for focused imaging, standard TNE is recommended for the other indications\(^12\).

For any indication, the first study must always be a full comprehensive study, or if focused TNE is performed in emergency situations such as pericardial tamponade, this should be followed by a comprehensive study as soon as the patient has been hemodynamically stabilized. Standard TNE can be considered as a...
functional follow-up study for patients without structural heart disease\textsuperscript{12}.

**Guidelines for Safe Practice for Neonatologists Performing Echocardiography\textsuperscript{13}**

For any neonatologist performing echocardiography, a few guidelines for safe practice are shown below-

**Training and Audit**

1- Consider whether a neonatologist will perform this procedure often enough to acquire and maintain a basic set of skills.

2- Attend a formal course in echocardiography and decide on the level of expertise a neonatologist wish to acquire. If wish to diagnose heart disease accurately, seek a training fellowship or placement within a pediatric cardiac center.

3- When begin practice, keep a log of scans, and ask a mentor to discuss and audit one’s progress.

**Examination**

1- Perform a clinical examination prior to echocardiography. If the echocardiographic findings do not fit the clinical picture, request a cardiology review. Always check the femoral or foot pulses.

2- Refer any child who has suspected or confirmed structural congenital heart disease for expert cardiology review.

3- It may be safer to initiate prostaglandin therapy on the basis of clinical suspicion rather than delaying treatment while a noncardiologist performs echocardiography.

4- Do not hesitate to rescan with an open mind if an infant’s clinical signs unexpectedly persist or change. Record all scans, audit performance, and reassess any diagnostic inaccuracies.

5- Know your limits: If not certain of the diagnosis, obtain a second opinion before altering management on the basis of the scan.

**Reporting Scans**

1- Establish a standard proforma (if forget to check something, go back and check!). Title the report “Neonatal Cardiac or Hemodynamic Assessment” or similar to avoid the impression that pediatric cardiologist echocardiography has been performed, which could delay referral later for clinical signs of cardiac disease.

2- Always write a full report and be careful to state if you consider heart disease has been excluded.

**Modes of Functional Echocardiography**

**Functional echocardiography** includes evaluation of the heart using two-dimensional (2D) pulsed wave Doppler (PWD) and continuous wave Doppler (CWD) and M-mode methods. In term and preterm infants a probe frequency range of 7.5 - 10 MHz provides excellent resolution with adequate tissue penetration\textsuperscript{14}.

**M-mode** method displays fine detail of cardiac structure along a time line. A single thin plane of ultrasound energy is focused onto a targeted region of the heart. All structures within the targeted plane of insonation are then displayed in real time as they change during various portions of the cardiac cycle. It is used for the evaluation of chamber size, wall thickness, valvular motion and quantification of myocardial contractility.

The measurement of the left atrial to aortic root ratio with M-mode. The green line shows the path of the M mode beam on the 2-dimensional image.

**Doppler method** allows for determination of the velocity and direction of moving objects. Because blood and myocardial tissue both are in motion throughout the cardiac cycle, either can be assessed by Doppler echocardiography.

**In pulsed-wave (PW) Doppler**, transducer crystals alternately fire pulses of energy and then “listen” for reflected signal return. This mode allows for determination of spatial signal position but limits the ability to measure blood traveling at higher velocities.

**In continuous-wave(CW) Doppler** echocardiography, half of the transducer crystals fire continuously while the other half “listen” continuously. This mode allows for unambiguous assessment of increased velocities but limits the ability to pinpoint the precise location at which the velocity is obtained. CWD is useful in assessing infants with cardiac lesions of velocity of $\geq 2$ m/sec like in restrictive ductus arteriosus, pulmonary hypertension and tricuspid regurgitation, valvular abnormalities or septal wall defects.

In combination, pulsed-wave and continuous-wave Doppler modes provide a complete picture of blood flow direction and velocity.

**Colour flow Doppler** useful in identifying areas of flow acceleration or regurgitation across valves, septal defects or transductal shunting.
Standard Views in Neonatal Echocardiography

<table>
<thead>
<tr>
<th>View</th>
<th>Demonstrates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transverse subcostal view</td>
<td>Normal situs Superior vena cava drains into right atrium, pulmonary veins into left intact intraatrial septum intact ventricular septum</td>
</tr>
<tr>
<td>Subcostal atrial and four chamber views</td>
<td></td>
</tr>
<tr>
<td>Apical four-chamber view</td>
<td>Normal mitral and tricuspid valves, with tricuspid positioned closer to the apex of the heart establish atroventricular concordance intact ventricular septum rotate to “five-chamber view” to identify normal aortic valve from the left ventricle Pulmonary artery from the right ventricle crossing over aorta, excluding transposition (ie, establishing ventriculo-arterial concordance)</td>
</tr>
<tr>
<td>Parasternal long axis view</td>
<td>Normal motion of mitral and aortic valves intact ventricular septum normal pulmonary valve</td>
</tr>
<tr>
<td>Parasternal short axis view</td>
<td>Intact ventricular septum normal pulmonary valve drainage of pulmonary veins into left atrium</td>
</tr>
<tr>
<td>Ductal view</td>
<td>Ductal patency and direction of flow</td>
</tr>
<tr>
<td>Arch view (suprasternal)</td>
<td>Exclusion of coarctation</td>
</tr>
</tbody>
</table>

Common echocardiographic windows and views used in functional echocardiography. LA, left atrium; RA, right atrium; Mv, mitral valve; Tv, tricuspid valve; LV, left ventricle; RV, right ventricle; Ao, Aorta; RPA, right pulmonary artery; Desc Ao, descending aorta; PDA, patent ductus arteriosus.

Components of Standard TNE

1. Evaluation of LV Systolic Function
   Hemodynamic instability in the neonate can be caused by LV dysfunction, and assessment of LV systolic function is a key component of TNE. Maturational differences make the immature myocardium susceptible to impaired performance. These developmental disadvantages make the neonatal myocardium vulnerable during a hypoxic ischemic insult or when subjected to preload or afterload compromise.

Left ventricular (LV) systolic performance can be assessed by shortening fraction (SF), ejection fraction or the rate-corrected mean velocity of circumferential fibre shortening (mVCFc).

Fractional shortening (FS) is the most reproducible and commonly used assessment of left ventricular contractility. It is assessed either in the long axis parasternal or short axis view using M-mode echocardiography.

\[ SF\% = \frac{LVEDD - LVESD}{LVEDD} \times 100 \]

Long axis parasternal view of the left ventricle- LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter.

Normal neonatal values for SF% are 28-40%. However, this measurement is affected by both preload and afterload. Errors may also occur because of the distortion of the left ventricle in the preterm infant and paradoxical septal wall motion associated with right ventricular dominance.

Mean velocity fiber shortening (velocity of circumferential fiber [VCF]) is an alternative measurement of contractility that is less sensitive to minor dimension discrepancies and involves no assumption about ventricular shape. It is determined by the following method

\[ mVCFc = \frac{(LVEDC - LVESC)}{LVEDC} \times \frac{ETc}{ET/\sqrt{RR}} \]

where LVEDC is left ventricular end diastolic circumference, LVESC is left ventricular end-systolic circumference, and ETc is left ventricular ejection time corrected for heart rate (ET/ square under root RR interval, where RR is the time between consecutive heart beats). However, it is also influenced by volume loading of the ventricle, which tends to increase both measurements.

Tissue Doppler imaging is a relatively new ultrasound technology that derives measurements of contraction and relaxation velocities directly from the myocardium. As a direct measurement, it is affected less by preload and afterload, and normal values have been documented; however, as yet it can only be seen as an area for further promising research in the neonatal population.

2. Assessment of LV Diastolic or Combined Function
   In contrast to systolic dysfunction, the impact of diastolic dysfunction on neonatal hemodynamic is less clear and more difficult to define by
echocardiography. In infants the available data on diastolic dysfunction assessment are limited and based on analysis of mitral inflow patterns. Transmirtial flow occurs in two phases: an early phase (E wave) of passive flow during which the majority of the filling occurs and a late atrial contraction phase (A wave) during which the remaining third of the venous return to the ventricle is delivered. In normal neonates, during the first week of life, there is gradual change from a fetal filling type with more dependence on filling during atrial contraction (A wave) toward a more mature filling pattern with higher early filling (E wave). This change is characterised by progressive increase in E wave velocities, increase in the E/A ratio and early filling fraction.

PW Doppler can be used to examine this biphasic pattern of transmirtial flow. In patients with diastolic dysfunction, the majority of filling occurs during the atrial phase as the stiff ventricular wall prevents passive early flow across the mitral valve. The immature fetal and preterm myocardium is characterized by impaired diastolic function. Maximum E and A wave velocities are compared as ratios. An E: A ratio of < 1 indicates diastolic dysfunction.

The Tei index (or myocardial performance index) is a quantitative echocardiography index of ventricular function by incorporating both systolic and diastolic performance of the right and left ventricles. It is defined as the sum of isovolumetric contraction and relaxation times divided by the ejection time, which requires measurement of the time interval between the end and onset of mitral or tricuspid inflow (the ‘a’ interval) and the ejection time of the LV or RV outflow (the ‘b’ interval). The Tei index is then calculated by the formula (a b)/b. Normal values in healthy neonates range from 0.25 to 0.38. It has a low degree of inter- and intraobserver variability.

3-Evaluation of RV Function The evaluation of RV function should be an integral part of TNE, especially in patients with pulmonary hypertension, but it is difficult to perform, because there is no good quantitative parameter for the assessment of RV function.

For the estimation of RV size, the ASE (American Society of Echocardiography) pediatric quantification guidelines recommend the measurement of end-diastolic diameters at the basal and mid cavity levels, end-diastolic length, and end-diastolic and end-systolic plani metered areas in apical four-chamber views. For the assessment of RV function, the pediatric guidelines recommend quantitative measurements such as fractional area change and tricuspid annular plane systolic excursion, but these measurements require further validation in the neonatal population. Because tricuspid annular plane systolic excursion is dependent on heart size, the normal values change with growth.

Tissue Doppler and RV strain measurements have great potential but need further validation. In daily practice, qualitative assessment of RV function is often used, but this requires expertise, especially in the newborn and infant populations.

4-Assessment of Atrial-Level Shunt.—A key component of TNE is the assessment of intracardiac and extracardiac shunting and its contribution to hemodynamic or respiratory instability.

Assessment of shunting across the atrial septum (patent foramen ovale or atrial septal defect) is therefore a required part of the TNE. Atrial shunting can be best evaluated from subxiphoid long-axis or short-axis views of the atrial septum. Color Doppler imaging is used to view the atrial shunt and shunt direction. Because velocities can be low, it might be necessary to lower the color scale. For TNE, the most important aspect is shunt direction. Normally, left atrial pressures are higher compared with right atrial (RA) pressures and a left-to-right shunt is present, although a bidirectional shunt can still be normal in the neonatal period. Right-to-left shunting is abnormal and in the absence of structural heart disease suggests elevated right-sided filling pressures, often related to pulmonary hypertension and RV hypertrophy. Bidirectional and right-to-left shunting can contribute to reduced arterial oxygenation. Apart from shunt direction, pulsed-wave or continuous-wave Doppler can be used to assess the pressure gradient across the atrial septum. The calculation of the mean gradient gives information on the pressure difference between left and right atria and the difference in filling pressures.

5-Assessment of PDA - Assessment of ductal patency, determination of ductal shunt direction, and measurement of ductal pressure gradients are an important part of every targeted neonatal echocardiographic study.

The diagnosis of a significant PDA by echocardiography precedes the development of clinical signs by a mean of 2 days. Bounding pulses and a murmur may be absent in up to 20%
of infants with a PDA. Therefore echocardiography remains the gold standard for PDA diagnosis. Echocardiography can reveal whether shunting is present, the size of the duct, and circulatory side effects such as pulmonary over circulation and reduced diastolic flow in systemic arteries.

**Direct 2D imaging:** Through high parasternal window slightly left to sternum PDA is visualised as three legged stool appearance.

![Echocardiograph showing ductus](image)

(A) This echocardiograph, from the high left parasternum, shows the ductus in its entirety.

**Color doppler:** When the color Doppler field is placed over the ductus shown on two-dimensional imaging, the characteristic red jet of the ductal shunt appears to be streaming back up the anterior wall of the MPA. The two blue streams of the LPA and the descending aorta are seen on either side of the ductal stream. Measurement of the internal ductal diameter by two-dimensional and colour Doppler imaging allows early prediction of significant PDA in preterm infants. Since the ductal walls may be hard to define in 2D mode, color Doppler has been used to determine the ductal diameter.

A color jet measurement greater than 1.6mm correlates with a significant left-to-right shunt in neonates weighing less than 1500 g.\(^8\) When using 1.5 mm as the threshold, there was a strong association with an hsPDA (81% sensitivity and 85% specificity)\(^9\).

In addition, color Doppler provides information regarding the direction of shunting across the PDA. A disadvantage of this technique is the over-saturation of the color filters leading to an overestimation of the smallest ductal diameter. This leads to a lack of correlation between the minimal ductal diameter by color when compared to angiographic measurements of the PDA\(^10\).

High parasternal view of patent arterial duct with left-to-right shunting.

**Direction of ductal shunting -** Pulsed Doppler identifies the direction and velocity of blood flow at the site of the range gate. The tracing displays left-to-right flow as a positive trace and right-to-left flow as a negative trace, with velocity plotted against time. The pattern of Doppler shunting is determined by the relative pressures at each end of the duct through the cardiac cycle. When the aortic pressure exceeds that in the MPA throughout the cardiac cycle, the shunt is pure left-to-right. When MPA pressure exceeds aortic pressure throughout the cardiac cycle, the shunt is pure right-to-left.

Pulsed Doppler at pulmonary end of DA is used to measure peak systolic velocity across PDA. DV \(<2\) cm/sec is associated with hemodynamically significant PDA\(^11\).

**Shunt flow pattern** - Doppler echocardiographic assessment of PDA shunt flow pattern during the first 4 days of life is useful for predicting the development of clinically significant PDA in premature infants\(^2\).

Four Doppler patterns are identified.

**Pulmonary hypertension pattern** - A bi-directional shunt with right to left shunt (downward away from the baseline) in early systole is followed by a small left to right shunt (upward away from the baseline) throughout the diastole. This pattern was seen in early postnatal life in the presence of high pulmonary vascular resistance.

**Growing pattern** - A bi-directional shunt, but the right
to left shunt decreased and a growing left to right shunt is seen. This pattern represents a growing left to right shunt through a large ductus accompanying a fall in pulmonary vascular resistance.

**Pulsatile pattern:** No right to left shunt is and a much greater left to right shunt was shown by a pulsatile flow of peak velocity of about 1.5 metres/sec.

**Closing pattern** The prominent difference between this and the pulsatile pattern is that the closing pattern did not show the rhythmically pulsatile change, but rather a continuous left to right shunt covering the whole cardiac cycle in the profile. Large left-to-right shunts characteristically have continuous left-to-right flow, but instead of continuous high-velocity flow seen in healthy babies before the duct closes, the higher velocity is found in late systole, and the velocity at end diastole tends to be low (less than 1 m/sec and less than half the peak velocity in systole). This flow pattern suggests that the aortic and pulmonary pressures are nearly equal at the end of diastole, which is not seen in healthy infants.

**Closed pattern** This pattern is to be sampled in the pulmonary artery, because the Doppler gate is placed in the pulmonary end of the ductus while it is closed, so true ductal sampling would have produced no Doppler signal at all. Thus the closed pattern is similar to the pulmonary artery flow pattern.

The range of ductal shunt pattern from pulsatile left-to-right (A) to bidirectional (B) to predominantly right to left (C).

**Pulmonary overcirculation**

The increase in effective pulmonary blood flow is estimated by the left atrial to aortic ratio (LA:Ao), pulmonary artery diastolic flow, left ventricular cavity size, transmitral flow patterns and left ventricular output.

Left atrial /aortic width ratio (La/Ao ratio): M mode pictures of the left atrium and the aortic root are obtained from a parasternal long axis view. LA/AO ratio $\geq 1.4:1$ is found to be associated with mod to large PDA.

LA: Ao can be measured using long parasternal axis view to obtain an m-mode tracing (yellow line).

The presence of diastolic blood flow in the left pulmonary artery is also a useful indicator of ductal significance; specifically, a high end-diastolic velocity represents a large left-to-right shunt and increased pulmonary perfusion.

Additional markers of increased pulmonary shunting also include a high LV output ($>350$ ml/min/ kg).14

**Transmitral Doppler flow measurement** may be a useful marker of left atrial pressure/volume loading. In premature infants, the early phase of passive filling (E wave) is less than the late active phase (A wave), resulting in an E: A wave ratio of $<1.0$. In neonates with a hemodynamically significant DA, an increase in passive transmitral flow secondary to increased left atrial pressure, results in a pseudonormalization of the E:A ratio which may be $>1.0$.

**Mean LPA velocity/end diastolic LPA velocity:** A mean LPA velocity of $\geq 0.42$m/s and/or an End Diastolic LPA velocity $\geq 0.2$ m/sec identify significant L-R SHUNT through PDA.

**LV/Aortic root width ratio**: RATIO of $\geq 2.2$ is found to be associated with mod to large PDA.

**Systemic hypoperfusion**

Absent or Retrograde diastolic flow in postductal aorta: Normally diastolic flow at the post ductal aorta is low-velocity forward flow, as ductal shunting increases, the diastolic flow becomes progressively absent, and then retrograde. The descending aorta is imaged best from the same high left parasternal position as the ductus. It is critical that the Doppler range gate be placed beyond the aortic insertion of the ductus. Retrograde diastolic flow in the descending aorta exceeding 30% of the antegrade flow is indicative of a mod- large left-to-right ductal shunt.

High parasternal views of (A) a healthy infant who has forward diastolic flow and (B) an infant who has reversed diastolic flow that is associated with high-volume left-to-right ductal shunt.
Diastolic flow in superior mesenteric artery/anterior cerebral artery/renal artery Decreased/absent diastolic blood low in SMA/MCA/RA is found to be associated with moderate PDA and retrograde flow is seen with large PDA.

LVO/SVC ratio ≥4 seems to be associated with significant L-R ductal shunting.23

In every neonate with a clinical suspicion of a PDA, a comprehensive echocardiographic study should be performed before medical or surgical treatment to exclude ductal-dependent congenital heart defects and define arch sidedness. Subsequent standard TNE helps in defining the hemodynamic significance of the PDA and is useful in clinical follow-up documenting spontaneous closure or the effect of treatment. In preterm infants with hemodynamic instability after ductus ligation, TNE can be helpful in identifying the cause12.

