Lalana Newborn Resuscitation

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Received Date: 14-10-2021, Accepted Date: 10-11-2021, Published Date: 17-11-2021

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Abstract

Background: Birth asphyxia is a leading cause of perinatal and neonatal morbidity and mortality predominantly in Asian countries. Effective resuscitation of newborns takes on priority in saving lives. Newly born resuscitation is unique in that displacement of fetal fluid filled lung requires continuous positive pressure ventilation by sustained nasal oxygen inflation as opposed to intermittent positive pressure ventilation to initiate breathing facilitating vital cardio-vascular changes from fetal to adult life.

Aim: Quick and safe resuscitation of hypoxic/asphyxiated newborns transiting from fetal fluid filled lungs to well aerated neonatal lungs with onset of rhythmic respiration triggering large reduction in Pulmonary Vascular Resistance (PVR), facilitating a series of cardiovascular changes essential for survival after birth.

Method: The study comprised of 1,383 consecutive singleton live births during 14-month period from 1st April 2016 to 31st May 2017, wherein 60% (n=830/1383) deliveries were attended, exclusion criteria 12 twin pregnancies and 10 stillbirths. Resuscitation of hypoxic/asphyxiated newborns involves three simple steps; STEP 1: Assessment of score zero to +5 by pulse oximetry based on peripheral oxygen saturation, STEP 2: Classification as “Normal” and hypoxic/asphyxiated newborns Graded I-V based SpO2, pattern of breathing and heart rate. STEP 3: Lalana Newborn Resuscitation (LNR) Protocol I and II by sustained nasal oxygen inflation, proven both scientifically and physiologically to initiate rhythmic respiration.
Results: Incidence of birth asphyxia was 21.4%, all 178 hypoxic/asphyxiated newly borns Graded I-V within 20-60 seconds of birth, were successfully resuscitated by sustained nasal inflatory, oxygen flow at rate of 4-15 Litres/minute directed to baby’s nostrils through a wide bore tube for up to 1 to 3 minutes, initiating rhythmic breathing, respiratory rate 30-60/min, heart rate 120-160 beats per minute (bpm) and, SpO₂ >96% monitored continuously by Pulse Oximeter.

Conclusion: ‘Lalana Newborn Resuscitation’ (LNR) proved effective in all 178 asphyxiated newborns, Grade I-V by continuous positive pressure ventilation with sustained nasal oxygen inflation at flow rates of 4-15 L/min, commenced rhythmic breathing within 1-3 minutes of birth, respiratory rate 30-60/min, heart rate 120-160 bpm and Zero pulse oximetry score, SpO₂ >96%.

**Keywords**

Lalana Newborn Resuscitation (LNR); Continuous Positive Pressure Ventilation (CPPV); Sustained Nasal Oxygen Inflation; Pulse Oximetry Score; SPO₂; Grade I to V

**Aims for Effective Resuscitation of Hypoxic/Asphyxiated Newborns**

- Effective resuscitation of asphyxiated newborns takes on priority in newborns in saving lives as well as without any residual neurological and other sequelae so children should be normal
- Unique newly born resuscitation is in transition of fetal fluid filled lungs to well aerated neonatal lungs by safe and quick resuscitation by sustained inflatory nasal oxygen flow proven both scientifically and physiologically to generate hydrostatic pressure gradient between airways and lung tissue to overcome the high resistance of moving fetal lung liquid through the airways and across the alveolar wall into the interstitial tissue to the lymphatic and thence to circulation
- Effective resuscitation with continuous distending pressure results in uniform recruitment of alveoli with functional residual capacity, preventing alveolar collapse, atelectasis and V/Q mismatch, to achieve optimal gas exchange
- Prevention of hypoxemia and hypercapnia that result in rise of arterial carbon dioxide causing reduced blood flow to the brain with ischemia resulting in altered mental status and ill effects
- Also stabilizing newborns at birth with low fraction of inspired oxygen (FiO₂) is difficult, as hypoxia is a potent inhibitor of spontaneous respiration, thus higher FiO₂ mitigates...
hypoxya-induced inhibition of breathing, stimulating the central respiratory center in initiating rhythmic respiration.

- Oxygenation mitigates hypoxya-induced inhibition of breathing and stimulates the central respiratory center to initiate rhythmic respiration, reducing Pulmonary Vascular Resistance (PVR) causing reflex physiological mechanism promoting vital cardio-vascular changes adapting to extra-uterine life.
- The primary measure of adequate initial ventilation is the prompt improvement in heart rate is a primary measure of adequate initial ventilation, based on the concept that a low heart rate indicates vagal-induced bradycardia in response to perinatal asphyxia. Pulse oximetry plethysmograph pulsatile waveform indicates cardiac function and pumping of oxygenated blood throughout the body.
- Monitoring of peripheral tissue oxygenation (SpO₂) with Pulse oximeter allows for real time assessment of newborns with classification within 20-60 seconds ‘Normal’ or hypoxic/ asphyxia newborns Graded I-V that determines oxygen flow rates, as well as discontinuation at 96%.
- Prevention of lung injury by avoiding potentially harmful Intermittent Positive Pressure Ventilation (IPPV) considered both physiologically and scientifically weak in transition of fetal fluid filled lungs to well aerated neonatal lungs, as entire tidal volume will only enter previously aerated regions due to much lower airway resistance causing overexpansion with intermittent collapse, surrounding atelectasis and V/Q mismatch with right to left shunting, perpetuating hypoxya and Persistent Pulmonary Hypertension (PPH) with poor outcome in neonates.

**Introduction**

Birth asphyxia accounts for 29% neonatal deaths, ranging from 20-40% with 2.76 million annual neonatal deaths with 97.8% or 2.02 million deaths occurring in the first week of life, of which 70% or 1 million deaths occurred within the first three days of life, 56.8% within the first day of life [1-3]. Globally of 2.5 million children who die in the first month of life, about one-third dies within 24 hours with similar intrapartum 1.2 million stillbirths, occurring predominantly in Asian countries, it is estimated that 4 to 9 million babies per year experience birth asphyxia with only 1 to 2 million successfully resuscitated [1,4]. Incidence varies from 2 to 28 per 1000 live births with three-fold higher risk of asphyxiated infants dying in the neonatal period compared to non-asphyxiated infants; however the major impact is on larger and more mature babies, who otherwise have a good chance of survival [5-10]. During 2020, 36.3% of 7,000 neonatal deaths took place within the first 24 hours comprising 47% of all child deaths under five years, up from 40% in 1990.

A slower decline in neonatal mortality is reported from 5 million in 1990 to 2.4 million in 2019, compared to under-five mortality rate, children facing the greatest risk of death in their first 28
days [12-15]. Misclassification of live born, apneic, cyanotic neonate with pulse who die due to non or inadequate resuscitation labelled as stillbirth are actually viable newborns as unskilled birth attendants are unable to distinguish between the two, have significant implications on national health policies and global strategies for reducing perinatal mortality, as even 1 in 100 stillbirths if effectively resuscitated will result in more than 30,000 lives that could potentially be saved each year. Worse still for every newborn baby that dies mainly by birth asphyxia at least another twenty newborn suffer birth injuries etc [16, 17].

Thus birth asphyxia constitutes one of the leading causes of preventable perinatal and neonatal morbidity and mortality predominantly in Low and Middle Income Asian countries. India reported high neonatal mortality rate (NMR) 22/1000 live births compared to about 1% in developed countries with vast technological advances in antenatal and neonatal critical care report low Perinatal Mortality Rate (PMR) of 6.1/1,000 births with 10-15% reduction in neonatal mortality rate and low incidence of birth asphyxia below 0.1% over the past decades, however stillbirth rates have remained unchanged, constituting 70% of perinatal deaths with 30% early neonatal deaths, corrected PMR 4.1/1,000 births excluding congenital anomalies, an unavoidable proportion of perinatal mortality, which constituted a leading cause in 34% [12,15,18,19]. In a study from Vellore, South India lethal congenital malformations was the third cause18.2% of early neonatal deaths following birth asphyxia 24.1% and respiratory distress syndrome 20%, followed by early onset neonatal sepsis 15%, intracranial haemorrhages 9.2% and extreme immaturity 4.3% ranked as sixth and seventh cause of early neonatal deaths [1,2,20,21]. In U.K. intrauterine growth retardation is the single largest contributor to perinatal mortality in non-anomalous fetuses. Pregnancies with IUGR have an eight-fold increased risk of stillbirth 19.8 versus 2.4/1,000 births in UK with over 50% of deaths being SGA having birth weight below 10th customized centile of whom only 30% were suspected antenatal [18].