6- Assessment of Right Ventricular Systolic pressure (RVSP) and Pulmonary Artery (PA) Pressures and Diagnosis of PPHN - Changes in pulmonary vascular resistance occur during the first weeks of life, so the assessment of PA pressures is an important component of every targeted neonatal echocardiography study.

The echocardiogram plays an essential diagnostic role and is an important tool for managing newborns with PPHN. It is defined by the echocardiographic determination of extra pulmonary venoarterial admixture (right-to-left shunting at the foramen ovale and/or ductus arteriosus), not simply evidence of increased Pulmonary Vascular Resistance (PVR) (i.e., elevated PVR without extra pulmonary shunting does not directly cause hypoxemia).

Assessment of right ventricular systolic pressure (RVSP) is possible in the presence of tricuspid regurgitation and calculated using the Bernoulli equation:

\[ \text{RVSP} = \text{right atrial pressure} + 4 \ (\text{Tricuspid Regurgitation JET V})^2 \text{ max where Vmax = peak velocity.} \]

The presence of PDA can also be used to estimate pulmonary pressures if systemic systolic pressures are known.

In every child with suspected pulmonary hypertension, comprehensive echocardiography should be performed to rule out structural heart disease. In neonates with PPHN, TNE allows assessment of the effect of treatment on PA pressures, RV function, and shunt direction at the atrial and ductal levels.

The measurements made with echocardiography can be used to predict or interpret the response or lack of response to various treatments. For example, in the presence of severe left ventricular dysfunction with pulmonary hypertension, pulmonary vasodilation alone may be ineffective in improving oxygenation. The echocardiographic findings in this setting include right-to-left ductal shunting (caused by suprasystemic PVR) and mitral insufficiency with left-to-right atrial shunting. In this setting, efforts to reduce PVR should be accompanied by targeted therapies to increase cardiac performance and decrease left ventricular afterload. This constellation of findings suggests that left ventricular dysfunction may contribute to pulmonary venous hypertension, such as occurs in congestive heart failure. In this setting, pulmonary vasodilation alone (without improving cardiac performance) will not cause sustained improvement in oxygenation. Careful echocardiographic assessment will provide invaluable information about the underlying pathophysiology and help guide the course of treatment12.

7- Assessment of Systemic Blood Flow- Left and right ventricular output can be measured Echocardiographically. Doppler assessment of left ventricular output is a useful adjunct to clinical assessment in infants with hemodynamic instability and provides the information regarding systemic blood flow.

Echocardiographically derived left ventricular output has been shown to correlate closely with Fick-derived measurements.

Assessment of LVO involves measuring the velocity time integral (VTI) across the ascending aorta from an apical five-chamber view using PW Doppler and determining the diameter of the aortic root from a parasternal long-axis view by M mode method.
Pulsed-wave Doppler measures blood flow across the aortic valve (white lines). The area under the curve is then traced to obtain the velocity time integral (C; yellow line). RV, right ventricle; LV, left ventricle; Ao, aorta; LA, left atrium.

With the help of aortic root diameter, aortic root cross sectional area (AoCSA) is derived from formula \( \pi \times \text{aortic diameter}^2 / 4 \). LVO is then derived by \( \text{LVO} = \text{AoCSA} \times \text{VTI} \times \text{heart rate} / \text{weight} \) and is expressed in ml/kg/min. Normal values range from 170 to 320 ml/kg/min.

Left ventricular output (LVO) does not necessarily equate to systemic flow. In the presence of a left-to-right ductal shunt, LVO cannot be used as a reliable reflection of systemic blood flow and oxygen delivery. If such a shunt exists, changes in LVO could reflect changes in systemic flow, ductal shunting, or a combination of the two.

Assessments of systemic flow, which are theoretically unaffected by ductal shunting, are Right ventricular output (RVO) and SVC flow. However, turbulence in the pulmonary artery from ductal flow can disturb the flow pattern making accurate determination of RVO difficult. LVO is increased by ductal shunting, but RVO may be decreased because of reduced systemic venous return.

Superior vena caval (SVC) flow
Subcostal approach is used to assess SVC Doppler signals and a high suprasternal view is used to measure SVC diameter.

Reduced flow in the SVC is common in premature infants in the first 24 h, reaching a nadir between 8 and 12 h which coincides with increased systemic vascular resistance. SVC flow less than 40 ml/kg/min in the first 24 hours of life has been associated with late intraventricular hemorrhage that tended to occur as perfusion improved. However, SVC return reflects blood supply to the brain and upper body and therefore no information regarding blood supply to the liver, kidney and gut can be derived. Measurement of SVC diameter beyond 48 h of life is difficult. In addition, the diameter of the vessel varies widely within the cardiac cycle resulting in wide margin of error from volumetric calculations. Groves et al. have also questioned the validity of this measurement due to high interobserver variability.

RVO is also affected by interatrial shunting across the often patent foramen ovale. Low RVO values below 150 ml/kg/min are found particularly in hypoxemic infants; infants with PPHN and high values may be found with large interatrial shunts. However, in the first 48 hours after birth, significant interatrial shunting is uncommon, and maximum velocity in the main pulmonary artery is the main determinant of RVO. Pulmonary artery maximum velocity (PA Vmax) can therefore be used as a screen for low RVO in the first 48 hours of life with a velocity of less than 0.35 m/sec being indicative of an RVO of less than 150 ml/kg/min.

Although no studies have explored the absolute threshold of low systemic blood flow and whether treatment improves outcome an SVC flowless than 30 ml/kg min−1 at 5 h of age and less than 45 ml/kg min−1 thereafter or a ventricular output (RVO or LVO) less than 150 ml/kg min−1 is associated with increased morbidity and mortality.

Infants with perinatal asphyxia
Comprehensive echocardiography is indicated in neonates with perinatal asphyxia with clinical or biochemical signs of cardiovascular compromise. Standard TNE, including the assessment of LV function, pulmonary hypertension, and ductal shunting, can help in optimizing therapy. The role of TNE in monitoring the cooling and rewarming phases of hypothermia needs further investigation.

Neonatal hypotension
In any neonate presenting with signs of hypotension, CHD needs to be excluded by comprehensive echocardiography. In the absence of structural heart disease, standard TNE can be used in the management of persistent hypotension, because it can be helpful in identifying the underlying mechanisms. With estimates of systemic blood flow one can more effectively treat hypotension and/or low blood flow using common...
cardiovascular medications according to their known effect on contractility and vascular resistance.

Low systemic blood flow with hypotension suggests a high systemic vascular resistance, and this situation might benefit most from increased contractility and afterload reduction with e.g. dobutamine or milrinone. With normal blood flow, dopamine can be used to increase the afterload and increase blood pressure.

Infants with congenital diaphragmatic hernia (CDH)
- All infants with CDH should undergo a comprehensive echocardiographic assessment of cardiac anatomy early in the course of postnatal management. Early diagnosis of CHD is mandated in the setting of CDH, which has a 10% to 18% incidence of associated CHD ranging from persisting atrial communications (patent foramen ovale and atrial septal defect) to more complex lesions, which impart a significantly higher mortality. More severe forms of CHD, especially those involving functionally single ventricles, are associated with such a poor prognosis that aggressive management may not be justified. Once CHD has been excluded, standard targeted neonatal echocardiographic studies can be used in follow-up. In CDH, TNE with focused imaging can also be used for checking line placement, which may be particularly difficult to assess radiographically because of distorted thoracic anatomy.

Focused TNE
- Assessment of pericardial fluid - Hemodynamic instability in a term or preterm infant can be caused by the presence of pericardial effusion. Echocardiography is an ideal technique to detect the presence of pericardial fluid and to assess its hemodynamic significance.

Subxiphoid coronal imaging may be sufficient to establish the diagnosis. Echocardiographic evidence of RA collapse at the onset of systole and RV collapse in diastole are signs of hemodynamic compromise.

Focused TNE can also be used for identifying catheter tip position after line placement and potential complications such as line thrombosis or infection. Echocardiography to rule out vegetations should be performed or interpreted by a pediatric cardiologist.

It is also a useful tool for neonates on ECMO, especially for evaluation of cannula position. When assessing PA pressure and ventricular performance, the impact of venoarterial ECMO on ventricular filling must be considered. Every child on ECMO must undergo comprehensive echocardiography.

Impact on neonatal outcomes
- The availability of functional echocardiography in the neonatal unit may influence management and short-term outcome.

In a retrospective review of 241 infants admitted to a tertiary NICU, echocardiography performed by neonatologists was associated with a change of management in 66% of infants examined. The diagnoses included structural heart disease (33%), hemodynamically significant PDA (3%), PPHN (6%), and LV dysfunction (3%).

In another retrospective study, the effect of serial echocardiography done by a neonatologist and early targeted medical PDA treatment was compared with historical controls. Serial echocardiography was associated with earlier identification and treatment of PDA, lower rates of severe IVH (from 36 to 10%, P = 0.046) and reduced ventilator days (from 13 to 9 days, P = 0.036).

In a prospective observational study of neonates in Pune (India), total of 348 echocardiographic studies were performed in 187 neonates (mean 1.86; SD 2.02). The most frequent indication was Patent Ductus Arteriosus (PDA) assessment (n = 174, 50%), followed by haemodynamic instability (n = 43, 12.36%). The results of ECHO modified treatment in 148 cases (42.50%) in the form of addition and/or change in the treatment or avoidance of unnecessary intervention.

Summary
- There is a growing acceptance that neonatologist-performed functional echocardiography is a useful tool in the NICU, with increasing evidence of improved patient outcomes. What is lacking at present is a formalised training and accreditation program necessary for the development of echocardiography skills. Echocardiography should supplement not replace clinical assessment and acumen. Extreme caution is needed with the infant who exhibits persistent cyanosis, and in general, a pediatric cardiologist should be consulted.

References
2- Skinner JR. Echocardiography on the neonatal unit: a job for the neonatologist or the cardiologist? Arch Dis Child. 1998;78: 401–402
Dear NNF Members,

NNF has started its monthly bulletin along with an active Website www.nnfi.org and quarterly journal. We invite your suggestions/articles/inputs for making them more pro active. Kindly send them to the undersigned.

Dr Ajay Gambhir
President, NNF
Email: president@nnfi.org

Dr Sunil K Mehendiratta
Secretary, NNF
Email: secnnf@nnfi.org
Skin Care in Dermatological Conditions in Newborns

Vibhu Mendiratta¹, Shiwangi Rana²
¹Director Professor, ²Senior Resident, Department of Dermatology & Venerology
Lady Hardinge Medical College & SSK Hospital, New Delhi

Abstract

Neonatal skin requires special care and support, especially in the conditions where the skin is damaged or diseased. We are describing few dermatological conditions with prominent skin involvement, manifesting at birth or within few weeks of life and which require intensive dermatological nursing with specialised management.

Introduction

Similar to adults, neonatal skin act as a first line of defence and protect against water loss, absorption of harmful substances, intrusion of microorganisms, and physical trauma. However, skin of newborn is not as morphologically and functionally specialized as adults and hence it gradually mature to adapt to the change in environment. Moreover, preterm newborns, during the first weeks of life, have an even less developed skin barrier and, therefore, are even more at risk. Special care procedures are required to ensure healthy development and to protect the neonatal skin from irritation and inflammation.

There are many dermatological conditions which manifest at or within few weeks of birth and require special care and management. As the presentation is early they pose a diagnostic challenge to the clinician. In this article we will briefly discuss few common dermatological conditions seen in neonates, with special emphasis on their management.

1) Neonatal Erythroderma

Erythroderma in neonates is a diagnostic and therapeutically challenging condition. There are multiple causes of erythroderma, the common ones are: infections, ichthyosiform erythroderma, drugs, atopic dermatitis and seborrheic dermatitis.

Management of neonatal erythroderma includes, a detail clinical evaluation with all the necessary laboratory investigation. Irrespective of the cause, the initial management is same and the main goal is to prevent various complications which are associated with erythroderma. Due to involvement of >90% of body surface area, these neonates are at higher risk of developing increased TEWL (trans epidermal water loss), hypernatremia, hypoalbumenemia, high cardiac output failure, infections and systemic toxicity of topically applied medicines.

Ideally these neonates should be managed in intensive care unit, with barrier nursing and humid environment. There should be strict temperature and daily input output charting. All routine investigations including the total blood count, serum electrolyte, serum albumin and uric acid levels should be sent, skin swabs for microbiological fungal culture can be positive in case staphylococcal scalded skin syndrome and cutaneous candidiasis and it should be repeated every alternate day. If available neonate should be kept in a humidifier incubator which can greatly reduces TEWL. Fluid and electrolyte imbalance needs to corrected promptly.

Daily bathing with water with or without a neutral pH cleanser should be done. After bath a bland emollient like petrolatum, with no perfume or preservatives should be applied all over the body, a frequent and liberal use of emollient significantly decreases TEWL and increases stratum corneum hydration.¹ In case erosions and blisters as seen in bullous ichthyosiform erythroderma and staphylococcal scalded skin syndrome potassium, permagnate soaks and zinc oxide paste can be advised. Use of salicylic acid, lactic acid and urea based cream is strictly avoided as they can be absorbed percutaneously leading to systemic toxicity. Use of topical steroid in seborrheic and atopic dermatitis induce erythroderma should be localised to limit area only, as significant percutaneous absorption can cause HAP axis suppression.

Once the condition of neonate is stabilised and the final diagnosis is made, the specific therapy can be started later.

2) Epidermolysis Bullosa

Epidermolysis bullosa (EB) is a group of genetic disorder, characterised by skin fragility, blistering and erosion on minor trauma. Depending upon the level of cleavage at dermo-epidermal junction, they are classified to four types:
1) EB simplex
2) Junctional EB
3) Dystrophic EB
4) Kindler

Management of EB includes wound care, skin care and other comorbidities. We will discuss the management as per the international consensus on best practice guidelines for skin and wound care in epidermolysis bullosa.²

Skin and wound care

General measures: Due to increased fragility of skin, these neonates should be given especial nursing care. The parents or care giver should be counselled regarding the avoidance of provoking factors (like trauma and friction) and gently handling of neonate. There are various blister prevention techniques (table 1) that can be administered when caring for a newborn that may help lessen the chance of infection and reduce pain.

Bathing and cleansing: There is a controversy regarding bathing practices, some advocate daily bathing while others discourage it. Daily bathing in severe EB can be beneficial in terms of general hygiene and wound cleansing, but many find this too difficult, painful and time-consuming. For the cleansing of wound various techniques has been recommended by various clinicians:

- Chlorhexidine baths before surgical procedures, in an attempt to reduce gram-positive organisms
- Vinegar soaks to gain control of gram-negative organisms, such as pseudomonas
- Diluted bleach bath, to reduce rates of infections
- Salt baths by its osmotic effect can reduce pain.

Blister and wound care: Once the active blister is formed, intact blisters should be lanced at their lowest point to limit tissue damage³, this can be done by using a hypodermic needle. The needle should pass through the blister roof lying parallel to the skin. The blister content should be gently emptied by using sterile gauze, and roof should lie intact.

Dressing can lead to overheating which increases the tendency to blister as sweating increases friction. Patient can develop new blister around the edge of dressing. For the neonates with wide spread skin loss dressing is required, however it should be removed once the wound is healed. To reduce friction a thin layer of white soft and liquid paraffin can be applied. Various types dressing are available for use in EB (table 3), which can be used according to the type of wound. Oral analgesia such as paracetamol and ibuprofen may be sufficient to manage mild pain, opioids and anxiolytics are necessary for severe pain associated with dressing changes.

Topical antimicrobials are recommended for infected and colonised wounds. The first choice of antimicrobials are, enzyme alginogel and polymeric membrane. Other agents are, honey, Polyhexamethylene biguanide, Hydrogen peroxide, Povidone iodine, silver, Cadexomer iodine, and Metronidazole gel.

Periwound skin care: Protecting periwound skin is also one of the important part in the management of EB, as this area is highly vulnerable to further damage. Any exudate in the periwound skin should be gently cleansed, adhesive dressings should be avoided, dressings with low adherence may be used with caution in patients who have extremely fragile skin. To protect periwound skin, barrier creams and cleansing agents can be used.

3) Collodion Baby

Collodion baby is refer to newborn born encased in a yellowish, adherent, supple, parchment like membrane that resembles plastic wrap. This membrane cracks with in few days after birth and peel off spontaneously in 3- 4 weeks. These newborn later develop one of the variety of icthyosis, the commonest ones are, lamellar icthyosis and non-bullous icthyosiform erythroderma. Other less common ones are, netherton syndrome, X-linked ichthyosis, neutral lipid storage disease, ichthyosis vulgaris, Sjogran-Larson syndrome.

Due to risk of developing various complications (table 3), these newborns needs special care and should be shifted to neonatal intensive care unit soon after birth.

The aim of management is to maintain the moisture in the skin and prevention of associated complications. The most important measure when treating these neonates is to keep them in a humidified incubator soon after birth, so as to prevent various complications resulting from excessive TEWL (like, hypernatremic dehydration and hypothermia).⁴,⁵

Consenses regarding optimal amount of humidification is not clear as some advocate a minimum of 40% to 60% humidity⁶ whereas others suggest 90% to 100%.⁷

Any derangement in electrolyte and fluid loss should be corrected promptly. Daily input output charting, electrolyte levels and weight monitoring should be done. Nasogastric feeding can be considered in
newborns who are unable to take breastfeeding due to taut facial membrane. As the natural course of the membrane is spontaneous peeling off, vigorous peeling of membrane should be avoided.

Buyse et al in their study found that the TEWL in a collodion baby at day 4 was 112 g/m²/h, compared with 18 g/m²/h in healthy babies. Use of petrolatum based emollients twice daily can decrease TEWL and thus preventing complications related to it.

The major concern regarding use of emollients is the increase risk of acquiring coagulase negative staphylococcus aureus, and other nosocomial infection. Therefore while using emollients in these newborn hand hygiene should be maintain. Prophylactic use of antibiotics is not recommended, however barrier nursing and daily clinical evaluation should be done to look for any sign of cutaneous infection.

Due to decrease barrier function there is risk of percutaneous absorption and systemic toxicity of topical medicines. Therefore any kind of medicated cream with salicylic acid, urea and lactic acid should be avoided. To prevent ocular dryness due to ectropion topical eye lubricant can be used.

Systemic retinoids therapy is often required in case of herliquin ichthyosis, where the scales are very thick with severe ectropion and eclabium. Oral acetretin (0.5-0.75mg/kg/day) or isotretinoin (2mg/kg/day) can be use to accelerate shedding of hyperkeratotic plaques, however there use in collodion baby is very rare as the membrane shed spontaneously.