Unique resuscitation in the newly borns is transition from fetal lungs containing about 30 ml/kg body weight of fluid, low protein content of 25mg/dl, that differs from both ultra-filtrate of plasma and amniotic fluid, requires that newborns make high forceful inspiratory efforts up to 60 cm H₂O at birth usually with the first cry, overcomes the resistance of inspiration of air into the liquid filled lungs, stretching the alveolar epithelial pore radius of 0.5mm impermeable to solute to 3.5 mm in radius that allows flow of fetal alveolar liquid down a protein osmotic pressure gradient into the interstitial tissue and thence absorbed via lymphatic’s into the circulation [22-25]. Subsequently the pores in the alveolar epithelium contract back towards their fetal size [26]. In fact meconium staining of amniotic fluid often results from normal labor contractions with hypoxia or even infection, inhibits fetal lung fluid reabsorption at birth, disturbing the ability of the lungs in vital transition to extra-uterine life and others on guidelines of basic newborn resuscitation with world-wide decline in neonatal asphyxiated deaths [4,5,11,27-31].


DOI: http://dx.doi.org/10.46889/JCMR.2021.2305
Neonatal Resuscitation Program (NRP) introduced in 1988, by American Academy of Paediatrics and American Heart Association and World Health Organization lacks scientific clarity and is considered physiologically weak regarding transition of fetal fluid filled lungs to well aerated neonatal lungs by inflating lungs through the application of Intermittent Positive Pressure Respiration (IPPR) by short bursts of air/oxygen with bag and mask or endotracheal intubation, is potentially harmful as entire tidal volume will only enter previously aerated regions due to the much lower airway resistance predisposing to lung injury and un-even alveolar ventilation that does not generate adequate intra-pulmonary pressure to remove fetal lung fluid, while also permitting lung fluid to re-enter the airways causing rising Alveolar-arterial (A-a) gradient and ventilation perfusion (V/Q) mismatch with right to left cardiac shunt through foramen ovale and ductus arteriosus, perpetuating hypoxia and persistent pulmonary hypertension with bradycardia resulting in delayed onset of breathing [23,32-37].

Intrapartum events cause deficient oxygenation defined as respiratory failure or oxygen insufficiency that requires resuscitative intervention to establish rhythmic respiration defined as birth asphyxia, since pulmonary arterioles remain constricted in the fetal circulation with the right to left shunting through foramen ovale and ductus arteriosus with only about 10% of cardiac output perfusing the lungs [35,37]. Sustained inflation with oxygen at 5 cm H2O pressure or oxygen flow at 8 litres/min, up to maximum 20 cm H2O pressure or oxygen flow up to 25 litres/min that extends over 1 to 3 minutes is proven both scientifically and physiologically achieves better post manoeuvre lung mechanics to effectively resuscitate asphyxiated newborns, allow for uniform alveolar recruitment and the increased FiO2 results in exponential increase of the alveolar surface area measured As Functional Residual Capacity (FRC) with alveolar pressure above atmospheric pressure, that enables the generation of intrinsic hydrostatic pressure gradient between airways and lung tissue to overcome the high resistance of moving liquid through the airways and across the alveolar wall that helps keep the air sacs to stay open, achieving optimal gas exchange, improving ventilation, thereby triggering large reduction in Pulmonary Vascular Resistance (PVR), with vasodilation of pulmonary arteriole causing a reflex physiological mechanism that converts fetal circulation to adult type [23,24,34,38-40].

Oxygen therapy is the only specific treatment to prevent or mitigate the effects of hypoxia with rapid reduction for the need of high FiO2, thus continuous monitoring by Pulse Oximeter not only gives accurate insights to peripheral oxygenation (SpO2) but also heart rate within matter of seconds empowering one to respond quickly and confidently to abnormal SpO2 reading to determine supplemental oxygen which is discontinued with zero score SpO2>96%, indicate successful resuscitation [38-43]. Delay in resuscitation by NRP can result in devastating consequences of the baby being deprived of oxygen causing damage to heart and brain and other organs sometimes even death [34,35,44]. Thus more severe the fetal asphyxia, the longer it will take before the infant starts to breathe spontaneously, in fact 20% to 40% of survivors suffer from considerable impairments depending on extent of asphyxial insult such as
blindness, deafness, autism, seizures and cognitive impairments with inability to develop fine motor skills, memory and mood disturbances etc to permanent neurological deficits with sequelae depending on extent of asphyxial insult, showing no decline in incidence of meconium aspiration syndrome and seizures due to HIE with no overall decrease in neonatal mortality, though asphyxial related deaths decreased significantly (p=<0.01) [11,44-49].

The trend in western developed countries indicates rate of asphyxia in 2/1000 births, resulting in mortality rate of 10-15% in NICU with cerebral palsy rate of 10-15% among survivors and eventually a rate of over 40% with considerable impairments such as blindness, deafness, autism, seizures and cognitive impairments, inability to develop fine motor skills, memory and mood disturbances. Thus the degree of morbidity remains high affecting quality of life in survivors as the rate of Hypoxic Ischemic Encephalopathy (HIE) has remained the same over previous decades [44-49].

Perinatal asphyxia mainly due to intrapartum events is estimated to be the fifth largest causes of under-five child mortality after pneumonia, diarrhoea, neonatal infections and complications of preterm births, is in reality much higher as non-breathing viable newborns, termed as stillbirth are left without resuscitative efforts at birth, who are in fact actually early neonatal deaths [14-17]. Many parts of low income Asian and African countries with limited resource, still lack skilled birth attendants and well outfitted resuscitation teams and even essential resuscitation equipment, such as bulb syringes, bag and mask devices etc. may be substandard or unavailable and ethnic Asian babies deserve better [30]. Despite concerted global and national efforts to improve child mortality, in the post neonatal phase with key child health interventions such as oral rehydration therapy, care seeking for acute respiratory infections and improved immunization rates has however resulted in neonatal mortality gradually increasing as a percentage of total under-five child mortality with less attention being given to determinants of perinatal and neonatal mortality despite new found focus on neonatal health the annual rate of reduction in NMR and ENMR still lags behind IMR and U5MR, with slow decline in perinatal mortality rates. Although problems in the perinatal and neonatal phases have been reported in India, little progress has been made towards implementing large-scale solutions to these problems and effective interventions to address risk factors such as essential newborn care and their implementation still has not resulted in a rapid reduction in perinatal and neonatal mortality rates [2,3,7,12].

Effective resuscitation is the need of the hour that is imperative in hypoxic/asphyxiated births will prove to be the single most significant strategy in reducing both perinatal and neonatal mortality and morbidity, so children should be normal, consequently reducing under-five years child mortality rates [16-18]. Sustained oxygenation rather than IPPV is the basis of quick reversal of hypoxic ill effects with early onset of rhythmic respiration, resulting in improved neonatal outcome with reduction of adverse life-long ill sequelae, as throughout the world, around 200 million children do not accomplished their age appropriate development, more highly prevalent in Asian countries, further compounded by the negative impact of covid19.
pandemic with hundreds of thousands more fatalities expected due to lack of medical facilities more so in developing Asian countries [45,50]. Thus neonatal period within the first 28 days of life, is the most vulnerable period in the life of a child with the highest risk of mortality per day than any other period during childhood, constituting 62% of under-five year child mortality in Africa and South Asia compared to 54% in developed European and Northern American countries in spite of low neonatal mortality in Sustainable Development Goal (SDG) regions, thus neonatal health has taken on eminence in reducing under five child mortality rates [14,15].

**Problem Definition**

1. Resuscitation of hypoxic newborns requires quick intervention to initiate breathing best adapted to transition from fetal fluid filled lungs to well aerated neonatal lungs, in reducing hypoxic birth injury so children should be normal

2. Sustained pressure ventilation generates hydrostatic pressure gradient between airways and lung tissue to overcome the high resistance of moving fetal lung liquid through the airways and across the alveolar wall into the interstitial tissue is scientifically proven

3. Counteract hypoxia by oxygenation with flow rates 2-15 Liters/min, stimulates central respiratory centre to initiate respiration and facilitate smooth physiological cardiovascular transition from fetal to neonatal circulation

4. Continuous assessment of newborn status by Pulse oximeter SpO2 and heart rate monitoring

5. Harmful Intermittent Positive Pressure Ventilation (IPPV) predisposes to lung injury as short intermittent inflation provides for inadequate ventilation in newly born in transition from fetal fluid filled lungs to neonatal life considered as physiologically and scientifically weak, hence best suited in cardiorespiratory arrest of infants, children and adults with previously aerated lungs

**Materials and Methods**

The study comprised 1,383 consecutive singleton live births during 14-month period from 1st April 2016 to 31st May 2017 at Shifa Hospital, a multispecialty centre in the metropolitan city of Bangalore. I attended 830 (60%) deliveries including vaginal deliveries both vertex and breech presentation, instrumental-vacuum and low/outlet forceps deliveries as well as surgical Lower Segment Caesarean Sections (LSCS) both Elective and Emergency surgery. Sources of data were Labor room records, neonatal charts and NICU register. Data was entered into EPI data version 3.1 and then exported to SPSS Version 21 for analysis and statistical significance, the threshold of significance was set at 0.05.
A sample pilot study was carried out on 30 newborns with the new innovative resuscitation technique using sustained nasal oxygen inflation at flow rates 2-15 Litres/minute (L/min) proved eminently successful with uneventful observation in NICU, who were then shifted to mother’s side for initiation of early breast feeding. A study was then undertaken on 830 newborns whose delivery I attended during the 14 month study period.

The status of all newborns are preferably assessed within 20-60 seconds after birth i.e. following complete expulsion of newborn, with immediate clamping and cutting of umbilical cord in hypoxic newborns or may be delayed 1-3 minutes in spontaneously breathing newborns. The Pulse Oximeter is placed across the foot of newborn to monitor peripheral tissue oxygen saturation (SpO₂), heart rate, plethysmograph waveform noting adequate cardiac output, the pattern of breathing observed or respiratory rate derived from Photoplethysmogram (PPG).

Lalana Newborn Resuscitation (LNR) proves ideal and consists of three steps. Step 1 Pulse oximetry score zero to +5 based on peripheral oxygen saturation (SpO₂). Step 2 Classification as “Normal”, healthy newborns with spontaneous onset of rhythmic respiration while hypoxic/asphyxiated newborns Graded I-V based on SpO₂, pattern of breathing and heart rate. Step 3 includes Protocols I and II, application of continuous positive pressure ventilation by sustained nasal oxygen inflation at flow rates 2-15L/min determined by Pulse oximetry score, SpO₂, pattern of breathing and heart rate for upto 1-3 minutes or till onset of rhythmic respiration, SpO₂ >96% and heart rate >120 bpm.

**Step-1**

**Newborn Pulse Oximetry Score**

Pulse oximeter automatically provides an estimate of newborn health status within seconds. Zero score Pulse Oximetry score SpO₂ 96%-100% indicates ‘Normal’ healthy newborns, +1 Pulse Oximetry score, SpO₂ 94%-95%, mild birth asphyxia, +2 Pulse Oximetry score, SpO₂ 92%-93%, moderate birth asphyxia, +3 Pulse Oximetry score, SpO₂ 90-91%, severe birth asphyxia, +4 Pulse Oximetry score, SpO₂ 89%-50%,Secondary apnea with absent breathing and + 5 Pulse Oximetry score Terminal apnea with absent breathing or ‘flat baby’. Zero to +5 Pulse Oximetry score based on SpO₂, for all newborns is seen in Table 1.
Table 1: Newborn pulse oximetry scoring for \( \text{SpO}_2 \).

<table>
<thead>
<tr>
<th>Score</th>
<th>( \text{SpO}_2 ) Pulse Oximeter Reading</th>
<th>Newborn Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zero</td>
<td>96%-100%</td>
<td>Normal / Healthy</td>
</tr>
<tr>
<td>1</td>
<td>94%-95%</td>
<td>Mild Asphyxia</td>
</tr>
<tr>
<td>2</td>
<td>92%-93%</td>
<td>Moderate Asphyxia</td>
</tr>
<tr>
<td>3</td>
<td>90%-91%</td>
<td>Severe Asphyxia</td>
</tr>
<tr>
<td>4</td>
<td>89%-50%</td>
<td>Secondary Apnea</td>
</tr>
<tr>
<td>5</td>
<td>&lt;50%</td>
<td>Terminal Apnea</td>
</tr>
</tbody>
</table>

Step-2

Classification of Newborns as Normal, Healthy or Hypoxic/asphyxia Grade 1 to V

The status of all newborns assessed within 20-60 seconds of birth classified as Normal, healthy newborns or hypoxic/asphyxiated newborns further graded into I-V based on Pulse Oximetry Score, \( \text{SpO}_2 \), breathing pattern and heart rate. Normal, healthy newborns, have Zero Pulse oximetry Score \( \text{SpO}_2 \) 96%-100%, with spontaneous onset of rhythmic breathing, respiratory rate 30-60/min and heart rate 120-160 bpm. Mild birth asphyxia, Grade I newborns +1 Pulse oximetry Score, \( \text{SpO}_2 \) 94%-95%, with regular/irregular breathing pattern, respiratory rate ±20-30/ min and heart rate 100 - 119 bpm, Moderate birth asphyxia, Grade II newborns +2 Pulse oximetry Score, \( \text{SpO}_2 \) 92-93%, with irregular breathing, respiratory rate ±15-20/min and heart rate 100 - 80 bpm. Severe birth asphyxia, Grade III newborns +3 Pulse oximetry Score, \( \text{SpO}_2 \) 90-91%, irregular or gasping breathing, respiratory rate 10-15/min and heart rate 80-60 bpm. Secondary apnea Grade IV newborns +4 Pulse oximetry Score, \( \text{SpO}_2 \) 89%-50%, absent respiration and heart rate 60-35 bpm, while Terminal apnea Grade V newborns +5 Pulse oximetry Score, \( \text{SpO}_2 \) <50%, absent respiration and heart rate < 35 bpm is also referred to as “flat baby”. However grading of hypoxic newborns into Grade I-V by criteria of +1 to +5 pulse oximetry score, \( \text{SpO}_2 \) <96%, respiratory rate <30/ min and heart rate <120 bpm, may vary as real time assessment of newborn’s \( \text{SpO}_2 \) is constantly changing due to continuous monitoring. The classification of newborns at birth based on Pulse oximetry score, \( \text{SpO}_2 \), respiratory rate and heart rate is seen in Table 2.
Table 2: Classification of newborns within 20-60 seconds of birth.