### Table 1: Blister prevention techniques.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remove from incubator unless prescribed for other medical condition such as prematurity</td>
<td>Heat and humidity exacerbate blistering</td>
</tr>
<tr>
<td>Remove cord clamp and replace with ligature</td>
<td>To prevent trauma to umbilical area</td>
</tr>
<tr>
<td>Line nappy with soft material</td>
<td>To prevent blistering at edges of nappy</td>
</tr>
<tr>
<td>Cleanse nappy area with 50% liquid/50% white soft paraffin in ointment or spray (Emollin™) form</td>
<td>To ensure cleansing without trauma.</td>
</tr>
<tr>
<td>Delay bathing until prenatal and birth trauma healed</td>
<td>To avoid damage from infant being handled naked</td>
</tr>
<tr>
<td>Nurse on neonatal incubator mattress</td>
<td>To enable infant to be lifted on mattress and avoid shearing forces from carer’s hands</td>
</tr>
<tr>
<td>Use long soft teat such as lamb’s teat or a Haberman Feeder</td>
<td>To avoid friction damage to underside of nose and oral mucosa</td>
</tr>
<tr>
<td>Apply teething gel to teat (use a preparation that is safe to use from birth)</td>
<td>To alleviate pain from blistered mucosa</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dressing type</th>
<th>Indications/functions</th>
<th>Contraindications/comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft silicone mesh</td>
<td>Wound contact layer</td>
<td>Increased risk of overgranulation in Junctional EB. Should not be used in patients with Dowling Meara</td>
</tr>
<tr>
<td>Lipido-colloid</td>
<td>Wound contact layer</td>
<td>Not suited to very moist wounds (problems with retention)</td>
</tr>
<tr>
<td>Soft silicone foam</td>
<td>Protection and absorption</td>
<td>Heat related blister Use as secondary dressing over primary layer of soft silicone or lipido-colloid mesh to prevent adherence Silfix: Adherence may be too strong for very fragile skin</td>
</tr>
<tr>
<td>Hydrogel</td>
<td>Cooling Pain and reduction</td>
<td>Do not allow to dry</td>
</tr>
<tr>
<td>Sheet hydrogel</td>
<td>Cooling Pain and reduction</td>
<td>Unusual pain reactions have been reported</td>
</tr>
<tr>
<td>Hydrofiber</td>
<td>Very moist wounds where it is difficult to keep dressings in place. Between digits where there is a risk of fusion</td>
<td>Lightly exuding or dry wounds Irrigate with water or saline to remove if necessary</td>
</tr>
<tr>
<td>Polymeric membrane</td>
<td>Chronic and acute wounds</td>
<td>Stimulates high levels of exudate — use barrier film to protect periwound skin if required. Distinct smell does not necessarily indicate infection. Can be difficult to retain on vertical surfaces</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dressing type</th>
<th>Indications/functions</th>
<th>Contraindications/comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft silicone mesh</td>
<td>Wound contact layer</td>
<td>Increased risk of overgranulation in Junctional EB. Should not be used in patients with Dowling Meara</td>
</tr>
<tr>
<td>Lipido-colloid</td>
<td>Wound contact layer</td>
<td>Not suited to very moist wounds (problems with retention)</td>
</tr>
<tr>
<td>Soft silicone foam</td>
<td>Protection and absorption</td>
<td>Heat related blister Use as secondary dressing over primary layer of soft silicone or lipido-colloid mesh to prevent adherence Silfix: Adherence may be too strong for very fragile skin</td>
</tr>
<tr>
<td>Hydrogel</td>
<td>Cooling Pain and reduction</td>
<td>Do not allow to dry</td>
</tr>
<tr>
<td>Sheet hydrogel</td>
<td>Cooling Pain and reduction</td>
<td>Unusual pain reactions have been reported</td>
</tr>
<tr>
<td>Hydrofiber</td>
<td>Very moist wounds where it is difficult to keep dressings in place. Between digits where there is a risk of fusion</td>
<td>Lightly exuding or dry wounds Irrigate with water or saline to remove if necessary</td>
</tr>
<tr>
<td>Polymeric membrane</td>
<td>Chronic and acute wounds</td>
<td>Stimulates high levels of exudate — use barrier film to protect periwound skin if required. Distinct smell does not necessarily indicate infection. Can be difficult to retain on vertical surfaces</td>
</tr>
</tbody>
</table>

### Table 2: Recommended dressings for neonates with EB

<table>
<thead>
<tr>
<th>Dressing type</th>
<th>Indications/functions</th>
<th>Contraindications/comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft silicone mesh</td>
<td>Wound contact layer</td>
<td>Increased risk of overgranulation in Junctional EB. Should not be used in patients with Dowling Meara</td>
</tr>
<tr>
<td>Lipido-colloid</td>
<td>Wound contact layer</td>
<td>Not suited to very moist wounds (problems with retention)</td>
</tr>
<tr>
<td>Soft silicone foam</td>
<td>Protection and absorption</td>
<td>Heat related blister Use as secondary dressing over primary layer of soft silicone or lipido-colloid mesh to prevent adherence Silfix: Adherence may be too strong for very fragile skin</td>
</tr>
<tr>
<td>Hydrogel</td>
<td>Cooling Pain and reduction</td>
<td>Do not allow to dry</td>
</tr>
<tr>
<td>Sheet hydrogel</td>
<td>Cooling Pain and reduction</td>
<td>Unusual pain reactions have been reported</td>
</tr>
<tr>
<td>Hydrofiber</td>
<td>Very moist wounds where it is difficult to keep dressings in place. Between digits where there is a risk of fusion</td>
<td>Lightly exuding or dry wounds Irrigate with water or saline to remove if necessary</td>
</tr>
<tr>
<td>Polymeric membrane</td>
<td>Chronic and acute wounds</td>
<td>Stimulates high levels of exudate — use barrier film to protect periwound skin if required. Distinct smell does not necessarily indicate infection. Can be difficult to retain on vertical surfaces</td>
</tr>
</tbody>
</table>

### Table 3: Various complications related with collodion membrane.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distruption of barrier function of skin</td>
<td>Increase transepidermal water loss (TEWL)</td>
</tr>
<tr>
<td>Ectropion</td>
<td>Dryness of eye</td>
</tr>
<tr>
<td>Eclabion</td>
<td>Poor feeding and failure to thrive</td>
</tr>
<tr>
<td>Taut membrane round nose and chest</td>
<td>Breathing difficulty</td>
</tr>
<tr>
<td>Constriction band around fingers, hands and toes</td>
<td>Interfear with blood flow, occasionally leading to loss of parts of digit.</td>
</tr>
</tbody>
</table>
4) Neonatal Pemphigus

Neonatal pemphigus is a transient condition caused by transplacental transmission of materal autoantibodies primarily antidesmoglein 3 IgG autoantibodies. In all the cases mother has a positive history of pemphigus vulgaris or foliaceous. The clinical presentation develops at or with few weeks after birth in form of flaccid bullae, erosions all over the body. Involvement of oral mucosa can occur rarely. Atypical presentation in form of vesicles and erosions over chest, nape, perianal region and penis, without involving mucosa has been described. This condition should be differentiated from other bullous disorder presenting in neonatal periode namely, bullous impetigo, congenital syphilus, epidermolysis bullosa. A positive maternal history of pemphigus with supportive investigations like Tzanck smear for acantholytic cells, histopathology from intact bulla and direct immunofluorescence from perilesional skin helps in confirming the diagnosis. Indirect immunofluorescence from the serum of neonates for IgG antibody is positive at birth. According to previously reported studies, seroconversion can occur around 5 days to 2 months after birth, however Tanaka et al reported a case where reaction remain slightly positive even at the age of 2.5 years.

The disease is transient and lesion resolves as the antibody titres falls. Systemic therapy is not required and in most of the cases the main stay of treatment is barrier nursing with topical paraffine gauze dressing. Topical antibiotics are required only if there is secondary infection. For cases with oral mucosal involvement, nasogastric tube feeding can be done till the erosions are healed.

5) Infections

a) Neonatal Herpes:

Neonatal herpes is caused by HSV (Herpes Simplex Virus), which is acquired from infected mother during birth (most common), intrapartum or postpartum. Both HSV 1 and HSV 2 can cause neonatal herpes infections, with majority of cases being caused by HSV 1 (75%).

In majority of HSV infected infants there is no history of genital herpes or any symptoms at delivery. The risk of transmission varies according to the type of infection in mother. Thus, the risk of transmission is highest (up to 60%) when newborn is born to mother with first-episode primary infection at time of delivery, ≤30% when mother have first-episode nonprimary infection. The lowest risk (at <2%) of neonatal transmission is, when maternal history of recurrent infection is present.

Due to HSV infection neonate can develop:
- Disseminated HSV
- Localized CNS HSV
- Skin, eye and mucous membrane (SEM) infection.

Clinically these neonates presents with grouped vesicular rash at birth or shortly afterwards, in some cases it may appear 5-6 week later. Vesicles can coalesce to form large bullae which rupture to leave behind large erosions and peeling of skin. If the infection is disseminated, there is likely to be lethargy, seizures, respiratory distress, hepatosplenomegaly with hepatitis.

Bedside investigations like tzanck, grams should be ordered, and all the investigations including liver and renal function test should be carried out. For the diagnosis, viral can be isolated by tissue cultures from the oropharynx, nasopharynx, skin lesions, mucous membrane (eye and mouth) swabs, rectal swabs, blood buffy coat and CSF. If facilities available, PCR testing of CSF, skin lesions, mucous membranes and blood can be done. When skin lesions are present direct immunofluorescence of virus-infected cells for the presence of HSV antigens, are of value.

Serological diagnosis is not of much value in NHSV, as immunoglobulin (Ig) G antibodies acquired transplacentally cannot be differentiated from IgG produced by the infant and the detection of HSV IgM antibodies have only variable and limited reliability. If mother has active lesions of herpes at the time of delivery, detection of HSV 1 and 2 antibodies in mother can help to diagnose primary or non primary infection.

The treatment of choice for treating NHSV is intravenous acyclovir. The dose is 60 mg/kg/day in three divided doses administered every 8 h for 2-3 week followed by oral acyclovir for 6 months. To limit the risk of dissemination, the treatment should be started even if only skin and mucosa is involved. Regular monitoring of blood counts, renal function test and maintenance of hydration is important as there is risk of neutropenia and nephrotoxicity with high dose of acyclovir.

In case of suspicion of secondary infection skin swabs should be sent and antibiotics are started as per the sensitivity. Proper cleaning with barrier nursing is very essential in neonates with involvement of larger body surface area.

b) Neonatal Scabies:

Scabies is a mite infestation caused by an obligate human parasite of the phylum Artropoda, Sarcoptes scabei var hominis. It is one of the common conditions seen in our day to day practice. A neonate
The mainstay of treatment is oral antifungal which non-responding atopic dermatitis. Examination for fever with papulovesicular rash and as presentations has been reported in literature in palms, and soles is a consistent finding. Atypical web space and involvement of the face, neck, scalp, and pustules. Classical burrows can be seen in the burrows. As a result there can be uncontrolled scratching for mite.

Although 5% permethrin is a safe and effective scabicide, however it is not FDA approved for its use in infants <2months. Use of topical 5-10% sulphur in petrolatum base has been found to be safe in neonates. It is applied all over the body including face and rinsed off after 24 hours and then reapplied every 24 hour for next 2 consecutive days. The only concern with sulphur is skin irritation.

c) Neonatal Candidiasis:
Candidiasis is an infection caused by yeast of genus candida. Neonatal candidiasis is seen in first week of life, whereas congenital candidiasis is present at birth. The infection is thought to be acquired from mother’s genital track.

Clinical manifestations includes oral thrush, diaper rash, localised palmar pustules and sometimes in the form of generalised rash. Infection over the diaper area can be confused with diaper dermatitis, in such cases presence of a well define margins and presence of satellite pustules can be helpful. Definite diagnosis can be made with KOH and fungal culture.

Invasive and disseminated candidiasis is a serious and common cause of late onset sepsis and has a high mortality. In addition to the above mentioned cutaneous manifestations there are multiple systemic involvements. Diagnosis is confirmed with a positive blood culture for candida. The route of transmission can be vertical or nosocomial. The common risk factor of developing invasive candidiasis are- a) low birth weight (<1500 g) b) use of broad spectrum and/or multiple antibiotics c) central venous catheters; d) parenteral alimentation and intravenous fat emulsion; e) colonization with Candida and/or previous episode of mucocutaneous candidiasis; f) prolonged urinary catheterization.

The mainstay of treatment is oral antifungal which includes, amphotericin drops and fluconazole. For oral thrush 2% miconazole oral gel can be used. Other topical anticanidial drugs like, ketoconazole 2%, sertaconazol 2%, clotrimazole 1% cream are used for cutaneous candidiasis. Treatment of mother is very essential to the prevent recurrence of infection.

6) Neonatal Lupus Erythematosus:
It is rare syndrome which is seen due to transplacentral transmission of maternal autoantibodies to the ribonucleoproteins (RNPs), Ro-SSA, La-SSB or U1-RNP. The mothers of these newborns have clinical or subclinical autoimmune connective tissue disease. The classical clinical manifestations are, transient skin lesions resembling subacute cutaneous LE, and/or congenital heart block.

The skin lesion appear at birth or with in first few weeks of life. Characteristic lesions are erythematous scaly annular or polycyclic plaques mostly involving the face and particularly periorbital skin (racoon sign/owl-eye/eye mask). These lesions are transient and resolve in 5-6 months without significant pigmentation and scarring, however there are reports of atropic scarring at birth which is suggestive of occurrence of the lesions during pregnancy.

Cardiac involvement can manifest as complete heart block can occur in around 60% of patients.

The skin lesions resemble subacute cutaneous LE, and/or congenital heart block. These newborns should be thoroughly investigated, to confirm the diagnosis skin biopsy for histopathology and direct immunofluorescence with complete autoantibody profile of both newborn and of mother should be done. A complete haematological and biochemical investigation should be done to rule out related complications, for cardiac involvement echocardiography and electrocardiography is done.

For only cutaneous involvement sunprotection is advised by using physical sunscreen, topical low potent steroid can be applied over the scaly erythematous lesions. Newborn with cardiac involvement, are manage in neonatal intensive care unit by pediatric cardiologist, and may require pacemaker insertion. There can be transient raise in transaminases levels which falls back spontaneously. Oral prednisolone 2mg/kg/day for 14 days may be required in patients with thrombocytopenia.

Mother of these newborn should be counselled regarding risk (approximately 25%) of having another affected child, in these cases serial fetal echocardiography should be done by expert pediatric cardiologist.

References
1) Garcia Bartels N, Scheufele R, Prosch F et al. Efect of


**Announcement**

**NNF Training Fellowship for Doctors and Nurses**

Dear NNF Members,

NNF invites applications for fellowship from its members (Doctors and Nurses). Details are on website www.nnfi.org. Kindly download the form and send it to NNF Office.

Dr Ajay Gambhir  
President, NNF  
Email: president@nnfi.org

Dr Sunil K Mehendiratta  
Secretary, NNF  
Email: secnnf@nnfi.org
Birth Weight in Relations to Maternal Weight Gain During Gestational Period and Birth Order in a Tertiary Care Hospital in Bhubaneswar, Odisha

Mishra Jayanti1, Panda Jyochnamayi2, Mishra Jyotiprakash3
1Professor Physiology, KIMS, KIIT University, Bhubaneswar, 2Associate Professor Obstetrics and Gynaecology, KIMS, KIIT University, Bhubaneswar, 3Paediatric Specialist, Capital Hospital, Bhubaneswar

Abstract

Introduction: Neonatal birth order may act as a predictor for the birth weight. There may also be a correlation of maternal condition like gain in maternal weight during pregnancy with birth weight. Studies related to birth weight and its predictors are of importance because birth weight specifies health. Moreover such studies have not been documented from Odisha.

Aims and Objectives: The present study has been taken up to look into the potential association of birth weight with maternal weight gain during pregnancy and birth order.

Materials and Methods: 200 mother-infant binomials were identified with information on the baby’s birth weight and birth order. The maternal weight gain during pregnancy was also recorded by standardised procedures.

Statistical Analysis: Correlation coefficient (r) was determined between neonatal birth weight and maternal weight gain during pregnancy. The difference in mean birth weight of the first born group was compared with that of the other group. Statistical analysis was done by the use of SPSS 16.0 software.

Result: The newborns having <2500gms showed a weakly positive correlation with maternal weight gain(r=0.04). Newborn having >2500 gm birth weight showed a strongly positive correlation(r=0.87). There was no statistically significant difference between the mean birth weight of the first born and other group. (P>0.05)

Conclusion: The birth weight shows a positive correlation with maternal weight gain during pregnancy. However there was no association of birth order with birth weight in the present study.

Key Words: Birth weight, Birth order, Maternal weight gain

Introduction

In both developed and developing countries, birth weight is probably the single most important factor that affects neonatal mortality, in addition to being a significant determinant of post-neonatal infant mortality and morbidity.1,2 Thus, birth weight has long been a subject of investigations and a target for intervention. Considerable attention has been focused on the causal determinants of birth weight, and especially of low birth weight (LBW), in order to identify potentially modifiable factors.1 Low birth weight is defined by WHO as a birth weight less than 2500 g (before 1976, the WHO definition was less than or equal to 2500 g), since below this value birth-weight-specific infant mortality begins to rise rapidly. 2000 g has been suggested as a lower cut-off point3-7. The lowest birth weights were reported for Asia, with mean values ranging from about 2700-2800 g in the Indian subcontinent to 3200-3300 g in China and Japan, and corresponding LBW rates of 30-40% and 5-6%, respectively. In West Africa, the range of mean birth weight was 2800-3000 g with an LBW rate of 10-20%, while in North Africa, the corresponding values were 3200-3300 g and 5-15%. The range of mean birth weights was 2900-3100 g with an LBW rate of 10-18% in Central America and, respectively, 3100-3300 g and 9-12% in South America1,2. Studies related to birth weight and its correlates are of importance because birth weight signifies health. Studies establishing relationship between birth order and birth weight are scarcely reported. Birth order may act as a predictor for the birth weight and maternal condition like weight gain during pregnancy may have relationship with the
birth weight. Therefore the present study has been taken up to look into the relations of birth order and maternal weight gain during pregnancy with birth weight.

**Materials and Methods**

This is a descriptive study conducted at department of Obstetrics and Gynaecology after obtaining institutional ethical permission over a period of 4 months, from May 2016 to August 2016. Two hundred women with uncomplicated singleton pregnancy who all gave consent were followed up. Pregnant women with PIH, severe anaemia, cardiovascular and respiratory disorders were excluded from the study. All the women belonged to the upper middle class category according to Kuppuswamy Scale. The maternal gain (Difference in weight between the first visit and just before delivery) in weight was noted by using libra weighing scale. The birth order of the newborn was noted. The birth weight was recorded by using the seca 354 baby scale with a least count of 10 gms. All the weights were converted from grams to Kg while doing a correlation test. The data collection was done between 9am to 11am in the morning. The first born were included in one group and others were put into the second category. Information about socio demographic factors of the subjects was obtained by interviewing and questionnaire.

**Statistical Analysis**

Correlation coefficient (r) was determined between mean neonatal birth weight and mean maternal weight gain in Kilogram during pregnancy in the Low birth weight as well as normal birth weight groups. The difference in mean birth weight of the first born group was also compared with that of the later born group. Statistical analysis was done by the use of SPSS 16.0 software.

**Results**

The newborns having <2500gms showed a weakly positive correlation with maternal weight gain (r=0.04). Newborn having>2500 gm birth weight showed a strongly positive correlation (r=0.87). There was no statistically significant difference between the mean birth weight of the first born (2880±0.52gms) and later born (2846±0.54gms). (Two tailed P Value = 0.64, 95%CI of this difference from -0.11 to 0.18)

**Discussion**

The findings are in agreement with some previous workers as far as maternal weight gain is concerned. The present study however contradicts the findings of previous workers regarding relationship towards birth order. Modifiable factors with large effects on intrauterine growth should be targeted for public health intervention. In developing countries future research should focus on factors like antenatal care, vitamins, trace elements, physical activity, stress and anxiety.

**Conclusion**

No association of birth order with birth weight was found in the present study. The birth weight shows a positive correlation with maternal weight gain during pregnancy. The maternal conditions play a role in determining the birth weight.
Acknowledgements: We are thankful to the paramedical staffs, students and the concerned authorities for their help and support.

References
11. Steve Selvin and Joseph Garfinkel The Relationship between Parental Age and Birth Order with the Percentage of Low BirthWeight Infants, Human Biology, Vol. 44, No. 3 (September 1972), pp. 501509

KANCHI KAMAKOTI CHILDS TRUST HOSPITAL, CHENNAI
NEONATOLOGY CONSULTANTS REQUIRED

We are a 200 bed tertiary care children’s teaching hospital. The Hospital has various National Board and other sub-specialty training programs.

We seek full time Senior & Junior Consultants (one each) in Neonatology.

The NICU is a 40-bed level 3 unit, with conventional ventilation, HFOV, Nitric Oxide etc. The unit is recognized by the National Board for DNB Neonatology (two seats / year).

Persons with appropriate qualifications / experience may please send their CV via e-mail to: kkcth@kkcth.org or via post to: Medical Director, KK Childs Trust Hospital 12A, Nageswara Road, Nungambakkam Chennai-600 034 Ph: 044 4200 1800, ext. 159
Neonatal Candida infection: Risk factors and sensitivity pattern

Rajesh Kumar¹, Pankaj Kumar², Manoj Kumar Singh², Sachin Singh³, Ankur Goyal⁴, Gyan Prakash⁵, Vineet Kumar Singh³

¹Associate Professor, Department of Pediatrics, SN Medical College Agra; ²Assistant Professor, Department of Pediatrics, SN Medical College Agra; ³Junior resident, Department of Pediatrics, SN Medical College Agra; ⁴Assistant Professor, Department of Microbiology, SN Medical College Agra; ⁵Assistant Professor, Department of Community Medicine, SN Medical College Agra

Introduction

Neonatal sepsis is one of the major cause of neonatal mortality, accounts for about 33% of neonatal death in India.³ Invasive fungal infections are now emerging as a major cause (9 - 13%) of all blood stream infections in neonatal intensive care units.² Candidiasis in neonates is a serious and common cause of late onset sepsis and has high mortality (25 - 35%).³ The incidence of such fungal infection has increased 11 fold over past 15 years. Candida species are the 3rd most frequent organism (after coagulase negative staphylococcus and staphylococcus aureus) isolated in late onset sepsis in very low birth weight (VLBW) infants (< 1.5 kg).³ Prematurity and low birth weight are important risk factors for Candida infection.⁶ Species identification and determination of anti fungal sensitivity patterns has utmost importance for proper management of systemic candidiasis and to prevent resistance. The increased isolation rates of non-albicans Candida species and a gradual shift in the anti fungal susceptibility profile have underlined the need of this study.

Methods

An observational study was conducted in neonatal intensive care unit (NICU) in the department of Pediatrics, S.N. Medical College Agra from March 2016 to December 2016. The study population consisted of 250 neonates with clinical signs and symptoms suggestive of sepsis and positive blood culture results. The study was approved by the Institutional Ethics Committee (IEC) and all the parents provided written informed consent. The data was collected prospectively and analyzed retrospectively. The main outcome measure was to study the profile of neonatal Candida septicaemia, associated factors and sensitivity pattern.

Objective: To study the profile of neonatal Candida septicaemia, associated factors and sensitivity pattern.

Design: Observational study

Setting: NICU of tertiary care centre in Agra

Methods: Culture positive 120 neonates were studied from 250 neonates those fulfill the criteria for inclusion and exclusion. Blood culture was done by using BACTEC 9050 system. Candida subspecies differentiation was done by using Corn meal agar medium. Antifungal sensitivity was performed for Fluconazole, Voriconazole and Amphotericin –B using disk diffusion method on Muller Hinton agar supplemented with 2% glucose and methylene blue Main outcome measure:

Primary: To study Candida septicaemia in Neonates

Secondary: Factors associated with Candida sepsis and antifungal sensitivity pattern.

Results: On blood culture growth was seen in 48% neonates, out of these 29.17% were Candida species cases. Candida albicans isolates were responsible for 60% and non- albicans Candida species were 40% of cases. Non-albicans Candida isolates were C. tropicalis (22.86%), C.glabrata (14.28%) and C. krusei (2.86%). Low birth weight (RR-1.647, 95% CI 0.7947-3.4134) and Prematurity (RR-0.7609, 95% CI 0.4180-1.3851) was found to be associated with increased risk of Candida infection. All Candida albicans isolates were sensitive to Amphotericin B (100%) followed by Voriconazole (80.95%) and Fluconazole (76.19%). Non albicans Candida were sensitive to Amphotericin-B (100%), Voriconazole (78.57%) and Fluconazole (57.14%). C. kruzi was sensitive to only Amphotericin B.

Conclusion: Candida infection is an important cause of neonatal sepsis specially in LBW babies. Growing resistance to various antifungal drugs is alarming. Amphotericin B is still showing no resistance.

Key Words: Neonatal sepsis, Candida albicans, Non albicans Candida sepsis.
2013 to September 2014. Neonates with signs and symptoms suggestive of sepsis such as refusal to feed, feed intolerance, lethargy, excessive irritability, high pitched cry, seizures, temperature instability, apnoea, respiratory distress, poor perfusion, tachypnea, bradycardia, abdominal distension, vomiting, and sclerema were included in study.

For early onset sepsis neonates having at least two of maternal or neonatal risk factor such as fever within 2 weeks prior to delivery, prolonged rupture of membrane (≥24hrs), foul smelling and meconium stained liquor, single unclean or >2 sterile vaginal examinations during labour, prolonged labour (sum of 1st and 2nd stage of labour ≥24hrs), low birth weight (<2500gm), prematurity (<37 wk gestation) and perinatal asphyxia (Apgar score <4 at 1 min) were also included in the study.

Infants who were already on antifungal treatment or those with major congenital anomalies and neonates of HIV positive parents were excluded from the study.

Blood samples were obtained from each neonate before starting antibiotics, which included haematological parameters like TLC, DLC, absolute neutrophil count (ANC), immature/total neutrophil count ratio (I/T ratio), micro ESR, CRP, blood culture and sensitivity. The samples were processed immediately after collection. In case of delay, culture bottles were kept in incubator at a temperature of 35°C. Pathological leucocyte indices such as TLC <5000/mm3, ANC <1800/mm3, I/T ratio >20% and micro ESR >15 mm were defined as abnormal.

For blood culture one ml blood was collected in enriched soybean plus casein broth media in proportion of 1:10 in BD BACTEC PD vial. Culture bottles were incubated at 35°C in BACTEC 9050 machine. When BACTEC 9050 gave a positive indication for the growth that bottle was taken out from machine with all aseptic precautions. Broth was taken from bottle through new syringe and subcultured on MacConkey’s agar, blood agar, Sabouraud’s dextrose agar and incubated at 37°C. Culture plates were examined after 24 hour for growth. The growth was confirmed by standard biochemical tests to know the exact pathogen and at the same time tentative pathogen was subjected for sensitivity test by standard Kirbybaeuer method as per CLSI guidelines. Culture was taken negative if there was no positive growth indication in BACTAC 9050 machine up to five days. Candida subspecies differentiation was done by using Corn meal agar. Antifungal sensitivity was performed for Fluconazole, Voriconazole and Amphotericin B using disk diffusion method on Muller Hinton agar supplemented with 2% glucose and methylene blue. Zone diameters were interpreted as per the approved National Laboratory standards (NCCLS) guidelines.

This study was approved by institutional ethical committee and written informed consent was obtained from the parents/ guardians before the commencement of study.

Statistical Analysis: Data are presented as number or percentage as appropriate. Categorical variables between groups were analysed using Fisher’s exact test or Chi square test by SSPS 18 software. A p value<0.05 was considered as significant. Relative risk was calculated for studying the effect of birth weight and gestational age on fungal sepsis.

Results
Based on the inclusion criteria, 250 neonates were included in the study. Out of 250 neonates, 174 (69.60%) were males and 76 (30.40%) were females. Majority of neonates 58% (145) were preterm and remaining 42% (105) were term, 63.2% (158) were low birth weight and 36.8% (92) were normal birth weight. Most of the newborns 226 (90.4%) were born. Blood culture was positive in 120 (48%) neonates. Culture positive neonates (120) were further studied.

Candida species were isolated in 29.17% (35/120) cases while bacterial culture was positive in 70.83% (85/120) cases. Of the total 35 Candida positive cases 74.29% (26) were male and 25.71% (9) were female. The male: female ratio of Candida culture positive cases was 2.9:1. Table 1 shows weight distribution of culture positive Candida cases and depicts that birth weight has inverse relation with risk of having Candida sepsis. Prematurity was another important risk factor (Table-2). Infants below 34 weeks GA were at higher risk of Candida sepsis. In our study low birth weight infants had a relative risk(RR) of 1.647 (95% Confidence interval i.e.CI 0.7947-3.4134, Z statistic 1.342), while Premature infants had a RR of 0.7609 (95%CI 0.4180-1.3851 Z statistic 0.894).

Majority of the Candida sepsis newborn were outborn 31(88.57%) while 4 (11.43%) were inborn (p value = 0.73). Among all cases with Candida sepsis 27 (77.14%) were delivered vaginally and 8 (22.86%) were delivered by caesarean section(p value =0.20). Of all Candida sepsis positive cases PROM was found in 14 (46.67%, p value =0.006), foul smelling liquor in 8 (26.67%, p Value = 0.02) and prolonged labour in 2 (6.66%, p Value = 0.026).

Distribution and drug sensitivity of albicans and non albicans Candida infection is shown in Table 3. Among the isolates of Candida albicans species all were sensitive to Amphotericin B (100%) followed by Voriconazole (80.95%) and Fluconazole (76.19%). Among nonalbicans Candida isolates all were sensitive to Amphotericin-B, followed by Voriconazole (78.57%) and Fluconazole (57.14%). C. kruzi was sensitive to only Amphotericin-B (Table3).
Discussion

Fungal infections are the emerging threat to the neonates in the tertiary care centres. Candida has been found to be the most common fungal pathogen in neonatal sepsis. This study was conducted to assess the profile of Candida septicaemia in neonates, sensitivity pattern of antifungal agents and various factors associated with neonatal Candida sepsis.

Candida growth was seen in 29.16% and bacterial growth was seen in 70.83% cases which were similar to several other studies. In our study Candida sepsis was more prevalent in males than females, results were similar to the study done by Avila-Aguero ML et al.8 Male preponderance in neonatal septicaemia may be linked to the X-linked immunoregulatory gene resulting in the host susceptibility to the infection in males. This may also be due to attitude of the parents in this region to seek medical services more for their male babies than female.

Among the cases of Candida sepsis 88.57% were out born. In our study though the percentage of out born neonates were more than inborn, the results were statistically not significant. Candida sepsis observed more in neonates born by vaginal route. The reason behind this may be, when a newborn is born vaginally he/she gets exposed to the birth canal of the mother which has Candida as the normal microflora and this normal commensal may turn pathogenic when host’s immunity is low.

Of all Candida sepsis positive cases premature rupture of membrane (p value =0.006), foul smelling liquor

<table>
<thead>
<tr>
<th>Table 1: Distribution of culture positive neonates according to Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth Weight</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>ELBW &lt; 1 Kg</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>VLBW (1-1.499kg)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>LBW (1.5-2.499kg)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Normal birth weight (2.5-3.999Kg)</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2: Distribution of culture positive neonates according to gestational age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (weeks)</td>
</tr>
<tr>
<td>--------------------------</td>
</tr>
<tr>
<td>&lt;30 weeks</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>30-34 weeks</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>35-36 weeks</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>&gt;37 weeks</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 3: Species differentiation and Sensitivity pattern of Candida positive cases:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organism</td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td>C. albicans</td>
</tr>
<tr>
<td>C. tropicalis</td>
</tr>
<tr>
<td>C. glabrata</td>
</tr>
<tr>
<td>C. kruzi</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>
Candida infection was inversely related to birth weight. Several other studies also reported low birth weight as the common risk factor for Candida sepsis. In our study prematurity was another risk factor for Candida sepsis especially when the gestational age was less than 34 weeks. Other studies also reported prematurity as the risk factor for neonatal candidiasis. Relative Risk of Candida infection was more for LBW (RR=1.647, 95% CI 0.7947-3.4134, Z statistic 1.342) as compared to normal babies (RR 0.7609 CI0.4180-1.3851 Z statistic 0.894) so low birth weight was associated more with increased risk of Candida sepsis.

In our study C. albicans isolates were more common than non albicans Candida sepsis. Similar results were reported in several other studies. Majority of the non albicans Candida isolates were C. tropicalis (22.86%) followed by C. glabrata (14.28%) and C. krusei (2.86%) and this is in accordance with results obtained in other studies. C.tropicalis was found to be the commonest non albicans Candida species in these studies.

All the Candida species isolates were sensitive to Amphotericin B. Sensitivity to Voriconazole for albicans Candida was 80.95% and non albicans Candida was 78.57%. Sensitivity to Fluconazole for albicans Candida was 76.19% and non albicans Candida was 57.14. C. kruzi was resistant to all anti fungal drugs except Amphotericin B. These results were similar to the results of studies done by Juyal et al and goel et al. 

Conclusion
Candida species is an upcoming organism responsible for neonatal sepsis in NICU. Candida infection was associated with LBW babies specially weighing < 1kg. Widely used antifungal drugs like Fluconazole and Voriconazole had shown significant resistance for both albicans and non albicans Candida species. Amphotericin B is found to be most promising drug for all type of Candida infections.

References
Central Lines in Newborn Infants in a Tertiary Hospital: A retrospective analysis

Babu B, Mallaiah R, Ahuja A
Department of Neonatology, Fortis La Femme Hospital, New Delhi

Abstract

Background: Central lines in newborns are used in the newborn care, more frequently with the increased survival of preterm babies and aggressive nutrition strategies including the parenteral nutrition. However, they are associated with many complications like sepsis. Before placing a central line, one must ensure that the benefit outweighs the risks involved.

Aim: To collect and present data on the use of Umbilical vein catheters and Peripheral inserted central catheters in newborn infants admitted to our NICU.

Methods: We identified all infants with central line admitted to our NICU at Fortis La Femme Hospital, New Delhi from April 2014 to May 2016. The rate of Central line related problems were studied retrospectively including the Central line associated blood stream infections.

Result: A total of 49 central lines were placed in 35 newborn infants of the 490 babies admitted in our NICU, out of which there were 46 PICC lines and 3 Umbilical vein catheters. Out of these infants, 5 babies developed CLABSI, which had blood culture positive and 5 babies had a rise in CRP within 48 hours of placing a central line. The most common reason for placing a central line was to provide Parenteral nutrition. Most number of central lines were placed in extremely low birth weight babies. Most number of CLABSI was seen in babies who had the central line for a prolonged period.

Conclusion: CLABSI is newborn infants is directly proportional to the duration of central line. Hand hygiene during the maintenance of the central line and clean visible central line insertions are other causes of CLABSI. Neonatologists should take utmost care in not just the insertion of the central line but also the sterile technique of maintenance of the central line along with the timing of removal of central line.

Introduction

Central lines are used commonly in the NICU’s worldwide in the management of newborn infants to provide venous access, for administration of parenteral nutrition and to provide high glucose concentrations to meet the demands of preterm babies. However, the use of CLs is associated with several complications including infection. Therefore, the decision to insert a central line should be made for every patient individually, looking at the benefits and the risks involved. Once inserted, special care should be taken for the maintenance of central line and should be removed at the earliest point, when it is no longer required.

Infection

Newborn and especially preterm infants are always vulnerable to infections. Strict asepsis should be followed while inserting the central line and its maintenance, so as to decrease the risk of infections. Most common isolated pathogens in CLABSI is Klebsiella pneumonia.

Infection can occur due to failure to maintain asepsis during insertion. Strict hand washing and keeping a clean sterile insertion area, repeated handling of the central line, contaminated IV fluids, clean visible taping of the central line would decrease the risk of CLABSI in neonates.

Insertion and Maintenance

Aseptic conditions during catheter insertion and management are vital for prevention of infectious complications. It has been shown that the incidence of CLABSI can be reduced by education and training for care providers who insert and maintain catheters.

Insertion

Insertion of central line is a bedside procedure. After a strict handwash, the site for insertion of central line is located. The skin is cleaned with Chlorhexidine solution, followed by Povidine iodine and again cleaned with Chlorhexidine solution. Sterile drapes are placed prior to insertion.
The line is flushed with 0.9% Normal Saline and after placement is again flushed and continuous infusion started. Catheter position after confirmation on X-ray is taped in such a way that the insertion site is visible.

**Maintenance**
There should be minimal handling of the central line. Insertion site should be checked frequently, inspected several times a day. The ideal position for the tip of the PICC is in the inferior or superior vena cava1,5,7.

**Anatomy**
The peripheral veins of first choice are the veins of the antecubital fossa, the basilic and cephalic veins, as well as the axillary veins. Other vessels used are the femoral and saphenous veins of the leg, the external jugular vein of the neck and the temporal vein of the scalp8.