<table>
<thead>
<tr>
<th>Normal Healthy newborn</th>
<th>Grade I Mild Asphyxia</th>
<th>Grade II Moderate Asphyxia</th>
<th>Grade III Severe Asphyxia</th>
<th>Grade IV Secondary Apnea</th>
<th>Grade V Terminal Apnea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zero Pulse oximetry Score - SpO₂ 96%-100%</td>
<td>+1 Pulse oximetry Score - SpO₂ 94% - 95%, Regular/irregular Respiration, rate 20-30/min. Heart Rate 100 - 119 bpm.</td>
<td>+2 Pulse oximetry Score - SpO₂ 92-93%, Regular/irregular Respiration, rate 15-20/min. Heart Rate 100 - 80 bpm.</td>
<td>+3 Pulse oximetry Score - SpO₂ 90-91%, Irregular/respiration, rate 10-15/ min. Heart Rate 80-60 bpm.</td>
<td>+4 Pulse oximetry Score - SpO₂ 89%-50%, Absent/respiration. Heart Rate 60-40 bpm</td>
<td>+5 Pulse oximetry Score - SpO₂ &lt;50%, Absent/respiration ‘Flat baby’. Heart Rate &lt;40 bpm</td>
</tr>
<tr>
<td>Spontaneous onset respiration, rate 30-60/min, Normal Heart Rate 120-160 bpm</td>
<td></td>
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</tbody>
</table>

Step-3

Effective aeration of the newly born’s lung is a function of applying an elevated pressure over sustained periods of 1-3 minutes that results in significant improvement of lung mechanics in efficiently overcoming the high resistance of moving liquid from lungs to interstitial with uniform lung aeration and prompt increase in heart rate monitored continuously by pulse oximetry with circulation of oxygenated blood throughout the body.

Newborns timed at birth at complete expulsion of fetus, the umbilical cord ligated and cut immediately in hypoxic/asphyxiated newborns, which may be delayed upto 1-3 minutes in “Normal” newborns with spontaneous onset of respiration. The pulse oximeter is placed on the baby’s foot to monitor superficial oxygen saturation (SpO₂), heart rate and the plethysmograph tracing records how well heart is pumping oxygenated blood throughout the body indicated by pulsatile changes. All newborns are classified as ‘Normal’ or hypoxic who are further Graded I to V, based on pulse oximeter score +1 to +5 respectively, SpO₂, pattern of respiration and heart rate within 20-60 seconds of birth.

Majority are ‘Normal’ Healthy newborns, active, pink in color, moving all four limbs with vigorous cry initiate spontaneous rhythmic respiration within 20-60 seconds of birth with Zero Pulse oximetry Score, SpO₂ >96% respiratory rate 30-60/min and heart rate of 120-160 bpm. Routine newborn care based on regional NICU protocol, baby wiped dry under radiant warmer to prevent hypothermia, nasal and oral suction maintaining asepsis, Vitamin K 0.5-1mg intramuscularly, stomach wash if delivered by LSCS, baby wrapped in warm clothing and cap,
is transferred to mother’s side for early feeding, breast feeding instituted within an hour after normal vaginal delivery or four hours after LSCS.

Lalana Newborn Resuscitation (LNR) for hypoxic newborns are further graded into Grade I - V based on +1 to +5 Pulse oximetry score, peripheral oxygen saturation (SpO₂) <95%, pattern of breathing and heart rate. Mild birth asphyxia, Grade I newborns, +1 Pulse oximetry Score, SpO₂ 94%-95% with regular/irregular respiratory rate ±20-30/ min and heart rate 100 - 119 bpm, require resuscitation by sustained nasal oxygen inflation at flow rate 2-4 L/min (FiO₂ 28% to 36%), upto 60 seconds till rhythmic pattern of respiration, oxygen is discontinued with normal pulse oximeter reading SpO₂ >96%. If however SpO₂ decreases to <94% oxygen flow rate is increased to 5-8 L/min or more (FiO₂ up to 50%), for upto 1-3 minutes till Zero Pulse oximetry Score, SpO₂ >96%, and heart rate >120 bpm.

Moderate birth asphyxia, Grade II newborns have +2 Pulse oximetry Score, SpO₂ 92%-93%, regular/ Irregular respiration, rate ±15-20/min and heart rate 100 - 80 bpm, resuscitated by sustained nasal oxygen inflation at flow rate of 5-8 L/min, (FiO₂ 40% to 52%) for upto 60-90 seconds till onset of rhythmic respiration, oxygen is discontinued with normal pulse oximeter reading SpO₂ >96% % and heart rate >120 bpm.

Severe birth asphyxia, Grade III, +3 Pulse oximetry Score, SpO₂ 90%-91%, irregular/gasping respiration, rate ±10-15/min and heart rate 80-60 bpm, resuscitation by sustained nasal oxygen inflation at flow rate of 10-12 L/min, (FiO₂ 56% to 64%) applied for 90-120 seconds till onset of rhythmic respiration, oxygen is then discontinued with normal pulse oximeter reading SpO₂ >96 and heart rate >120 bpm.

Secondary apnea Grade IV, +4 Pulse oximetry Score, SpO₂ 89%-50%, absent respiration and heart rate 60-40 bpm, ventilation by sustained nasal oxygen inflation at flow rate of 12-14 L/min, (FiO₂ 64% to 76%) up to 120-180 seconds till onset of rhythmic respiration, rate 30-60/min and heart rate >120 bpm, oxygen is discontinued with normal pulse oximeter reading SpO₂ >96%. However if heart rate is <45 bpm, endotracheal intubation undertaken with continuous distending pressure ventilation by sustained oxygen at flow rate of 15 L/min (FiO₂ 100%) for 120-240 seconds or more till onset of breathing and heart rate increases to > 100bpm extubate and continue with nasal oxygen inflation flow rate of 10-12 L/min (FiO₂ 60-68%). Grade IV newborns are usually subjected to severe perinatal asphyxia and are at greater risk of intrauterine (stillbirth) or early neonatal death often delivered by judicious quick obstetric intervention by emergency LSCS, may be effectively resuscitated by sustained nasal oxygen with tactile stimuli, back rubs, nasal and oral suctioning till onset of rhythmic respiration. Oxygen discontinued at Zero pulse oximetry score, rhythmic pattern of respiration, rate 30-60/min SpO₂ >96% and heart rate >120 bpm.

Terminal apnea, Grade V newborns +5 Pulse oximetry score, SpO₂ <50%, with absent respiration and heart rate <40 bpm ‘flat baby’ may respond to continuous distending pressure ventilation by sustained nasal oxygen inflation up to 15 L/min (FiO₂ 64% to 76%) for 120-240 seconds.
seconds or more till onset of rhythmic respiration or if no recording on pulse oximeter of SpO₂ or heart rate, immediately intubate with endotracheal tube and resuscitate by positive airway distending pressure with oxygen flow at rate of 15 L/min upto 25 L/min (FiO₂ 100%), if no breathing or heart beat within 60 seconds give cardiac compression about 120/min with medication of epinephrine, volume expander 5% dextrose saline at 10 ml/kg and Carbicarb 2.5meq/kg, a mixture of Na₂CO₃/NaHCO₃ which does not generate CO₂ slow infusion over one hour. If heart rate increases > 100 bpm with onset of breathing, shift to sustained nasal oxygen inflation up to 12 L/min (FiO₂ 64%) for 60-120 seconds and oxygen discontinued with rhythmic breathing, rate 30-60/min, normal SpO₂ >96% and heart rate >120 bpm.

However Grade V newborns are at high risk of intrauterine death (fresh stillbirth) or if born with signs of life who are often un-responsive to resuscitative intervention and dying shortly after birth termed early neonatal deaths, are usually delivered by emergency LSCS, which impacts the more mature, larger newborns with birthweight around 3500-4000 g, born 39 weeks or later, most of whom on survival may be associated with high incidence of HIE and serious neurological sequelae with lifelong disability, cerebral palsy etc. Hence it is recommend that resuscitative efforts may be aborted if neonate unresponsive after three to five upto ten minutes of resuscitation with sustained nasal oxygen inflation at 15 L/min (FiO₂ 76%) or through endotracheal tube, FiO₂ (100%).

Preterm <32 weeks and <1250g with incidence of 1% among 830 deliveries attended. Among total nine preterms, VLBW, five were 28-32 weeks gestation and four were 28 weeks gestation. Three preterm weighed <1000g and remaining six between 1000-1250 g. Five delivered normally and three by emergency LSCS and one preterm 32 weeks gestation, weighing 1180 g born by assisted breech delivery had placenta previa. Of the two deaths, one preterm 28 weeks gestation weighing 740 g died on2nd post-natal day due to extreme immaturity and RDS. Another preterm 28 weeks weighing 960 g had obstetric complications of MSAF and PROM died on 3rd post-natal day of RDS and sepsis, the remaining seven preterm VLBWs survived. However one preterm 28 weeks gestation and 1010g birthweight had polyhydraminos with duodenal atresia was surgically corrected at a referral hospital.

LNR Protocol II for resuscitation of preterm newborns, gestational age <32 weeks and birthweight <1250g by CPPV by sustained nasal oxygen inflation at flow rates of 2 L/min up to 12 L/min (FiO₂ 28-60%), through wide bore oxygen tube or nasal prongs till heart rate improves and regular respiration established following which bubble CPAP with blender and FiO₂<30% through nasal prongs started, to maintain oxygen saturation around 95%, if less than 28 weeks gestation the SpO₂ maintained between 88-95%, the preterm is then transferred to NICU for observation and further management/treatment of complications if any. In preterm with secondary or terminal apnea endotracheal intubation with sustained oxygen flow at rate of 12 L/min (FiO₂ 100%) is administered for 2-3 minutes or more till breathing established and heart rate >120 bpm, continued with CPAP (FiO₂<30%) through nasal prongs and baby shifted to NICU for observation and management/treatment of any complications.
Delivery room use of sustained nasal oxygen inflation during resuscitation triggers physiological transition of fetal fluid filled lungs to well ventilated neonatal lungs initiating rhythmic breathing. In spontaneously breathing preterm <32 weeks and <1250 g birth weight, Continuous Positive Airway Pressure (CPAP) with blender and FiO₂ <30%,with oxygen bubbling through 5 cm water in a bottle producing small airway pressure oscillations which on reaching the newborn’s lung results in improved gas exchange and lung function. Preterm <32 weeks and VLBW <1250 g CPAP (FiO₂<30%) maintain oxygen saturation around 95%, preterm <28 weeks gestation the SpO₂ maintained between 88-95%. Preterms are more prone to birth asphyxia as opposed to term babies and extremely immature preterms are at greater risk of cerebral palsy, delay in development, hearing and sight problems, hence it is recommend that resuscitative efforts may be aborted in terminal apnea.

The present study all 178 hypoxic newborns Grade I-V were effectively resuscitated with onset of rhythmic breathing by Lalana Newborn Resuscitation (LNR) outlined in Protocol I and II resulted in the wellbeing of neonates with normal pulse rate, respiratory rate and oxygen saturation during observation in NICU, blood glucose checked as well as blood gas study for acid base balance with temperature control to prevent hypothermia and minimize oxygen consumption and shifted to mother’s side for institution of early breast feeding if uneventful stay NICU during observation for four hours.

Lalana Newborn Resuscitation (LNR) provides for quick and safe resuscitation by application of continuous positive airway pressure by sustained nasal oxygen inflation monitored by Pulse oximetry SpO₂ in determining oxygen flow rates of 2 L/min up to 15 L/min (FiO₂ 28%-76%), blown to the baby’s nostrils through wide bore oxygen tube for up to 60-180 seconds to initiate rhythmic respiration, SpO₂>96% and heart rate 120-160 bpm. Higher FiO₂ stabilizes hypoxic newborns at birth, reducing risk of hypoxia-induced inhibition of breathing and leading to a more stable breathing pattern with better aeration of the lung and increased lung volume, pulmonary compliance with Functional Residual Capacity (FRC), facilitating reflex cardiovascular changes compatible with adult life. The primary measure of adequate initial ventilation is the prompt improvement of heart rate and adequate cardiac output noted on plethysmograph waveform with circulation of oxygenated blood throughout the body resulting in aerobic cellular metabolism and removal of lactic acid, mitigating hypoxia positively impacts postnatal adaptation of newborns with minimal ill effects thus decreasing the morbidity and mortality associated with hypoxic ischemic tissue (brain, heart, gut and kidney) injury and untoward long-term sequela.

DOI: http://dx.doi.org/10.46889/JCMR.2021.2305
**LNR METHODOLOGY**

**Protocol I**

Lalana Newborn Resuscitation (LNR) Protocol I, provides quick and safe resuscitation by sustained nasal oxygen inflation oxygen flow rates 2 L/min up to 15 L/min (FiO₂ 28% to 76%) determined by Pulse oximetry score (L/min-Litres per minute, HR / beats per minute-Heart Rate/bpm, ET- Endotracheal Tube) (Table 3).

<table>
<thead>
<tr>
<th>Classification</th>
<th>Protocol I</th>
</tr>
</thead>
<tbody>
<tr>
<td>‘Normal’ Healthy</td>
<td>Zero Pulse oximetry Score - SpO₂ 96% - 100%, spontaneous onset of rhythmic breathing, rate 30-60/min and HR±120-160 bpm. Routine newborn care maintaining asepsis and thermo-control. Shift newborn to mother’s side and initiate early nutrition, by breast-feeding within an hour in normal delivery and four hours after LSCS.</td>
</tr>
<tr>
<td>Grade I</td>
<td>+1 Pulse oximetry Score - SpO₂ &gt;96%, regular/irregular respiration, ± rate 20-30/min and HR ±100–119 bpm. Sustained nasal oxygen at flow rates 2-4 L/min (FiO₂ 28% to 36%), directed towards the nostrils through the wide bore tube for up to 60 seconds. Newborn wiped dry under radiant warmer with tactile stimuli, nasal and oral suction. Discontinue oxygen with Zero Pulse oximetry Score SpO₂&gt; 96%, with rhythmic breathing pattern, rate 30-60/min and HR 120-160 bpm. Shift newborn to NICU for observation for 4 hours and then to mother’s side and institute breast-feeding.</td>
</tr>
<tr>
<td>Grade II</td>
<td>+2 Pulse oximetry Score - SpO₂ 92-93%, irregular/respiration ± rate 15-20/min and HR ±100–80 bpm. Sustained nasal oxygen flow rate 5-8 L/min (FiO₂ 40% to 52%), directed towards the nostrils through the wide bore tube for up to 60-90 seconds. Neonate wiped dry under radiant warmer with tactile stimuli, nasal and oral suction. Discontinue oxygen with Zero Pulse oximetry Score SpO₂&gt; 96 with rhythmic breathing pattern, respiratory rate 30-60/min and HR &gt;120 bpm. Shift to NICU for observation for 24 hours or management and treatment of complications if any.</td>
</tr>
<tr>
<td>Grade III</td>
<td>+3 Pulse oximetry Score - SpO₂ 90-91%, gasping respiration, ± rate 10-15/min and HR ± 80 - 60 bpm. Sustained nasal oxygen flow rate 8-12 L/min (FiO₂ 52% to 64%) directed towards the nostrils through the wide bore tube for up to 90-120 seconds or more. Neonate wiped dry under radiant warmer with tactile stimuli, back rubs, nasal and oral suction. Discontinue oxygen</td>
</tr>
</tbody>
</table>
### Table 3: Classification of newborns within 20-60 seconds of birth.