**Indications**
Drug administration, parenteral nutrition & fluid therapy are the main indications. All medications can be given through the PICC line after checking for terminal site compatibility.

Drug incompatibility is a frequent cause of line occlusion9. Given the risk of occlusion, blood products should only be given exceptionally4. Injections and temporary infusions should be avoided, minimizing the handling, given the risk of infection.

**Aim**
To collect and present data on the use of Umbilical vein catheters and Peripheral inserted central catheters in newborn infants admitted to our NICU.

Clinical data and complications including central line – associated blood stream infections (CLABSI) – Blood C/S positive and CRP rise were studied retrospectively in different gestational ages.

**Methods**

**Setting and Design**
This was a retrospective study which covered the period from April 2014 to May 2016 in the Neonatal Intensive Care Unit at Fortis La Femme Hospital, New Delhi.

Infants who fulfilled the following criteria were included:
– Infants born during the above mentioned period.
– CL placed or in place in our NICU.

**Definitions**

**Central line Associated Blood Stream Infection:** Primary blood stream infection associated with the usage of a central line

**Time of CLABSI onset and CRP positive Sepsis** were defined as parameters arising 48 hours or after the introduction of Central line and within 24 hours of discontinuation of central line and not secondary to an infection arising from other foci.

For each central line placed for infant, we recorded gestational age (GA), birth weight, clinical indication for central line, duration of catheter use, cause of catheter removal, CRP maximum, CL dwelling time, complications.

**Results**

<table>
<thead>
<tr>
<th>No. of central lines days</th>
<th>339</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of babies included</td>
<td>35</td>
</tr>
<tr>
<td>Total number of central line episodes</td>
<td>49</td>
</tr>
<tr>
<td>Average duration of central line/episode</td>
<td>6.91</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type of lines</th>
<th>No. of babies with Central Line</th>
</tr>
</thead>
<tbody>
<tr>
<td>PICC Line</td>
<td>46</td>
</tr>
<tr>
<td>UVC</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gestational Age</th>
<th>No. of babies with Central Line</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 – 28 weeks</td>
<td>28</td>
</tr>
<tr>
<td>28 – 32 weeks</td>
<td>14</td>
</tr>
<tr>
<td>32 – 36 weeks</td>
<td>04</td>
</tr>
<tr>
<td>&gt; 36 weeks</td>
<td>03</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Day of life</th>
<th>No. of babies with Central Line</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – 3</td>
<td>15</td>
</tr>
<tr>
<td>3 – 7</td>
<td>17</td>
</tr>
<tr>
<td>7 – 14</td>
<td>7</td>
</tr>
<tr>
<td>14 – 28</td>
<td>6</td>
</tr>
<tr>
<td>&gt; 28</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Birth Weight</th>
<th>No. of babies with Central Line</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1000 gm</td>
<td>31</td>
</tr>
<tr>
<td>1000 – 1500 gm</td>
<td>09</td>
</tr>
<tr>
<td>1500 – 2500 gm</td>
<td>07</td>
</tr>
<tr>
<td>&gt; 2500 gm</td>
<td>02</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Indication</th>
<th>No. of babies with Central Line</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Parenteral Nutrition</td>
<td>35</td>
</tr>
<tr>
<td>Hypoglycaemia</td>
<td>3</td>
</tr>
<tr>
<td>No IV Access</td>
<td>10</td>
</tr>
<tr>
<td>For Peritoneal Dialysis</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reasons for Removal</th>
<th>No. Of babies with Central Line</th>
</tr>
</thead>
<tbody>
<tr>
<td>Removed after completion of Aim</td>
<td>33</td>
</tr>
<tr>
<td>Occlusion</td>
<td>08</td>
</tr>
<tr>
<td>Swelling</td>
<td>05</td>
</tr>
<tr>
<td>CRP rise</td>
<td>03</td>
</tr>
</tbody>
</table>
Discussion

We report results from a retrospective study of neonates with central lines, UVCs and PICC lines. The central lines were used only in selected cases, in infants with extreme prematurity, ELBW babies, Severe IUGR babies who were not expected to reach full feeds soon or those requiring high glucose infusion rates to maintain their blood sugar levels.

CLABSI has become a major concern in neonates. A retrospective cohort study performed by Odetola et al. at a Pediatric intensive care unit suggested that 90% of nosocomial BSIs were related to intravascular catheter devices.

In the present study the incidence of CLABSI was around 10% and blood stream infection in terms of CRP positivity and blood culture negative was also 10%. However, it included 2 infants whose CRP increased immediately post surgery.

One of the purpose of our study was to determine the risk factors for CLABSI in the NICU. The causes of nosocomial bloodstream infections are multifactorial. In addition to central line exposure, there are many other factors in the NICU environment, that can contribute to the development of a BSI. Therefore, it is difficult to pinpoint a true independent contribution to the development of CLABSI.

Several factors have been noted in earlier studies to have a role in the development of CLABSI. These include low gestational age, low birth weight, administration of parenteral nutrition and prolonged duration of catheter use. Several studies have evaluated the effect of increased duration of catheter use on the incidence of CLABSI.

Several limitations should be considered when interpreting our data. Our study had a small sample size (n = 49). These factors can be patient-related such as underlying health state, environmental such as hospitalization and intubation. We did not have a control group. It would have been valuable to compare the occurrence of BSIs with a population without any central line.

Our study contributes to increased knowledge of the use of central lines in a very selected population of preterm infants. With the high incidence of CLABSI, a prospective and a more detailed study is planned to determine the risk factors leading to CLABSI. Asepsis during insertion, asepsis during maintenance, multiple handling, long dwelling time of central line, use of TPN, use of Bayonets or TPN filters is to be evaluated and their impact on the incidence of CLABSI to be studied. Further studies on preterm infants are needed to provide better understanding of CLABSI to improve clinical practices.

References

4. Guidelines at the Neonatal departement at Karolinska University Hospital, Danderyd.

<table>
<thead>
<tr>
<th>Type of Infection</th>
<th>No. of babies with Central Line</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLABSI – Blood C/S positive</td>
<td>5</td>
</tr>
<tr>
<td>CRP Positive, Blood C/S negative</td>
<td>5</td>
</tr>
<tr>
<td>CRP positive post operatively</td>
<td>2</td>
</tr>
</tbody>
</table>
Prediction of Nutritive Sucking in Preterm Babies (<34 weeks); an Essential Tool for Optimal Care of LBW Babies

Nisha Kumari1, Ashish Jain2, Siddarth Ramji2

1Post Graduate, Department of Pediatrics, 2DM (Neonat), Assistant Professor, Department of Neonatology,
3MD, Director Professor & Head, Department of Neonatology, Maulana Azad Medical College, New Delhi-110 002

Background: Many infant and maternal factors influence the feeding readiness in preterm babies. Understanding these would lead to early breastfeeding. Currently methods that are subjective and lack evidence, guide the practices in feeding low birth weight (LBW) babies. This results in delayed breastfeeding and unwanted alternate feeding. Thus, an objective but simple tool to guide readiness to feed, could be an important adjuvant skill, to optimize the feeding of LBW babies.

Objective: To determine predictors of nutritive sucking in babies <34 weeks and estimate the appropriate preterm sucking readiness (PTSR) score as an indicator of readiness and success of nutritive sucking.

Methods: Design: Prospective longitudinal observational study Setting: Neonatal unit of a referral hospital attached to Medical College Participants: Forty nine inborn neonates of 28-34 weeks gestation, not on intravenous fluids and on full gavage feeds.

Outcome measures:
• Predictors of achievement of good nutritive sucking estimated by a suck: swallow ratio of 2:1.
• Determination of the best PTSR score which measures achievement of nutritive sucking in advance to mature suck–swallow ratio.

Results
• Nutritive sucking was achieved at a median age of 14 days (7 to 50)
• Lower birth weight (<1531.1 ± 142.8) and lesser gestational age (<32.8 ± 1) were poor predictors of established nutritive sucking at 14 days of age. They reported to have a significant independent negative association with age at which established nutritive sucking was achieved.
• PTSR score of >9 had the best prediction for achievement of nutritive sucking at 14 days of life, with a sensitivity of 92.3% and specificity of 100%.

Conclusion: A PTSR score is a sensitive and specific tool to predict the readiness for nutritive sucking in preterm babies <34 weeks. It may be an objective, simple and important adjuvant in optimization and early initiation of breastfeeds in LBW babies.

Keywords: Nutritive sucking, preterm infant, Preterm Readiness Sucking Scale

Introduction
A desired milestone for the moderate to severe preterms is to acquire and attain an efficient breastfeeding behavior for the optimal breast milk delivery and subsequent growth. Hence, a successful breastfeeding is not only essential for growth, but a one of the key determinants of a preterm infant’s readiness for hospital discharge.1,2 With advances in medical technology and better accessible neonatal care, we now see more and more survival of moderate and very preterm neonates. The proper discharge care and nutrition makes it very important to understand the issues related to feeding skills. Any follow-up clinic has greater than 40% of infants with feeding disorders that were former preterm infants. Despite, this undisputed importance, there is little objective guidance available currently for health care professionals to decide when to initiate breastfeeding in these small babies. Many infant and maternal factors influence the development of these skills and the length of this feeding progression.3,4 A better understanding of these factors is needed for early facilitation of transition of preterm infants from...
gavage to breastfeeding. Currently, a traditional and subjective methodology, rather than objective evidence-based approach, have been used to guide the feeding practices in LBW babies. This decisions, often results in unwanted delays and restrictions on breastfeeding. Thus, a presence of a simple and objective tool would guide health professional to optimally feed and facilitate early breastfeeding in LBW babies.

In addition to the estimation of the predictors for the early establishment of nutritive sucking, we hypothesized that, if these preterm babies less than 34 weeks are assessed for the readiness to breastfeed objectively by the personnel taking care of them using a structured scale on a daily basis, it may be possible to initiate breastfeeding earlier. We used a simple objective tool called Preterm Sucking Readiness (PTSR) Score (annexure I) for this purpose.

**Research question**
What are the predictors of early establishment of nutritive sucking in preterm babies less than 34 weeks? Can the use of simple objective tool “Preterm Sucking Readiness (PTSR) Score”, when used by the personnel taking care of these babies to assess for the readiness to breastfeed result in early initiation of breastfeeding?

**Objectives**

**Primary**
To identify predictors of established nutritive sucking in preterm of 28 to 34 weeks of gestation.

**Secondary**
To determine the appropriate score of Preterm Sucking Readiness (PTSR) Scale that is indicative of nutritive sucking in preterms 28 to 34 weeks of gestation.

**Methodology**

**Study design**: Prospective longitudinal observational study

**Study site**: Neonatal unit of a referral hospital attached to Medical College

**Participants**: Forty nine inborn preterm infants of gestation between 28-34 weeks gestation.

**Sample size**: Since this was a pilot study, it was decided a-priori to enrol 40 eligible neonate in the study.

**Time frame**: The study was carried out from 2015-16.

**Ethics**: The study protocol was approved by the institutional Ethics Committee.

**Inclusion criteria**
Inborn neonates admitted to the NICU were eligible for enrolment if they were born between 28-34 weeks of gestational age, not on intravenous fluids and only on gavage feeding.

**Exclusion criteria**: Encephalopathy, major congenital malformation, oronasal malformation, receiving any respiratory support or sedative drugs like morphine/midazolam, and had undergone any surgery.

**Outcome measures**
The primary outcome was “Nutritive sucking” defined as a suck to swallow ratio of 2:1 over a 3 minute observation of feeding on an empty breast assessed by videography at 7, 14, 21 and/or 28 days after enrollment. The study also attempted validation of the Preterm Sucking Readiness scale (PTSR) for predicting achievement of nutritive sucking.

**Data Collection**
In all enrolled neonates maternal characteristics (age, socioeconomic status, education, parity, relevant medical and obstetric history, and mode of delivery) were recorded. Maternal involvement in the care of the infant in terms of breast feeding visits, was also recorded. Neonatal characteristics of the enrolled neonates (gestational age, birth weight, intrauterine growth status, Clinical Risk Index for Babies [CRIB] score,7 morbidities and feeding details) was also recorded.

**Assessment for sucking Readiness**
All enrolled neonates were assessed once every day at a fixed feeding session for their sucking readiness while sucking on an empty breast (non-nutritive sucking) for 3 minutes using the Preterm Sucking Readiness scale (PTSR) as described by Crowe et al.8 Continuous monitoring of oxygen saturation was done during the entire period of feeding.

In addition to the assessment by the PTSR score every day, the babies were assessed at 7, 14, 21 and 28 days for attainment of nutritive sucking using the established suck swallow ratio. As soon as the babies attained an established nutritive sucking (defined as suck swallow ratio of 2:1) on any of these four assessment points of examination viz 7, 14, 21 and 28 days, they were no longer assessed.

**Videographic recording**
Starting from day 7 of enrolment weekly video graphic recording were done on day 14, day 21 and day 28 by a high quality Nikon Coolpix L840, 16 megapixel. The dynamic video-graph frame ensured the capture of the maternal breast (to monitor latching of the baby), baby’s mouth and neck (to monitor sucking and swallowing). Based on these observation the
Figure 1: Flow chart representing assessment tools and timeline used in Study.
suck to swallow ratio was estimated during play back of the video recording independently by two of the investigators (NK, AJ).

**Figure 2**: Sample photo of videographic assessment.

**Figure 3**: Sample photo of videographic assessment.

### Data management

All base line and outcome data were recorded in a predesigned and pre-tested proforma. The data were then entered into Microsoft Excel spreadsheet. The data were checked for completion, consistency and accuracy. Videography recording of baby were arranged date wise and stored in DVD external drives. All records were checked by an independent neonatal consultant.

**Figure 4**: Progress of enrolled subjects represented as per the STROBE guideline\(^{18}\)

### Statistical analysis

The predictors of nutritive sucking at 7, 14, 21 and 28 days were assessed by univariate analysis. Multivariate analysis was done for significant variables. Categorical data was compared by Chi Square/Fisher exact test. Sensitivity and Specificity of PTSR score was done using ROC analysis to determine the most appropriate PTSR cut-off score. A p-value of 0.05 was taken as significant. Since this was a pilot study, it was decided a-priori to enrol 40 eligible neonate in the study.

### Results

#### Study flow

The study enrolled 49 preterm infants, of whom 41(83.6%) completed the study. Of the 49 neonates enrolled, 20 were a result of twin pregnancy and 5 a result of triplet pregnancy. Figure 4 provides the flow of the study.

**Table 1**: Baseline characteristics of study subjects

<table>
<thead>
<tr>
<th>Maternal characteristics (n = 49)</th>
<th>Estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of mother (yrs) [mean(SD)]</td>
<td>26.5 (5.8)</td>
</tr>
<tr>
<td>Socioeconomic status</td>
<td></td>
</tr>
<tr>
<td>Lower middle n(%)</td>
<td>40 (18.4)</td>
</tr>
<tr>
<td>Upper lower n(%)</td>
<td>9 (41.6)</td>
</tr>
<tr>
<td>Primigravida n(%)</td>
<td>24 (49.0)</td>
</tr>
<tr>
<td>Singleton n(%)</td>
<td>24 (49.0)</td>
</tr>
<tr>
<td>Antenatal visits ≥3 (%)</td>
<td>38 (77.5)</td>
</tr>
<tr>
<td>Mode of delivery</td>
<td></td>
</tr>
<tr>
<td>Vaginal (%)</td>
<td>43 (87.8)</td>
</tr>
<tr>
<td>LSCS (%)</td>
<td>6 (12.2)</td>
</tr>
</tbody>
</table>

**Neonatal characteristics, (n = 49)**

| Gestational age (weeks) [mean(SD)] | 32.2 (4.7) |
| Birth weight (g) [mean(SD)]        | 1418.1 (288.9) |
| Gender                            |           |
| Male (%)                          | 21 (42.9) |
| Intrauterine growth status        |           |
| AGA (%)                           | 45 (91.8) |
| SGA (%)                           | 4 (8.2)   |
| CRIB score [mean(SD)]             | 1.4 (1.9) |
| Illness                           |           |
| RDS (%)                           | 2 (4.1)   |
| Sepsis (%)                        | 2 (4.1)   |
| Hyperbilirubinemia (%)            | 1 (2.1)   |
| Respiratory support therapy       |           |
| IPPV (%)                          | 3 (6.1)   |
| CPAP (%)                          | 7 (3.2)   |
| Supplemental oxygen (%)           | 18 (36.7) |
| Age at starting of enteral feeding (Days) Median (Range) | 0 (0-10) |
| Age at parentral fluids discontinuation (Days) Median (Range) | 0 (0-15) |
| Weight at discontinuation of parentral fluids (g) [mean(SD)] | 1385.2 (245) |

LSCS- Lower Segment Cesarean Section, AGA – Appropriate for Gestational Age, SGA- Small for Gestational Age, CRIB- Clinical Risk Index for Babies, RDS- Respiratory Distress Syndrome, CPAP- Continuous Positive Airway Pressure.
Baseline characteristics

Table 1 summarizes the characteristics of the enrolled neonates.

Primary Outcome (Nutritive sucking predictors):
The median age for achievement of nutritive sucking was 14 days (range 7-50 days). Table 2 depicts the association of predictor variables and age of achievement of nutritive sucking. Neonates with higher gestational age, birth-weight and lower illness severity (lower CRIB score) achieved nutritive sucking significantly earlier. On multivariate analysis it was observed that gestation (p=0.049) and birth weight (p=0.003) had a significant independent negative association with age at achievement of nutritive sucking.

Secondary Outcome (Prediction by PTSR score)
It was observed that a PTSR score of ≥9 had the best predictive score for attainment of nutritive sucking (ROC analysis). For achievement of nutritive sucking by day 7, a PTSR score of ≥9 had a sensitivity of 86.7% and specificity of 100.0%. Similarly for achievement of nutritive sucking by day 14 (n=26), a PTSR ≥9 had a sensitivity of 92.3% and specificity of 100%.

Discussion
In the present study nutritive sucking was achieved at a median age of 14 days amongst preterm neonates 28-34 weeks of gestation. Birth weight and gestation had a negative independent association with the age at achievement of nutritive sucking. A PTSR score of 9 or more had a high sensitivity and specificity in identifying achievement of nutritive sucking in this population of preterm neonates.