<table>
<thead>
<tr>
<th>Classification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Asphyxia</strong></td>
<td>with Zero Pulse oximetry Score SpO2&gt;96% with rhythmic breathing pattern, respiratory rate 30-60/min and HR &gt;120 bpm. Shift newborn to NICU for observation, management and treatment of complications if any.</td>
</tr>
<tr>
<td><strong>Grade IV Secondary Apnea</strong></td>
<td>+4 Pulse oximetry Score - SpO2 89%-50%, absent respiration and HR ±60-40 bpm. Sustained nasal oxygen flow rate 12-15 L/min (FiO2 64% to 76%), directed towards the nostrils through the wide bore tube for up to 120-180 seconds or more. Neonate wiped dry under radiant warmer with tactile stimuli, back rubs, nasal and oral suction. Discontinue oxygen with Zero Pulse oximetry Score, SpO2&gt;96%, with rhythmic breathing pattern, respiratory rate 30-60/min and HR &gt;120 bpm. Shift newborn to NICU for observation, management and treatment of complications if any.</td>
</tr>
<tr>
<td><strong>Grade V Terminal Apnea</strong></td>
<td>+5 Pulse oximetry Score - SpO2 &lt;50%, absent respiration and HR &lt;40 bpm, ‘Flat baby’ or no recording on pulse oximeter of SpO2 and heart rate and occasional heart beats on auscultation, immediately intubate with endotracheal tube and ventilate with continuous distending airway pressure by oxygen flow at rate of 15 L/min (FiO2 100%) for 120-240 seconds or more, if no onset of breathing within 60 seconds start cardiac compression around 120/min and medications of epinephrine or volume expanders, 5% dextrose saline at 10 ml/kg also combats hypoglycemia and Carbicarb 2.5 meq/kg (a mixture of Na2CO3/NaHCO3) but without the generation of CO2 slow infusion over one hour to combat metabolic lactic acidosis secondary to hypoxemia and cardio pulmonary disturbances or Sodium bicarbonate if newborn is breathing diluted at 8 ml eq/kg. If onset of rhythmic respiration and heart rate increases to &gt; 100bpm, remove ET tube and continue with sustained nasal oxygen inflation at flow rate 12-15 L/min ( FiO2 64% to 76%) directed towards the nostrils through the wide bore tube till onset of rhythmic breathing under radiant warmer with tactile stimuli, back rubs, nasal and oral suction. Discontinue oxygen with Zero Pulse oximetry Score, SpO2&gt;96%, rhythmic breathing pattern, respiratory rate 30-60/min and HR &gt;120 bpm. Shift newborn to NICU for observation, management and treatments of any complications. OR abort resuscitation after 5-10 minutes if unresponsive either fresh stillbirth or early neonatal death.</td>
</tr>
</tbody>
</table>
Protocol II

Protocol II-Lalana Newborn Resuscitation (LNR) of preterm newborns with gestational age <32 weeks and birthweight <1250g followed by bubble CPAP with blender and FiO₂<30% through nasal prongs to maintain SpO₂ around 95-96% (Table 4).

<table>
<thead>
<tr>
<th>CLASSIFICATION</th>
<th>PROTOCOL II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Healthy Preterm</td>
<td>Zero Pulse oximetry Score - SpO₂ &gt; 96% with onset of with rhythmic breathing pattern, respiratory rate 30-60/min, HR 120-160 bpm. Routine newborn care given. Start Bubble CPAP at 5 cm H₂O, FiO₂&lt;30% with blender through nasal prongs or Oxygen Hood with oxygen flow rate to maintain SpO₂ at 88-95%. Shift to NICU for observation, management and treatment of complications if any.</td>
</tr>
<tr>
<td>Grade I Mild Asphyxia</td>
<td>+1 Pulse oximetry Score - SpO₂ 94% - 95%, regular /irregular breathing, respiratory rate ± 20-30/min, HR ± 100-120 bpm. Sustained nasal oxygen at flow rate at 2-4 L/min (FiO₂ 28% to 36%), directed towards the nostrils through the wide bore tube for up to 60 seconds, gently wipe dry with tactile stimuli, nasal and oral suction under radiant warmer till SpO₂ ~ 95%, with rhythmic breathing pattern, respiratory rate 30-60/min and Heart Rate 120-160 bpm. Start Bubble CPAP at 5 cm H₂O, FiO₂&lt;30% with blender through nasal prongs or Oxygen Hood with oxygen flow rate to maintain SpO₂ between 88-95%. Shift to NICU for observation, management and treatment of complications if any.</td>
</tr>
<tr>
<td>Grade II Moderate Asphyxia</td>
<td>+2 Pulse oximetry Score - SpO₂ 92-93%, regular/irregular breathing, respiratory rate ± 15-20/min and HR ± 100 – 80 bpm, Sustained nasal oxygen flow rate 4 -6 L/min (FiO₂ 36% to 44%), directed towards the nostrils through the wide bore tube for up to 60-90 seconds, gently wipe dry with tactile stimuli, nasal and oral suction under radiant warmer. Discontinue oxygen flow when SpO₂ ~ 95%, with rhythmic breathing pattern, respiratory rate 30-60/min and Heart Rate &gt;120 bpm. Start Bubble CPAP at 5 cm H₂O, FiO₂&lt;30% with blender through nasal prongs or Oxygen Hood with oxygen flow rate to maintain SpO₂ between 88-95%.</td>
</tr>
</tbody>
</table>


DOI: http://dx.doi.org/10.46889/JCMR.2021.2305
| Grade III Severe Asphyxia | +3 Pulse oximetry Score - SpO2 90-91%, irregular/gasping breathing, respiratory rate ± 10-15/min and Heart Rate ± 80 - 60 bpm. Sustained nasal oxygen flow rate 6 -8 L/min (FiO2 44% to 52%) directed towards the nostrils through the wide bore tube for up to 90-120 seconds, gently wipe dry with tactile stimuli, nasal and oral suction under radiant warmer. Discontinue oxygen flow when SpO2 ~ 95%, with rhythmic breathing pattern, respiratory rate 30-60/min and Heart Rate >120 bpm. Start Bubble CPAP at 5 cm H2O, FiO2<30% with blender through nasal prongs or Oxygen Hood with oxygen flow rate to maintain SpO2 between 88-95%.

Shift to NICU for observation, management and treatment of complications if any. |
| Grade IV Secondary Apnea | +4 Pulse oximetry Score - SpO2 89%-50%, absent respiration and HR 60-35 bpm. Sustained nasal oxygen flow rate of 8 - 10 L/min (FiO2 52% to 60%), directed towards the nostrils through the wide bore tube for up to 120-180 seconds or more, gently wipe dry with tactile stimuli, back rub, nasal and oral suction under radiant warmer. Discontinue oxygen flow when Pulse oximetry SpO2 ~ 95%, with rhythmic breathing pattern, respiratory rate 30-60/min and Heart Rate >120 bpm. Start Bubble CPAP at 5 cm H2O, FiO2<30% with blender through nasal prongs or Oxygen Hood with oxygen flow rate to maintain SpO2 between 88-95%.

Shift to NICU for observation, management and treatment of complications if any. |
| Grade V Terminal Apnea | +5 Pulse oximetry Score - SpO2 <50%, absent respiration and HR <35 bpm 'Flat baby' or no reading on pulse oximeter of SpO2 and heart rate, with occasional heart beats on auscultation, immediately intubate with endotracheal tube and ventilate with continuous distending airway pressure by oxygen flow at rate of 12-15 L/min (FiO2 100%) if no breathing attempts by 60 seconds start cardiac compression around 120/min and medications of epinephrine or volume expanders, 5% dextrose saline at 10 ml/kg and start Carbicarb 2.5meq/kg, a mixture of Na2CO3/NaHCO3 safer with no generation of CO2 slow infusion over one hour that does not affect cerebral blood flow. If onset of rhythmic respiration and heart rate increases to >100bpm, remove ET tube and |
continue with sustained nasal oxygen inflation at flow rates of 4-6 L/min (FiO2 36% -44%), directed towards the nostrils through the wide bore with tactile stimuli, back rubs, nasal and oral gently wipe dry with tactile stimuli, back rub, nasal and oral suction under radiant warmer.

Discontinue oxygen flow when SpO2 ~ 95%, rhythmic breathing pattern, respiratory rate 30-60/min and HR>120 bpm. Start Bubble CPAP at 5 cm H2O, FiO2<30% through nasal prongs or Oxygen Hood with oxygen flow rate to maintain SpO2 between 88-95%.