As was noted in the present study, Pickler et al9 and White-Traut et al10 reported that older GA at birth was a significant predictor of higher frequency of feeding readiness behaviours. Birth weight was another significant predictor of feeding readiness in preterm neonates in the present study. This was consistent with the findings reported by White-Traut et al.10 who observed that birth weight was positively associated with the number of feeding readiness behaviours and indirectly predicted efficiency. This may be because higher birth weight is related to improved coordination of breathing, sucking and swallowing, thus leading to better feeding as observed by Reynolds et al.11 The infant’s medical condition also influences the transition from gavage to full oral feedings Bazyk et al12 and Dodrill et al13. The present study also found that illness severity (CRIB Score) is directly proportional to the time required for transition from tube to breastfeeding. There are some studies showing association between mother’s previous or current experience with breastfeeding and achievement of breastfeeding. But in the present study we did not found any significant relationship between these two. The Neonatal Oral-Motor Assessment Scale contains separated 13 characteristics of jaw movement and 13 characteristics of tongue movement into categories of normal, disorganized, and dysfunctional. NOMAS14 is not a reliable tool as the inter-rater agreement with respect to the diagnosis was moderate to substantial. Recently, a debate was raised regarding the validity of NOMAS when used in preterm infants as this scale was developed from term infants15. PIBBS16 developed based on the observations of preterm infants from 30-36 weeks of gestation during a breastfeeding session at anytime during the day. Six items (rooting, areolar grasp, latch, sucking, longest sucking burst and swallowing) were assessed with a score being attributed to each item. Behavioural observation was done by two observer and mother. There was acceptable agreement between the observer but lower agreement between mothers and observers. The EFS17 is a 36-item observational measure of oral feeding skill that was divided in three parts to assess feeding readiness, feeding skill and feeding recovery. In our study we studied behavioural state and the effect of handling significant predictor of feeding readiness in preterm neonates in the present study.

Table 2: Association of predictor variables and age when nutritive sucking achieved.

<table>
<thead>
<tr>
<th>Predictor Variables</th>
<th>Age nutritive sucking achieved</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Within 7 days (n=5)</td>
</tr>
<tr>
<td>Age of mother (yrs) [mean(SD)]</td>
<td>26.4 (5.0)</td>
</tr>
<tr>
<td>Lower-middle socio-economic status (%)</td>
<td>2 (40)</td>
</tr>
<tr>
<td>Primigravida (%)</td>
<td>2 (40)</td>
</tr>
<tr>
<td>Singleton (%)</td>
<td>5 (100)</td>
</tr>
<tr>
<td>Gestational age (weeks) [mean(SD)]</td>
<td>33.2 (0.4)</td>
</tr>
<tr>
<td>Birth weight (g) [mean(SD)]</td>
<td>1561 (138.9)</td>
</tr>
<tr>
<td>Intrauterine growth retardation (SGA) (%)</td>
<td>0</td>
</tr>
<tr>
<td>CRIB Median (range)</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Breastfed previous children (%)</td>
<td>4 (80)</td>
</tr>
</tbody>
</table>

CRIB- Clinical Risk Index for Babies, SGA- Small for Gestational Age
on it along with infant feeding behaviour in infants of 28-34 weeks gestational age. We had done weekly videographic recording of the breastfeeding session which was reviewed by two independent observer for excluding interrater bias. We could not find any studies validating the Preterm Sucking Readiness (PTSR) scale developed by Crowe et al8 other than the original study. Also there are no earlier studies which have provided any cut-off values that indicate the preterm infant’s readiness for nutritive sucking.

Strength of study
• As the PTSR score was assigned to all neonates by single investigator so, the inter-observer variability was eliminated.
• This is the first time that the PTSR score is being validated in the Indian preterm population with identification of the cut-off scores for achievement of nutritive sucking.
• All the Videographic recording of outcomes was independently confirmed by another observer, this ensured that the outcome measure was accurately assigned.

Limitation of study
• The results of the study may not be extrapolatable to very preterm neonates <30 weeks of gestation since the sample size in that gestational strata was very few.

Conclusion
• Preterm babies less than 34 weeks having lower gestational age and birth weight achieve nutritive sucking later to those babies having comparatively higher gestational age and birth weight. The other factors like sickness had no effect on the attainment of nutritive sucking.
• The Preterm sucking readiness scale (PTSR) can be used with relative ease in babies less than 34 weeks. When serially assessed a PTSR score of 9 or more indicates a readiness to nutritive sucking in these preterm babies.

Implications
Babies with lower gestational age and birth weight have delayed establishment of nutritive sucking. Hence, these babies require special support for optimizing their feeds.

PTSR score may be an objective, simple and important adjuvant which can be used by health care providers at all levels for early initiation of breastfeeds in LBW babies. This skill can be up scaled to the grass root health care provider for wider use, translating into better care of LBW babies in community.

What is known and what does this study add?

What is already known?
• Achievement of nutritive sucking is dependent on various infant and maternal factors.
• Currently, no objective and evidence based models are available to guide the feeding practices in LBW babies.

What this study adds
• The gestational age and birth weight are important factors affecting achievement of nutritive sucking compared to many other factors including sickness of babies.
• PTSR score can be used as an objective, simple and important adjuvant in optimization and early initiation of breastfeeds in LBW babies.

Bibliography


Annexure I

Preterm Sucking Readiness Scale (PTSR)

<table>
<thead>
<tr>
<th>S.No</th>
<th>Variable</th>
<th>Method of assessment</th>
<th>Scoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Respiratory rate</td>
<td>Baseline RR counted before feeding session 30-40 breaths/minute</td>
<td>Yes=1. No=2</td>
</tr>
<tr>
<td>2.</td>
<td>Oxygen saturation</td>
<td>1. Baseline saturation &gt;90%</td>
<td>Yes=1. No=2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Direction of change</td>
<td>increase =1, decrease =2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. &lt;=5-10% difference from baseline</td>
<td>Yes=1. No=2</td>
</tr>
</tbody>
</table>

Feeding Readiness Behaviour

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behavioural state just prior to disruption at feeding time</td>
<td>Asleep</td>
<td>Drowsy</td>
<td>Crying</td>
<td>Active alert</td>
</tr>
<tr>
<td>Transition between behavioural states during care/handling</td>
<td>Remains asleep</td>
<td>Briefly alert but goes quickly asleep during care/handling</td>
<td>Briefly alert but drowsy during care/handling</td>
<td>Alert during care but then becomes drowsy in immediate post-care/handling period</td>
</tr>
<tr>
<td>Feeding readiness behaviours during care/handling</td>
<td>Displays no readiness behaviours</td>
<td>Displays occasional feeding readiness behaviours</td>
<td>Displays intermittent feeding readiness behaviours</td>
<td>Displays frequent feeding readiness behaviours</td>
</tr>
</tbody>
</table>

*Feeding readiness behaviours include behaviours such as sucking on dummy, tube or hand, mouthing, rooting behaviour and showing interest at breast.
Quality Improvement Initiative to Prevent Hypothermia at Admission in Neonatal Intensive Care Unit Among Preterm Neonates < 32 Weeks’ Gestation

Sindhu Sivanandan, M Jeeva Sankar, Ashok Deorari
Division of Neonatology, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi- 110029

Introduction
Hypothermia is associated with increased mortality in neonates. Preterm neonates are at higher risk of hypothermia because of their large surface area–to–volume ratio, immature skin, paucity of subcutaneous fat layer and lack of non-shivering thermogenesis.

Abstract

Objectives: Hypothermia is an important contributor of mortality and morbidity. The objective of the current quality improvement (QI) effort was to prevent hypothermia during resuscitation and initial stabilization among preterm neonates by implementing a bundle of standardized thermal care practices (‘thermoregulation bundle’).

Methods: This QI initiative used a stepwise plan-do-study-act (PDSA) approach to implement a thermoregulation bundle among inborn preterm neonates (< 32 weeks’ gestation) at a level III neonatal intensive care unit (NICU) in New Delhi. After the baseline phase (June - August 2015), we implemented a thermoregulation bundle (September-December 2015) in steps followed by a post-intervention phase (January - April 2016). A multidisciplinary QI team was formed and the improvements in thermal care were introduced stepwise in PDSA cycles: cycle-1- use of plastic bags, cycle-2- reinstitution of cling film in place of plastic bags and education of delivery room nurses, cycle-3- incorporation of previous interventions plus attention to delivery room temperature and warm transport. Frequent feedback with run charts of admission temperature and appraisal in monthly meetings were done to motivate stakeholders and encourage compliance. Primary outcome was axillary admission temperature within 10 minutes of admission to the NICU. Secondary outcomes were the incidence of moderate hypothermia (axillary temperature of 32.0°C to 35.9°C) at admission and relevant clinical outcomes.

Results: A total of 79 neonates were enrolled in the study (24 in baseline phase, 23 in implementation phase and 32 during the post intervention phase). The mean (± SD) birth weight (1191 ± 320 vs. 1078 ± 312 g), gestational age (29 ± 1.3 vs. 29 ± 1.6 weeks) and other demographic characteristics were comparable between the baseline and post-intervention phase. However, more neonates in post-intervention phase were singleton and delivered after spontaneous conception. The statistical process control chart for admission temperatures over time of all enrolled neonates demonstrated both a sustained increase in mean admission temperature and a decreased variability. The mean axillary temperature at NICU admission increased from 35.9°C to 36.5°C (mean difference -0.6°C; 95%CI-0.9 to -0.3). The incidence of moderate hypothermia decreased from 50% to 12.5% (RR 0.25; 95% CI 0.09 to 0.7). There was no difference in in-hospital mortality or other short term morbidities.

Conclusions: Effective implementation of thermal care practices through a stepwise PDSA driven approach increased axillary temperature and decreased the incidence of moderate hypothermia at NICU admission in preterm neonates. A multidisciplinary team, education of heath providers and frequent feedback using run charts helped in sustaining the improvement.

Key words: Quality improvement, thermoregulation, admission temperature, admission hypothermia
maintenance of delivery room temperature between 23°C to 25°C, warm blankets, plastic wrapping without drying, cap, and thermal mattress) to reduce admission hypothermia among preterm infants less than 32 weeks of gestation (2). During an audit of admission temperatures of preterm <32 weeks’ gestation neonates admitted to our NICU, the mean admission temperature was noted to be 35.6°C in spite of our practice of use of plastic wraps during resuscitation and a transport incubator.

This prompted us to initiate a quality improvement effort with the following objectives; the primary objective was to compare the mean axillary temperature at NICU admission among neonates <32 weeks’ gestation before and after a stepwise introduction of improvements in thermal care practices at birth driven by PDSA cycles. The secondary objectives were to compare the incidence of moderate hypothermia (axillary temperature 32.0°C to 35.9°C) at NICU admission and short term morbidities before and after the intervention.

**Methods**

The study subjects were neonates with a gestational age between 25 to 31 6/7 weeks who were born in our centre between June 2015 and April 2016. Neonates born during June to August 2015 formed the baseline cohort, during September to December 2015, the implementation cohort and those during January to April 2016, the post intervention cohort. Expectant parents were approached for informed consent if considered at high risk of having a preterm delivery. Exclusion criteria were deliveries occurring in the hospital other than in the delivery room or maternal operation theatre (OT) and major congenital malformations. The study was approved by the Institute Ethics Committee.

**Study setting:** Our neonatal intensive care unit (NICU) is an 8 bedded level 3 inborn unit with a 20 bedded level 2 nursery along with a high-risk maternal-fetal medicine service. There are about 2800 deliveries each year, a majority of them being high risk due to the referral nature of the centre. Delivery of a preterm neonate (<32 weeks’ gestational age) is attended by one or two neonatal fellows in training, a pediatric resident, and a nurse. The consultant neonatologist is called for in cases where resuscitation is anticipated to be extensive or when gestational age is <26 weeks. The delivery rooms are equipped with an oxygen blender, a pulse oximeter in addition to a radiant warmer with in-built T-Piece resuscitator.

**Delivery room resuscitation and thermal care practices in the baseline phase:** During resuscitation, neonates were received by the resident doctor over a plastic sheet (if gestation was <28 weeks) spread out on a warm sterile towel. We attempted delayed cord clamping in vigorous neonates for at least 30 seconds during which period the neonate’s tone and respiratory efforts were observed without active resuscitation. After cord was clamped, the neonates were placed under radiant warmer and the edges of the plastic sheet brought closer to wrap the neonate well without drying. A pulse oximeter was applied on the right-hand and resuscitated as per NRP guidelines. Hats were used occasionally and respiratory gases in delivery room were not heated or humidified. Neonates were transferred from to the NICU (a distance of 200 feet) in a transport incubator fitted with an oxygen source. In the NICU, the axillary admission temperature was recorded using a digital thermometer. We follow standard practices as per unit policy for the administration of surfactant, respiratory and nutritional management in these neonates.

**Planning and implementation of the intervention**

**Baseline phase:** No new interventions related to thermal care was introduced. A healthcare provider who was not part of the resuscitation team was commissioned as an observer to note the practices in the delivery room in a pretested proforma. We standardized the measurement of temperature at admission for all neonates admitted to the NICU. Accordingly, the admitting nurse recorded the axillary temperature with a hospital supplied digital thermometer (Infinity Mediquip India with an accuracy of 0.1°C between temperature ranges of 32°C to 42.9°C) within 10 minutes of neonate’s arrival in the NICU. The resuscitation team received no feedback on admission temperatures.

**Planning and formation of QI team:** During an audit, we noted that neonates <32 weeks’ gestation admitted to our NICU had a mean admission temperature of 35.6°C. This prompted us to initiate this QI effort to prevent admission hypothermia in preterm neonates. Our QI team included three neonatologists, all neonatal fellows, a nurse educator and the charge nurses of NICU, labor room and maternal OT. Two senior neonatologists played advisory roles and over saw the implementation of the QI. The team reviewed the literature on evidence based practices for thermal care, presented the recommendations informally which were then agreed upon or modified for local implementation. The panel 1 shows the recommendations for thermal care for preterm <32 weeks gestation adopted as the thermoregulation bundle.

General measures taken by the QI team to implement the thermoregulation bundle included orientation of pediatric and neonatal residents to the bundle recommendations and education of NICU nurses with a power point presentation on equipments for heat loss prevention and adverse effects of hypothermia. To plan our first PDSA, we performed a cause and effect analysis.
of admission hypothermia using a fishbone diagram (Figure 1) and constructed a key driver diagram (Figure 2). We used the data from delivery room observations of 24 births in the baseline phase and noted plastic wrap to be crumpled and exposing the neonate in 17/21 cases, team member roles not assigned in 12/24, equipments not checked in 7/24 and plastic wraps not used in 3/24 cases. This was used to construct a Pareto chart (Figure 3) and we identified improper application of cling wrap as a major contributor of admission hypothermia. We then conducted 3 PDSA cycles over 4 months and used run charts of admission temperature to study the progress.

Panel 1: Components of the Thermoregulation bundle

<table>
<thead>
<tr>
<th>Situation</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticipatory preparation</td>
<td>o Prepare resuscitation kit. Check equipments and organize a team. Call for additional help if necessary.</td>
</tr>
<tr>
<td>Delayed cord clamping</td>
<td>o In uncomplicated preterm birth delayed cord clamping should be attempted for a minimum time of 30 seconds after delivery</td>
</tr>
<tr>
<td>Thermoregulation</td>
<td>o Maintain DR temperature of at least 26 °C for all deliveries &lt; 32 weeks. Switch off air conditioner in the DR</td>
</tr>
<tr>
<td></td>
<td>o Pre-warm the radiant warmer to 100% heater output for at least 10 minutes prior to delivery</td>
</tr>
<tr>
<td></td>
<td>o Use polythene bags/ wraps for thermoregulation in delivery room for all neonates &lt; 32 weeks gestation. Do not dry the neonate. Do not remove the bag until neonate is transferred to the NICU and normal temperature is recorded</td>
</tr>
<tr>
<td></td>
<td>o Cover the head with the plastic bag. Use of hat is recommended</td>
</tr>
<tr>
<td></td>
<td>o Use a transport incubator to transfer neonates from DR to NICU. Pre-warm the baby boundaries and the transport incubator prior to use</td>
</tr>
<tr>
<td></td>
<td>o Measure axillary temperature within 10 minutes of NICU admission</td>
</tr>
</tbody>
</table>

Figure 1: Fishbone diagram showing cause–effect analysis of admission hypothermia
Figure 2: key driver diagram for improving the admission temperature of preterm neonates.

Figure 3: The Pareto chart shows the “few defects” causing most of the problems. The Y axis shows the frequency of deficiency identified in each of the categories.

PDSACycle-1 (Sep-October 2015): We introduced food grade plastic bags that were available in the market as an alternative to the existing cling films to cover neonate at birth. Residents were educated on their proper use through images in group emails and bags were made available in the unit. The admission temperatures and compliance with use of bags were documented and run charts of temperature for 10 neonates enrolled in cycle 1 were reviewed. We did not identify any new non-random signal corresponding to a process change in the run chart (Figure 4). The QI team received feedback from residents that the bags reopened leaving the neonate exposed and the obstetricians opposed the use of unsterile bags during caesarean sections.
PDSA Cycle-2 (November 2015): The QI team decided to reinstitute the use of cling films but with a better method of application, which was then disseminated among residents and nurses. This cycle also focused on education of delivery room nurses on thermal care practice and helped them adopt key roles during resuscitation. The run chart in cycle-2 depicted a new non-random change, a shift (6 consecutive points above the median line that is encircled) that can be attributed to a process change (Figure 4). The run charts were updated and visibly displayed in delivery room and NICU and the progress was shared with obstetricians in monthly meetings. The QI team reinforced the rationale for complying with thermal bundle at these meetings and also capitalized on the discussions generated to identify issues related to hypothermia. Some of these were the cold delivery rooms, lack of co-ordination with the NICU admitting nurse and ancillary staff for warm transport.

PDSA Cycle-3 (December 2015) was implemented to address the above issues. A room thermometer was installed near the baby corner in delivery room and the nurses were advised to target 26°C either by switching off the air conditioner or by using a blow by warmer. Warm transport was facilitated by ensuring better team work between resuscitation team and NICU staff and by switching on the transport incubator well in advance.

Post intervention phase: Between January 2016 and April 2016, the QI team encouraged the implementation all the components of the thermoregulation bundle, continued to monitor admission temperatures with run chart and provided feedback to resuscitation team and clinicians. To identify opportunities for process improvement, the QI team continued to meet with clinical teams, audited cases of admission hypothermia and addressed logistic issues related to supplies and equipment.