Shift to NICU for observation and management / treatment of complications.

However resuscitative efforts may be aborted after 5-10 minutes in the event the preterm is unresponsive due high incidence of neurological, deficits cerebral palsy etc. or other organ deficits and untoward ill life-long sequelae.

Table 4: Classification of preterm <32 weeks and <1250g within 20-60 seconds of birth.

Results

The incidence of birth asphyxia was 21.4% among 1,383 consecutive singleton live births, during 14-month period from 1st April 2016 to 31st May 2017, I attended 60% (n=830/1383) deliveries, including vaginal deliveries both vertex and breech presentation, instrumental-vacuum and low/outlet forceps deliveries and surgical lower segment caesarean sections (LSCS) both emergency and elective. All newbons were assessed and classified within 20-60 seconds of birth as normal, healthy neonates or hypoxic/asphyxia Grade I-V who were all, successfully resuscitated utilizing continuous positive pressure ventilation by sustained nasal oxygen inflation at varying flow rates of 2-15 L/min for upto 1-3 minutes or more based on pulse oximetry readings.

Among 830 deliveries attended, a majority 78.5% (n=652/830) were ‘Normal’, healthy newborns with zero Pulse oximetry score, SpO2 96% -100%, heart rate 120-160 bpm with spontaneous onset of rhythmic respiratory rate of 30-60/min. There was a high incidence 21.4% (n=178/830) of birth asphyxia. The distribution of 830 deliveries attended revealed 78.5% Normal, healthy newborns and 21.4% hypoxic/asphyxiated newborns Grade I to V is seen in Table 5.
Majority 78.5% (n=653/830) of births attended, were normal, healthy newborns who established spontaneous rhythmic respiration at birth, while 15.1% (n=126/830) Grade I suffered from mild asphyxia, and 3.7% (n=31/830) Grade II had moderate asphyxia, only 2.1% (n=17/830) Grade III newborns had severe asphyxia while 0.4% (n=3/830) Grade IV had secondary apnea. Just 0.1% (n=1/830) Grade V newborn had terminal apnea. Sex distribution revealed five females to four males. The distribution of 830 births attended according to Grade I-V is seen in Table 6.

Distribution of 21.4% (n=178/830) hypoxic/asphyxiated newborns among births attended, revealed a majority 70.8% (n=126/178) Grade I newborns had mild birth asphyxia, +1 Pulse oximetry score, SpO₂ 94%-95%, while 17% (n=31/178) Grade II newborns with moderate asphyxia, +2 Pulse oximetry score, SpO₂ 92%-93% and only 9.5% (n=17/178) Grade III newborns had severe asphyxia, +3 Pulse oximetry score, SpO₂ 90-91% while 1.7% (n=3/178) Grade IV newborns suffered from secondary apnea, +4 Pulse oximetry score, SpO₂ 89%-50%, with absent respiration and Heart Rate <50 bpm while 0.5% (n=1/178) with Grade V had terminal apnea, +5 Pulse oximetry Score, SpO₂ <50%, with absent respiration and Heart Rate <30 bpm or ‘Flat baby’. Distribution of 178 newborns with birth hypoxia/asphyxia, Grade I to V is seen in Table 7.
In the present study all 178 hypoxic newborns Grade I-V were effectively resuscitated with onset of rhythmic breathing, by Lalana Newborn Resuscitation (LNR) outlined in Protocol I and Protocol II based on birthweight and gestation with wellbeing of the newborns during observation in NICU for four hours to monitor pulse, respiratory rate and oxygen saturation on pulse oximeter, temperature maintained to prevent hypothermia and minimize oxygen consumption, blood glucose checked as well as blood gas study for acid base balance etc newborn then shifted to mother’s side and breast feeding instituted with uneventful early neonatal period.

Discussion

Lalana Newborn Resuscitation (LNR) with effective resuscitation proves ideal for hypoxic newborns in improving neonatal health and reducing perinatal mortality and neonatal mortality and morbidity rates. India with a population of over 1.3 billion has 124, 419, 96 thousand births each year, approximately 10% of newborns require assistance to breathe with incidence of birth asphyxia ranging from 2 to 28 per 1000 live births with 6.6 lakh newborn dying in the neonatal period of whom 5.1 lakhs die within the first week of life with Early Neonatal Mortality Rate (ENMR) 20 per 1000 live births and Neonatal Mortality Rate (NMR) 26 per 1000 live births is concerning, Nigeria ranked second with 270, 000 newborn deaths being almost one half neonatal deaths reported in India, indicating that strategies aimed at reduction of early neonatal deaths will substantially reduce under-five child mortality rate, perinatal mortality rate being a sensitive indicator for monitoring health care status (51, 52).

The incidence of Birth asphyxia was 21.4% with all 178 hypoxic/asphyxiated Grade I-V newborns successfully resuscitated by Lalana Newborn Resuscitation (LNR), the most safe resuscitative method that is proven both scientifically and physiologically that application of continuous positive pressure ventilation by sustained nasal oxygen inflation because lungs are filled so fluid, studies have shown that high pressure 25-30 cm H$_2$O is needed for the first inflation for about five seconds so whole lung becomes inflated and foetal lung fluid has been displaced from the alveoli then lungs continued to be inflated at lower 10-15 cm H$_2$O (38-40). Thus oxygen at flow rates of 2-15 Litres/min (FiO$_2$ 21% to 76%), is key to effective resuscitation in quick reversal of hypoxia with onset of rhythmic respiration with prompt increase in heart rate as being a sign of adequate lung aeration based on the concept that a low heart rate indicates vagal-induced bradycardia in response to perinatal asphyxia facilitates smooth physiological cardiovascular changes transiting from fetal to neonatal life monitored continuously by Pulse oximetry SpO$_2$ achieve aim of effective resuscitation with reduction in perinatal and neonatal mortality and morbidity in reducing adverse long-term hypoxic neurodevelopmental ill sequelae, so children should be normal.

In contrast non-physiological resuscitation by NRP by bag and mask or invasive endotracheal intubation with short intermittent inflation lacks scientific clarity regarding transition of fluid filled fetal lungs to well aerated neonatal lungs, as short intermittent bursts of air/oxygen does
not generate adequate intrapulmonary pressure but also proves potentially harmful as entire tidal volume will only enter previously aerated regions due to the much lower airway resistance predisposes to lung injury with overexpansion and intermittent collapse of alveoli causing ventilation perfusion (V/Q) mismatch, persistent pulmonary hypertension and bradycardia that further perpetuates hypoxia with delay in onset of breathing [29,30,35,37]. Thus continuous distending airway pressure by sustained oxygen inflation is the key to mitigating hypoxia-induced inhibition of breathing [53,54].

**LNR Includes 3 Steps:**

**Step 1:** Assessment of newborn by continuous Pulse oximetry monitoring that automatically and within few seconds provides an estimate of newborn’s health status. The pulse oximeter is clamped to baby’s foot within 20-60 seconds after birth timed at complete expulsion of fetus. In hypoxic newborns with immediate clamping and cutting of umbilical cord, however umbilical cord ligation may be delayed up to 3 minutes in healthy newborns with spontaneous onset of respiration and heart rate >120 bpm [54].

**Step 2:** Classification of newborns based on zero pulse oximetry score by SpO₂, as ‘Normal’, healthy newborns. ‘Normal’ healthy newborns have zero pulse oximetry score, SpO₂ 96%-100%, spontaneous onset of rhythmic breathing pattern, respiratory rate 30-60/min and heart rate of 120-160 bpm. Hypoxic/asphyxiated newborns are further graded into Grade I to V based on +1+5 Pulse oximetry score, SpO₂ <96%, presence or absence of breathing and heart rate. However grading of hypoxic newborns into Grade I-V by criteria of +1 to +5 pulse oximetry score, SpO₂ <96%, respiratory rate <30/ min and heart rate <120 bpm, to determine sustained nasal oxygenation may vary as real time assessment of newborn’s SpO₂ is constantly changing due to continuous monitoring, oxygen is however discontinued at SpO₂ 96%.