Data Collection: Pertinent maternal and neonatal data were collected from case records. Admission temperature recorded by the nurses was noted from the nursing chart. All temperatures were classified based on World Health Organization definitions(3): hyperthermia >37.5°C, normal 36.5°C to 37.5°C, cold stress/mild hypothermia 36.0°C to 36.4°C, moderate hypothermia 32.0°C to 35.9°C, and severe hypothermia < 32.0°C. Other outcomes collected include in-hospital mortality, duration of mechanical and non-invasive respiratory support, BPD defined as need for supplemental oxygen at 36 weeks and classified as per NICHD criteria(4), culture late onset sepsis (≥ 72 hours of life), necrotizing enterocolitis stage ≥ 2 based on Bell’s criteria(5) and retinopathy of prematurity (ROP) needing treatment(6).

Sample size and statistical analyses: Sample size estimation was based on the primary outcome (mean admission temperature at NICU admission). In a retrospective chart review of 14 inborn neonates < 32 weeks of gestation delivered consecutively in early 2015, the mean axillary temperature at NICU admission temperature was noted to be 35.6°C (SD = 0.9). A sample size of 22 neonates per phase was planned with a power of 90% for an alpha of 0.05 to increase the mean admission temperature to 36°C.

Analyses were performed with Stata 11 (Stata Corp.
Baseline characteristics and outcomes were compared between the baseline and post-intervention cohort using Student’s t test or Wilcoxon rank-sum tests for continuous data and $\chi^2$ or Fisher’s exact tests for dichotomous data as appropriate. Because continuous staff education, audit and feedback were expected to lead to improved quality over time, changes in admission temperature were further evaluated with statistical process control (XMR or P) charts created with QI Macros trial version (KnowWare International Inc, Denver, CO).

Results
A total of 79 neonates were enrolled in the study (24 in baseline phase, 23 in implementation phase and 32 during the post intervention phase). The mean ($\pm$ SD) birth weight (1191 $\pm$ 320 vs. 1078 $\pm$ 312 g), gestational age (29 $\pm$ 1.3 vs. 29 $\pm$ 1.6 weeks) and other demographic characteristics were comparable between the baseline and post-intervention phase (Table 1). However, more neonates in post-intervention phase were singleton and delivered after spontaneous conception. The study flow with the numbers enrolled is depicted in the panel 2. The neonates enrolled during the implementation phase (mean gestational age 28.3 $\pm$ 1.6 weeks and birth weight 967 $\pm$ 306 grams) were more immature and had higher CRIB II scores compared to baseline and post-intervention phase; at least a quarter of them were < 28 weeks’ gestation and about a half weighed less than 1000 grams.
Table 1: Demographic characteristics of neonates enrolled in the study

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Baseline N=24</th>
<th>Implementation phase N= 23</th>
<th>Post intervention phase N=32</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Maternal characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal age (Years)</td>
<td>29 ± 5</td>
<td>29 ± 4</td>
<td>30 ± 6</td>
</tr>
<tr>
<td>Spontaneous conception</td>
<td>12 (50)</td>
<td>21 (91)</td>
<td>31 (97)</td>
</tr>
<tr>
<td>Singleton pregnancy</td>
<td>9 (37)</td>
<td>20 (87)</td>
<td>22 (69)</td>
</tr>
<tr>
<td>Any antenatal steroids</td>
<td>24 (100)</td>
<td>22 (96)</td>
<td>31 (97)</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>3 (12.5)</td>
<td>2 (9)</td>
<td>0</td>
</tr>
<tr>
<td>Maternal hypertension</td>
<td>4 (17)</td>
<td>11 (48)</td>
<td>6 (19)</td>
</tr>
<tr>
<td>Maternal diabetes</td>
<td>0</td>
<td>3 (13)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>10 (42)</td>
<td>8 (35)</td>
<td>10 (31)</td>
</tr>
<tr>
<td>FHR abnormal</td>
<td>3 (13)</td>
<td>4 (17)</td>
<td>3 (9)</td>
</tr>
<tr>
<td><strong>Neonatal characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational age in weeks</td>
<td>29.8 ± 1.3 30 (29-31)</td>
<td>28.3 ± 1.6 28 (27-30)</td>
<td>29.6 ± 1.4 30(29-31)</td>
</tr>
<tr>
<td>GA &lt; 28 weeks</td>
<td>1 (4)</td>
<td>6 (26)</td>
<td>3 (9)</td>
</tr>
<tr>
<td>Birth weight grams</td>
<td>1191 ± 320</td>
<td>967 ± 306</td>
<td>1159 ± 295</td>
</tr>
<tr>
<td>Birth weight &lt;1000 g</td>
<td>6 (25)</td>
<td>13 (56)</td>
<td>9 (28)</td>
</tr>
<tr>
<td>Male sex</td>
<td>11 (46)</td>
<td>9 (39)</td>
<td>13 (41)</td>
</tr>
<tr>
<td>AGA SGA</td>
<td>17 (71)</td>
<td>16 (70)</td>
<td>21 (66)</td>
</tr>
<tr>
<td>Apgar score at 1 min</td>
<td>5.5 (3-7)</td>
<td>7 (4-7)</td>
<td>7 (6-7)</td>
</tr>
<tr>
<td>Apgar score at 5 min</td>
<td>7 (7-8)</td>
<td>8 (7-8)</td>
<td>8 (7-8)</td>
</tr>
<tr>
<td>Apgar score at 10 min</td>
<td>7 (6-7)</td>
<td>7 (7-8)</td>
<td>7 (7-7)</td>
</tr>
<tr>
<td>Cord pH.</td>
<td>(N=11) 7.03 (7.19 to 7.29)</td>
<td>(N=5) 7.04 (7.03 to 7.17)</td>
<td>(N=10) 7.18 (6.91 to 7.3)</td>
</tr>
<tr>
<td>Cord base excess</td>
<td>-2.8 (-5.5 to +1.5)</td>
<td>-12 (-12.9 to -8)</td>
<td>-5 (-7.2 to -4.4)</td>
</tr>
<tr>
<td>CRIB II score</td>
<td>5 (3.5-6.5)</td>
<td>8 (4-11)</td>
<td>4 (3-6)</td>
</tr>
<tr>
<td>Respiratory distress syndrome</td>
<td>14 (58)</td>
<td>16 (69)</td>
<td>18 (56)</td>
</tr>
</tbody>
</table>

* Data are expressed in N (%), mean ± SD and median (IQR). AGA (appropriate for gestational age) and SGA (small for gestational age), FHR (fetal heart rate), CRIB (Clinical Risk Index for Babies)

Table 2: Admission temperature and incidence of hypothermia among neonates enrolled in observation phase and post-intervention phase

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Baseline N=24</th>
<th>Post intervention phase N=32</th>
<th>Mean difference (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean admission temperature (°C)</td>
<td>35.9±0.7</td>
<td>36.5 ± 0.4</td>
<td>-0.6 (-0.9 to -0.3)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Incidence of moderate hypothermia</td>
<td>12 (50)</td>
<td>4 (12.5)</td>
<td>0.25 (0.09 to 0.7)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Admission temperature of enrolled neonates: Figure 5 shows a statistical process control chart for admission temperature for neonates enrolled during baseline, implementation and post-intervention phases. The trend of admission temperatures over time demonstrates both a sustained increase in mean admission temperature and a decreased variability as reflected in the narrowing of the control limits. The control chart also depicts a non-random change beyond the baseline phase corresponding to two junctures where there are 8 consecutive points above the central line (shown as red dots in PDSA cycle 2 and in post intervention phase).

Mean axillary temperature at NICU admission increased from 35.9°C to 36.5°C (mean difference -0.6°C; 95% CI -0.9 to -0.3; P=0.0002) and the incidence of moderate hypothermia decreased from 50 % to 12.5% (RR 0.25; 95% CI 0.09 to 0.7; P=0.003) in the post-intervention cohort (Table 2). The proportion of moderate hypothermia at admission during each study month is depicted in the p-chart (Figure 6). The p-chart shows a decrease in incidence of moderate hypothermia after the 1st PDSA cycle which is sustained in the post-intervention phase.

We did not find any difference in in-hospital mortality and in other short term morbidities like need for mechanical ventilation in 1st week of life, duration of mechanical ventilation in days, incidence of culture positive late onset sepsis, incidence of hemodynamically significant patent ductus arteriosus requiring treatment, incidence of moderate or severe bronchopulmonary dysplasia and the incidence of retinopathy of prematurity requiring therapy (Table 3).

Compliance with the thermoregulation bundle and balancing outcome: Analysis of various processes in the delivery room care was noted as a measure of compliance with implementation of the thermoregulation bundle and to identify opportunities for improvement. There was universal implementation of equipment check, role assignment and the use of plastic wraps in the post-intervention period. As a balancing measure, we chose the incidence of
Table 3: In-hospital mortality and short term morbidities of neonates enrolled in baseline and post-intervention phase

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Post intervention phase</th>
<th>Pre-intervention phase</th>
<th>RR/Mean difference (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital mortality</td>
<td>N= 32</td>
<td>6 (19)</td>
<td>1.1 (0.3 to 3.5)</td>
<td>0.54</td>
</tr>
<tr>
<td>Need for mechanical ventilation in first week of life</td>
<td>13 (41)</td>
<td>13 (54)</td>
<td>1.0 (0.3 to 3.5)</td>
<td>0.31</td>
</tr>
<tr>
<td>Duration of oxygen requirement in days</td>
<td>3 (1-22)</td>
<td>6.5 (3-20)</td>
<td>-</td>
<td>0.33</td>
</tr>
<tr>
<td>Duration of non invasive ventilation in days</td>
<td>2.5 (1-8)</td>
<td>4 (1-10)</td>
<td>-</td>
<td>0.73</td>
</tr>
<tr>
<td>Duration of mechanical ventilation in days</td>
<td>0 (0-6.5)</td>
<td>1 (0-6)</td>
<td>-</td>
<td>0.41</td>
</tr>
<tr>
<td>BPD (day 28 of life)</td>
<td>9 (28)</td>
<td>6 (25)</td>
<td>1.6 (0.4 to 5.8)</td>
<td>0.24</td>
</tr>
<tr>
<td>Moderate or severe BPD at 36 weeks PMA</td>
<td>2/27 (7)</td>
<td>4/21 (19)</td>
<td>0.4 (0.1 to 1.9)</td>
<td>0.13</td>
</tr>
<tr>
<td>Postnatal steroids for BPD</td>
<td>4 (12.5)</td>
<td>3 (15)</td>
<td>1.0 (0.2 to 4.0)</td>
<td>0.8</td>
</tr>
<tr>
<td>Treatment for ROP</td>
<td>1 (4)</td>
<td>0</td>
<td>-</td>
<td>0.35</td>
</tr>
<tr>
<td>PDA requiring therapy</td>
<td>1 (3)</td>
<td>4 (17)</td>
<td>0.2 (0.02 to 1.6)</td>
<td>0.15</td>
</tr>
<tr>
<td>NEC stage 2 or more</td>
<td>3 (9)</td>
<td>2 (8)</td>
<td>1.1 (0.2 to 6.2)</td>
<td>0.89</td>
</tr>
<tr>
<td>Time of achievement of full feeds (days)</td>
<td>5 (3-11)</td>
<td>9.5 (6-17)</td>
<td>-</td>
<td>0.07</td>
</tr>
<tr>
<td>Duration of TPN in days</td>
<td>5 (0-12)</td>
<td>10 (0-15)</td>
<td>-</td>
<td>0.24</td>
</tr>
<tr>
<td>Late onset sepsis (culture positive)</td>
<td>4 (14)</td>
<td>0 (6)</td>
<td>-</td>
<td>0.16</td>
</tr>
<tr>
<td>Any late onset sepsis (both culture positive and culture negative)</td>
<td>15 (47)</td>
<td>7 (29)</td>
<td>1.6 (0.8 to 3.3)</td>
<td>0.17</td>
</tr>
<tr>
<td>Duration of hospital stay in days</td>
<td>32 (22-37)</td>
<td>38 (29-50)</td>
<td>-</td>
<td>0.41</td>
</tr>
<tr>
<td>PMA at discharge home (weeks)</td>
<td>35 (34-36.5)</td>
<td>35.5 (35-37)</td>
<td>-</td>
<td>0.16</td>
</tr>
<tr>
<td>Mean weight at discharge (grams)</td>
<td>1711 ± 457</td>
<td>1870 ± 459</td>
<td>-</td>
<td>0.25</td>
</tr>
</tbody>
</table>

Data are expressed in N (%), mean ± SD and median (IQR). TPN (Total parenteral nutrition), PMA (Post menstrual age)

hyperthermia (admission temperature >37.5°C) as a surrogate of adverse effect related to implementation of thermal bundle and did not observe any episode of hyperthermia in the enrolled neonates.

Discussion

This quality improvement effort studied a step wise introduction of improvement in thermal care practices during resuscitation and stabilization driven by PDSA cycles. We showed improvement in mean axillary admission temperatures among preterm neonates < 32 weeks’ gestation without adverse effect of hyperthermia-a key balancing measure. The mean admission temperature increased by 0.6°C and the proportion of neonates with moderate hypothermia at admission dropped to 12.5%. Given that the optimal temperature for neonates has a range of 1°C only, (36.5°C- 37.5°C) moving the population mean by more than half a degree (0.5°C) is both clinically and statistically significant. This favourable outcome is most likely due to the stepwise introduction of thermoregulation bundle as seen from the abrupt change in the mean admission temperature in the control chart (Figure 2) with the introduction of process changes. This improvement was sustained throughout the post-intervention phase. The increase in mean admission temperature was also associated with a decrease in standard deviation of this measure, which suggests less variability and better thermal control.

Several other centres have also shown better admission temperatures and a decreased incidence of hypothermia in preterm neonates by implementing quality initiatives focused on thermoregulation at birth (7-14). A common theme in all the studies is the use of a combination or a ‘bundle’ of interventions for prevention of heat loss namely, a radiant warmer, polyethylene occlusive wrap, chemically activated warming mattress, hat, warm blankets etc and attention to delivery room temperature. Pinheiro et al. used battery powered radiant warmer in addition to transfer neonates to NICU (13). We implemented the thermal care interventions by having a written unit policy on thermoregulation, multi-disciplinary team, education of staff and real-time feedback to clinical team using run charts. Additionally the interventions were introduced stepwise in PDSA cycles. The PDSA model of improvement has been successfully used by Pinheiro et al (13) and Billimoria et al(7) to implement thermal care practices in their respective centres. In our case, each PDSA cycle helped us to test small interventions leading to valuable learning and refinement of the thermal control processes. Our first PDSA cycle did not give expected results but we learnt that plastic...
Figure 5: Statistical process control chart of admission temperatures of all neonates enrolled in the study. UCL: Upper control line (+ 3 SD), LCL: lower control line (-3 SD), CL: Control line (mean). The red squares signal a non-random change (8 consecutive points above the central line). The time period of implementation of the PDSA cycle is also depicted in the figure.

bags may not work well in our setting and identified areas for improvement (proper application of plastic sheets and a focus on staff education). Clinical team was motivated with prominent display of run charts of temperature which served as an instant display of outcome. This enabled team ownership, enthusiasm, participation and an opportunity to improve.

As a balancing measure, we did not have even a single episode of hyperthermia during and after implementation of the thermoregulation bundle. One reason might be that we did not use chemical warming mattress in our unit. Most episodes of hyperthermia had been noticed in relation to the use of warming mattress (15, 16). We monitored short term clinical outcomes like in-hospital mortality and major morbidities because hypothermia has been shown to be associated with significant late-onset sepsis and death and did not find any differences in outcome when compared to baseline. However, with our restricted sample size and limited study duration, we were not powered to detect small differences in these outcomes.

We developed the following system changes in order to sustain the improvement in admission temperature; a) routine use of a checklist for equipment and supplies in the delivery room. This ensures that supplies are replenished in time, equipments are serviced promptly...
and also helps the nurse to keep a track on the logistics 
b) admission temperature is used as a quality indicator 
that is entered in the nursing records and neonatal case 
records c) use of a room thermometer in the baby corner 
and noting of delivery room temperature each shift 
increased the awareness among the staff to switch off 
the air conditioner or to use a room warmer. We plan 
to incorporate the entry of admission temperature of 
all neonates admitted to the NICU from delivery rooms 
in the electronic database for routine surveillance.

Our study has the following limitations. Being a single 
centre study, all the interventions implemented by 
us may not be generalizable to other settings as the 
delivery room design (proximity to NICU, temperature 
of delivery room) and modes of thermal care employed 
(plastic bags, sheets, hats, chemical warming mattress) 
and the availability of a battery powered transport 
incubator differ across centres. We did not find the 
commercially available food grade plastic bags to 
work in our scenario but the same cannot be true in 
other settings. We employed multiple interventions 
and implementation strategies. Although it has a 
positive aspect to it, because single intervention 
(warming delivery room, plastic bags or chemical 
warming mattress alone) in addition to radiant warmer 
incompletely protects against hypothermia than many 
put together as a bundle(17-19). However, as some 
PDSAs incorporated more than one strategy, it was not 
possible to tease out the effect of each of these changes 
on admission temperatures. Presence of an observer 
in the delivery room may to monitor compliance with 
the interventions may have introduced a Hawthorne 
effect with healthcare workers displaying better 
performance just by being observed. However, the 
observer was present even in the baseline phase and

Figure 6: p-chart showing the incidence of moderate hyperthermia in each month. The CL line depicts the average incidence of hypothermia (26%). The control limits are set at 3 SD from the central line. The upper control limit (UCL) has a stepped appearance in a p-chart as the control limit is calculated for each individual measure and depends on the denominator in the percentage. The lower control limit (LCL) in the above chart is 0%.
the outcome parameter ‘admission temperature’ was an objective measure recorded by the admitting nurse in the NICU. Surveillance of admission temperatures through an electronic database in future will help us to determine whether our achievements are sustained when a prospective audit by an observer no longer exists. Finally, our study was not powered to evaluate the effect of the QI on clinical outcomes like mortality and morbidity in our population.

Conclusion
Our study shows the successful implementation of a bundle of evidence based practices in delivery room care focused on thermal protection during resuscitation and stabilization driven by a stepwise rapid cycle PDSA based approach. Integration of process changes in the system and continued surveillance needs to be explored as solutions for sustenance of our quality improvement effort.

References

What this study adds?
• A QI initiative focusing on evidence based thermal care practices at birth can be successfully implemented through a stepwise rapid cycle PDSA based approach to prevent hypothermia at NICU admission
• A multidisciplinary QI team, education of heath providers and frequent feedback using run charts can help in sustaining the improvement in admission temperature

What we already know?
• Hypothermia is associated with increased mortality among preterm neonates
• Preterm neonates rapidly lose heat at birth and a large proportion of them are hypothermic at the time of NICU admission
Different Spectrum of Manifestation Neonatal Lupus Erythematosus in Dizygotic Twins: A case report

Rameshwar Prasad
Senior Resident, Department of Neonatology, IPGMER, Kolkata, India

Abstract

Neonatal lupus is a rare autoimmune disease. Dizygotic twins had different manifestations of neonatal lupus. First twin had rhizomelic chondrodysplasia punctate. Second twin developed transient cardiomyopathy, thrombocytopenia and conjugated hyperbilirubinemia. First twin had feeding difficulty. In second twin, symptom resolved with conservative management. Genetic factors play role in the pathogenesis of neonatal lupus.

Key words: cardiomyopathy, conjugated hyperbilirubinemia, rhizomelic chondrodysplasia punctate, systemic lupus erythematosus, thrombocytopenia

Introduction

Most common manifestation of neonatal lupus erythematosus (NLE) is skin rashes and congenital heart block. Hematologic, hepatobiliary, central nervous, pulmonary and skeletal system are also involved. NLE is caused by transfer of maternal ant-Ro/SSA and anti-La/SSB and less commonly ant-U1RNP autoantibodies. Chondrodysplasia Punctata (CDP) refers to punctate calcification of cartilages and associated with shortening of long bones, midfacial hypoplasia, coronal clefts of vertebral bodies and cataract. CDP is found in disorders of peroxisomal, cholesterol, or vitamin K metabolism, maternal malabsorption of vitamin K and warfarin or phenytoin use during pregnancy. Curry et alfirst described an association between maternal connective tissue disorder and CDP. Since then there are multiple case reports describing SLE with CDP. Cardiac manifestations of NLE are congenital heart block and cardiomyopathy which may lead to heart failure. Hepatobiliary involvement is underreported in NLE. Hematologic manifestations are anemia, neutropenia and thrombocytopenia which are benign. In our case, first twin presented with rhizomelic chondrodysplasia punctate similar to warfarin embryopathy. Second twin didn’t had any dysmorphic feature but developed transient cardiomyopathy, conjugated hyperbilirubinemia and thrombocytopenia in first week of life that resolved gradually. To the best of our knowledge this is the first case report of its kind in which both twins had different manifestations of neonatal lupus.

Case presentation

A twin was born to a 27 year old G3 P0+2 mother at 34 weeks of gestation by caesarian section (indication – twin with fetal distress). Previous two pregnancies were spontaneous abortions in first trimester. Mother had been diagnosed to have systemic lupus erythematosus at the age of 24 years when she presented with malar rash, symmetrical polyarthritis and photosensitivity. Mother later developed lupus nephritis, myocarditis, hypertension and autoimmune thyroiditis. Mother had leucopenia (TLC-4200/mm3), positive Antinuclear antibody (titer>1:640), positive dsDNA, positive anti-Sm antibody, positive U1RNP, positive anti-SSA Ro and anti-SSB La antibodies. Her anticardiolipin antibody (IgG and IgM) and complement C3 and C 4 levels were normal and HLA B27 was negative. Mother was on hydroxychloroquin, prednisolone, amlodipine, metoprolol and levothyroxine since last 2 years and continued throughout this pregnancy. Aspirin (75mg/d) was started at 6 weeks of gestational age during this pregnancy. There was no history of taking any anticoagulant, alcohol or anticonvulsant during pregnancy.

The twin babies were diamiotic dichorionic and both were girl. Antenatal USG at 8 weeks of gestational age and anomaly scan at 20 weeks of gestational age were both normal with concordant growth pattern of both fetuses. Antenatal USG at 29 weeks of gestational age showed polyhydramnios in gestational sac and rhizomelic shortening of both upper limbs of fetus 1. Fetus 2 was normal having normal liquor in gestational sac. At birth, APGAR score of first twin was 7 and 9 at 1 and 5 minutes respectively. Birth weight of first twin was 1596 gm, head circumference was 30 cm and length was 39 cm. First twin had short both upper limbs, depressed nasal bridge, poorly developed brow ridges, large philtrum and prominent occiput. Radiological examination revealed short bilateral humeri and
stippled calcification in both ankles (Fig 1) and right upper end of humerus. Pelvis and vertebra appeared normal. Ultrasonography of brain, ophthalmologic examination, echocardiography and hematologic parameters were normal.

Figure 1: Rhizomelic shortening of proximal upper limbs, depressed nasal bridge, large philtrum, poorly developed brow ridges.

At birth Apgar score of second twin was 7 and 8 at 1 and 5 minutes respectively. Second twin had birth weight of 936 gm, head circumference 27 cm and length 37cm. Second twin was IUGR. There was no dysmorphic features. On day 4, Baby had respiratory distress, tachycardia, hepatomegaly and poor perfusion. Chest x-ray was showing cardiomegaly and pulmonary edema. Sepsis screen was negative and blood culture was sterile. On echocardiography, there was poor cardiac contractility, dilated LV and RV and engorged IVC. Furosemide and dobutamine was started and later on dopamine was added. Inotropes were gradually tapered off on day 9 and furosemide was stopped on day 10 of life. Baby’s platelet count at birth was 78000/mm$^3$ which decreased to 15000/mm$^3$ on day 5 of life. Baby received three units of platelet concentrate. Baby developed conjugated hyperbilirubinemia on day 9 without elevation of aminotransferases. Her total serum bilirubin was 20.3mg/dL, direct bilirubin 12.2mg/dL, SGOT 50 U/L, SGPT 20 U/L and serum alkaline phosphatase was 183U/L. At present baby’s serum bilirubin and platelet counts are normal and gaining regular weight. Thyroid profile of both babies was normal.

Figure 2: Calcific stippling of heel

Discussion

Incidence of NLE is 1 in 20000 livebirths\textsuperscript{1}. Transplacental transfer of maternal antiRo/SSA and antiLa/SSB antibody is found in 98 % infants. However, neonatal SLE presents in only 1-2% of mother with positive autoantibodies. First twin presented with CDP in which calcific stippling involved both heels and right upper humerus only with midface hypoplasia and proximal shortening of both upper limbs. Pathogenic role of maternal anti Ro/SSA and anti-La/SSB antibody has been proposed in CDP and possible target proteins are osteocalcin, osteoprotegerin and calreticulin. Elcioglu and Hall\textsuperscript{3} proposed the role of maternal autoantibodies on vitamin K metabolism thus causing bleeding in epiphyseal cartilages. Second twin manifested with cardiac, hepatobiliary and hematologic features. Coexistence of three organ involvement in NLE is rare. A national research registry for neonatal lupus was established in 1994 in US to provide database for translational research. 9 % (19) of the enrolled NLE patients had hepatobiliary diseases. 16 of them had associated cardiac or cutaneous manifestations and 3 had hepatobiliary disease as sole manifestation. Clinical variants were liver failure, conjugated hyperbilirubinemia with/without elevated aminotransferases and mildly increased aminotransferases.\textsuperscript{4} Isolated cardiomyopathy was found in 2.5% of the cases in national registry.\textsuperscript{5} Monsour et al\textsuperscript{6} described a case of dizygotic twins born to a mother diagnosed with SLE after delivery. One male twin had features of CDP. Other female twin was normal. Even monozygotic twins may be discordant for NLE\textsuperscript{7}. Maternal or sibling microchimerism has also been proposed for NLE discordance in twins\textsuperscript{8}.

Conclusion

Our case emphasizes the association of rhizomelic CDP with maternal SLE. Neonatal SLE is not only autoantibody mediated but placental and genetic factors also play role in the pathogenesis emphasizing need for further research.

References


**NNF Members Directory**

We appeal to all NNF members to send their updated address, phone numbers (residence, office and mobile) and email ID's. Please send this information on email: info@nnfi.org.

**PROFORMA**

Membership No.__________________________
First Name__________________ Middle Name_________________ Last Name  ___________________
Qualification __________________________________________________________________________
Communication Address ________________________________________________________________
____________________________________________________________________________________
____________________________________________________________________________________
City ___________________ State ___________________ Pin Code _____________________________
Telephone Nos. (with area code)
Office ___________________ Residence ___________________
Mobile _____________________________
E-mail ______________________ Fax ____________________

Dr VP Goswami  Dr Alok Bhandari  Dr Mahavir Jain

---

**TARIFF FOR ADVERTISEMENT IN NNF BULLETIN/NNF JOURNAL**

<table>
<thead>
<tr>
<th>Advertisement Type</th>
<th>Tariff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Back cover page colour</td>
<td>Rs. 2,50,000/-</td>
</tr>
<tr>
<td>Back inside cover page colour</td>
<td>Rs. 2,00,000/-</td>
</tr>
<tr>
<td>Front inside cover page colour</td>
<td>Rs. 2,00,000/-</td>
</tr>
<tr>
<td>Full colour page</td>
<td>Rs.1,50,000/-</td>
</tr>
<tr>
<td>Half colour page</td>
<td>Rs. 75,000/-</td>
</tr>
<tr>
<td>Black &amp; white full page</td>
<td>Rs. 40,000/-</td>
</tr>
<tr>
<td>Black &amp; white half page</td>
<td>Rs. 20,000/-</td>
</tr>
</tbody>
</table>

Note: Advertisement must be sent as soft copy through CD/DVD or Pendrive along with Cheque/Draft/Pay order in favour of “National Neonatology Forum” payable at Delhi

National Neonatology Forum
803, 8th Floor, Northex Tower, A-9, Netaji Subhash Place
Pitampura, Delhi-110034

Dr. Sunil K Mehendiratta
Secretary, NNF
Olmesartan Intake During Pregnancy Leading to Reversible Renal Failure and Skull Hypoplasia in a Preterm Newborn

Lata Bhat1, Supriya Bisht2, Kavita Khanijo3

1Senior Consultant, 2Consultant, 3Associate Consultant, Department of Neonatology, Fortis Hospital, Noida, UP, India

Abstract

Drugs acting on renin angiotensin aldosterone system are contraindicated during pregnancy, since they cause severe fetopathic effects like renal failure, oliguria, prematurity and skeletal hypoplasia. Renal failure is progressive in majority of cases. We are presenting a rare case of renal failure in a preterm newborn with skull hypoplasia with history of maternal intake of olmesartan (angiotensin-II receptor antagonist) throughout her pregnancy. Baby had deranged renal profile and was managed conservatively. Postnatal renal failure improved after conservative management. Her hypoplastic skull bones also had improved. This case emphasize the need for cautious selection of antihypertensives during pregnancy to avoid fetotoxicity. It also highlights that although rare, renal failure and skull hypoplasia can be reversible in such cases.

Introduction

Angiotensin-II receptor 1(AT1) antagonists, also known as “sartans” are one of the commonly used drugs for managing hypertension. Their mechanism of action is inhibition of angiotensin II/AT1-receptor interaction, leading to decreased effect of angiotensin II. This suppress renin-angiotensin system (RAS). Maternal intake of the drug, in the second or third trimester of pregnancy can cause fetotoxic effect in view of decreased RAS activity in the fetal circulation. As fetal renal function and urine production starts at the end of first trimester, by 20 week gestation, fetal urine constitutes over 90% of the amniotic fluid. The decreased renal vascular tonus suppresses fetal urine output. Fetal renal dysfunction subsequently cause oligohydramnios, and leads to further complications.

We are reporting a rare case of antenatal olmesartan intake in mother which lead to severe oligohydramios, renal failure and skull hypoplasia in the newborn. The renal failure and skull hypoplasia improved completely after conservative management.

Case Report

A twelve day old female baby was referred to us with deranged kidney function test (KFT) since birth. Baby was born vaginally in a private hospital at 32 weeks preterm to G2P1, with birth weight 1.6 kg. Mother had history of irregular periods. She was hypertensive, for which she was taking olmesartan 20 mg and hydrochlorothiazide 12.5 mg combination since many yrs.

Mother did not have antenatal checkup, and continued with the medications. Her first antenatal ultrasound done at 32 weeks was suggestive of oligohydramnios with fetal renal hypoplasia. Soon, she developed leaking per vaginum, and underwent dry labour within 48 hrs. Baby required resuscitation after birth, and developed respiratory distress which was managed initially with CPAP and antibiotics. At 30 hrs of life, she developed pulmonary haemorrhage, and was started on mechanical ventilation. Subsequently baby developed frank renal failure with decreased urine output (<1ml/kg/hr) and metabolic acidosis. Investigations revealed blood urea 65.6 mg/dL, S creatinine 1.4 mg/dL, S Sodium 118 mmol/L and S potassium 7.2 mmol/L. Her respiratory distress settled and she was extubated on ninth day. Though urine output improved, S creatinine increased progressively upto 4.3 mg/dL, along with blood urea 127 mg/dL and hence was referred to us on twelth day of life.

At admission in our unit, HR- 126/min, RR-70 /min with SpO2 85% in room air. Capillary refill time and pulses were normal. BP was 64/38 (47) mm Hg. On general examination, there was no dysmorphism, except high arch palate and widely separated sagittal suture > 1.5 cm, with anterior and posterior fontanelle felt in continuation. Systemic examination was normal.

Baby had minimal oxygen requirement. Investigations revealed venous blood pH: 7.35, pCO2-40, HCO3-22. CBC and peripheral smear was normal. Serum sodium was: 138 mmol/L, Potassium : 3.1mmol/L, Serum calcium : 7.7 mg/dL, S creatinine : 4.5 mg/dL and blood urea was 65 mg/dL. As sepsis screen was negative, urine
output adequate (>4ml/kg/hr), and tachypnea settled, feeds were started on second day of admission and conservative management continued. USG abdomen suggested that both kidneys were mildly enlarged and hyperechoic, with normal corticomedullary differentiation and no hydronephrosis. Further investigations were done to evaluate the fetotoxic effects of olmesartan. Liver function tests (LFT) were slightly deranged and urinalysis showed trace RBC. 24 hour urinary Creatinine and urinary protein was 7.90 mg/dl and 18.7 mg/dl respectively. Spot urine albumin creatinine ratio was 171.11 mg/g creat, suggesting microalbuminuria. Gradually, S creatinine decreased to 2.4 mg/dL on fourth day of admission, and 0.6 mg/dL on tenth day. Her urine output was adequate throughout. X ray skull revealed bilateral parietal bone hypoplasia. USG cranium, ECHO, hearing assessment was normal. Repeat X ray skull after four weeks revealed progressive ossification of parietal bone with reduction in the width of parietal suture. LFT also improved, Spot urine albumin creatinine ratio was normal 9.47 mg/g creatinine. Repeat USG abdomen done after four weeks reported same findings. Her kidney function tests remained normal throughout, and was discharged.

Discussion

Fetotoxic effects of “sartans”-angiotensin-II receptor antagonist losartan was first reported in 2001. These were similar to those seen in exposure to angiotensin converting enzyme (ACE) inhibitors during pregnancy³.

Abnormalities are oligohydramnios, pulmonary hypoplasia, hypoplastic skull bones, limb contractures, with subsequent fetal or neonatal death¹³. The expression of AT1 receptors is less during the initial stages of renal development, and increases later in pregnancy in mature renal tissues². Adequate amniotic fluid is necessary for normal fetal lung maturation. Hence, oligohydramnios due to any cause may result in pulmonary hypoplasia.

In a study of 15 newborns with maternal intake of “sartans” in second/third trimester, outcome was poor as 6(40%) cases died due to severe hypotension, pulmonary hypoplasia, and anuria. Renal failure improved with treatment in only 3(20%). Hypoplastic and poorly ossified skull bones, and widely open sutures, was seen in 9 cases².

Fetal membranous bones are highly vascular and require high oxygen tension for growth². Possible reason of skull hypoplasia is decrease in fetal blood flow due to reduced activity of the RAS. It may cause low oxygen supply, which may inhibit mineralization and ossification of the skull. Oligohydramnios may further cause the uterine muscles to exert direct impact on the developing fetal skull, which may interfere with skull ossification⁴.

In another similar set up, fetal ultrasound at 29 weeks gestation suggested oligohydramnios with normal fetal kidneys. Stopping olmesartan, maternal rehydration along with furosemide reversed the renal impairment. Baby was born at term with normal renal function, suggesting that renal impairment due to olmesartan may be reversible².

In a similar study of seven newborns, oligohydramnios was present in all and fetal kidneys were hyperechogenic on ultrasound. Majority 4(57%) did not survive. Few 2(28.5%) survived with renal impairment requiring chronic dialysis. Complete recovery of renal function was rare 1(14%). Other features were cranial ossification defect, flaccid paralysis of hands and feet and sensorineural hearing loss⁶.

In our case, the renal parameters of the baby improved completely with conservative management. Angiotensin-II receptor antagonists are contraindicated in the second and third trimester of pregnancy because of the risk of adverse fetal effects. It is strictly advised that hypertensive women who become pregnant while taking an angiotensin-II receptor antagonist, should be changed to another antihypertensive agent that does not impair RAS function².

References

Global Health at University of California in Los Angeles (UCLA, USA) and National Neonatology Forum (NNF, India) will hold Advances in Neonatology and Pediatrics (ANP) on March 4 & 5, 2017 in Hyderabad, India.

Focus of this conference will be infection and respiratory problems. Many internationally known speakers from USA and India will address topics like:

- Genomics in Neonatology
- Immunity and Molecular diagnosis of Sepsis
- Antibiotic stewardship and Multiple drug resistance
- Universal influenza vaccination and load of dengue
- malaria, chikungunia and zika during pregnancy
- Advances in delivery room resuscitation
- HFNC vs CPAP

Emerging concern of BPD and best papers in 2016. Audience participation during didactic lectures, case presentations, debates and journal club will be encouraged.

**Registration:** (INR): 1000/- for PG/Nurses & FELLOW, Rs. 2500/- for all others.

Cheque/Draft may be in favour of “NATIONAL NEONATOLOGY FORUM” and send to NATIONAL NEONATOLOGY FORUM, 803, 8th Floor, A-9, Northex Tower, Netaji Subhash Place, Pitampura, Delhi-110034, Ph. 011-27353535, Mobile : 8527453535

**FOR NEFT/RTGS:**
Account No. : 91191010001308
Bank Name : Syndicate Bank
Branch : DTC Wazirpur, New Delhi-110035
IFSC Code: SYNB0009119
Account Name: National Neonatology Forum
Type of account - Current

For further details please contact
Dr Ajay Gambhir (drajaygambhir@rediffmail.com 9811557085)  
Dr Dinesh Chirla (dchirla@gmail.com, 9849790003)
Dr Uday Devaskar (udevaskar@mednet.ucla.edu)  
Dr Suhas Kallapur (Suhas.Kallapur@cchmc.org)

---

**President, NNF:**
Dr Ajay Gambhir

**Secretary, NNF:**
Dr Sunil Mehendiratta

**President-Elect, NNF:**
Dr B D Bhatia

**Treasurer, NNF:**
Dr Alok Bhandari