**Step 3:** Lalana Newborn Resuscitation Protocol I and II, by continuous positive pressure ventilation by sustained nasal oxygen inflation, flow rates determined by Pulse oximetry score, facilitate onset of rhythmic breathing with effective resuscitation maintaining thermo-control and asepsis.

Among 830 deliveries attended, majority 78.5% (n=653/830) were normal, healthy newborns who established spontaneous rhythmic respiration, rate 30-60/min at birth with zero Pulse oximetry score, SpO₂ 96%-100%, heart rate of 120-160 beats per minute (bpm). While among newborns with birth asphyxia, Grade I newborns, 15.2% (n= 126/830) had mild birth asphyxia +1 Pulse oximetry Score, SpO₂ 94%-95% with regular/irregular respiration, rate ±20-30/ min, heart rate ±100 - 119 bpm, Grade II newborns comprised 3.7% (n=31/830) had moderate birth asphyxia +2 Pulse oximetry Score, SpO₂ 92-93% with regular/ irregular breathing, respiratory rate 15-20/min, ± heart rate 100 - 80 bpm and Grade III newborns 2.1% (n=17/830), had severe birth asphyxia +3 Pulse oximetry Score, SpO₂ 90-91% with irregular or gasping respiration, rate 10-15/min, heart rate 80-60 bpm and Grade IV newborns 0.4% (n=3/830), with secondary apnea +4 Pulse oximetry score, SpO₂ 89-50%, heart rate < 60 bpm with absent respiratory effort. Grade V newborns constituted 0.1% (n=1/830) with terminal apnea +5 Pulse oximetry score, SpO₂ <50%, absent breathing and heart rate < 30 bpm, in the event of no recordable
pulse oximeter readings for SpO\(_2\) and heart rate within 60 seconds continuous distending pressure ventilation through endotracheal intubation of sustained oxygen flow at 15 L/min (FiO\(_2\) 100%) with cardiac compression of 100-120/min and medications of epinephrine or volume expanders, 5% dextrose saline at 10 ml/kg, to also combat hypoglycemia. Sodium carbonate in ventilating newborns or Carbicarb 2.5meq/kg (a mixture of Na\(_2\)CO\(_3\)/NaHCO\(_3\)) for metabolic lactic acidosis secondary to hypoxemia and cardio pulmonary disturbances which does not generate CO\(_2\), newborn is extubated at onset of breathing and resuscitation continued with sustained nasal oxygen flow at 8-12 L/min (FiO\(_2\) 52% to 60%), till Zero Pulse oximetry score, SpO\(_2\) 96%-100%, regular breathing pattern respiratory rate 30-60/min and heart rate of 120-160 beats per minute (bpm), oxygen flow is discontinued [56].

Grade V newborns with terminal apnea are often subjected to severe perinatal asphyxia especially after prolonged labour due to failed trial with undetected cephalo-pelvic disproportion often associated with high risk of intrauterine death i.e. fresh stillbirths and usually delivered by quick obstetric intervention by emergency LSCS, termed as fresh stillbirth if born without signs of life or early neonatal death with signs of life with failed resuscitation including endotracheal intubation upto 5-10 minutes with CPPV and 100% oxygen flow at 15 L/min (FiO\(_2\) 100%) may abort resuscitative efforts due to high incidence of HIE with lifelong untoward neurological sequelae.

However though introduction of Neonatal Resuscitative Program (NRP) resulted in significant worldwide reduction in asphyxial neonatal deaths but nearly half of survivors suffered from permanent neurological deficits depending on the extent of insult, varying from mild ill effects to severe hypoxic ischemic encephalopathy or multi-organ complications and death within the first few days [11,13,31,44-49]. Since mild perinatal hypoxia occurs more frequently than severe events, it is associated with substantial long-term effect on the population, who are at increased risk of low intelligence or Intelligent Quotient (IQ) scores <80 affects a large proportion of adults with poor scholastic performance and other deficits include impaired cognition, mild autism, lack of development of fine motor skills, memory and mood disturbances etc. with over 200 million children not attaining age appropriate development while severe perinatal asphyxia in survivors may result in hypoxic ischemic encephalopathy which over past few decades has remained the same [45,47-49].

Fetal asphyxia first evokes gasping but prolonged asphyxia depresses central nervous system including respiratory centre, such that newborns do not respond to normal stimuli augmenting onset of breathing. However dramatic transition takes place at birth, as organ of gas exchange switch from placenta in the fetus to the lungs in the newborn occurring at onset of rhythmic breathing, often within 10 seconds of birth or even after 60-90 seconds at time of clamping of cord which however predisposes to hypoxia that acts as a major stimulus to breathing including chilling of the skin at birth and stimulation of receptors near larynx when airways are cleared of liquid as well as the increased sensitivity of carotid chemoreceptors to hypoxia have all shown to augment breathing [57-59].

The more severe the perinatal asphyxia the longer it will take longer for the newborn to breathe more so with Neonatal Resuscitation Program (NRP) that requires a team of usually four or more skilled birth attendants administering IPPV resuscitation with bag and mask or
endotracheal intubation if heart rate remains below 60 beats per minute for external cardiac massage using two fingers to depress the lower sternum at approximately 120 times a minute while continuing with respiratory assistance in a ratio of 1:5. Medications such as Epinephrine or volume expanders at recommended dose of 10ml/kg of saline is administered, which can be repeated to increase cardiac output [29,30].

Resuscitative efforts aborted after 10-20 minutes with NRP justified due to association of high mortality or morbidity in survivors with severe neuro-developmental disability and hence a coordinated approach by obstetrician, neonatal team and parents is important. Resuscitation may also be withheld in extremely immature newborns with gestational age <23 weeks and birth weight below 400g or in newborns with lethal congenital malformations, not compatible with life, e.g. anencephaly etc. [29,30].

In contrast resuscitation by LNR methodology by three simple steps may be administered by a single birth attendant, is dramatic due to impact of oxygenation with onset of regular breathing as continuous positive pressure ventilation with varying oxygen flow rate (Litres per minute) that not only helps keep airway open but also maintains ventilation perfusion, by improving oxygenation prevents hypoxic pulmonary vasoconstriction decreasing right to left intrapulmonary shunting, significantly reduces fraction of cardiac output passing through unventilated alveoli [53]. Air has 21% oxygen or FiO$_2$ 0.21 which mixes with oxygen, increasing concentration of oxygen, approximately by 4% per litre. At the first breath the peak inspiratory flow is 20-30 L/min, thus CPPV with oxygen at flow rate of 10 L/min, mixes with 20 L/min of air, with FiO$_2$ 0.60, hence pure 100% oxygen is never administered [55,56]. However in NRP, use of tight fitting mask or endotracheal intubation can increase FiO$_2$ up to 100%. In addition oxygen saturation stated by NRP seems unacceptable with long delay in hypoxic new-borns to achieve SpO$_2$ >90%, as stated in protocol, oxygen saturation at 1 min 40-45%, 2 min 65-75%, 3 min 70-75%, 4 min 75-85%, 5 min 80-85% and 10 min 85-95% [29,30]. In LNR even oxygen flow rate of around 2 L/min creates continuous distending pressure throughout respiratory cycle with onset of breathing neonates provides intrinsic Positive End Expiratory Pressure (PEEP), helps keep alveoli open to achieve optimal gas exchange facilitating quick physiological transition from fetal to neonatal life soon after birth, monitored by pulse oximeter requires minimal training of birth attendants in contrast to highly trained birth attendants a prerequisite in NRP [60].

NRP recognizes several significant gaps in knowledge related to neonatal resuscitation as current recommendation are based on weak evidence lacking well designed large well controlled trials (RCTs) as opposed to a large controlled study of LNR versus NRP that may be undertaken in the delivery room [29]. In LNR the quick reversal of hypoxia by supplementary oxygenation is the key to successful resuscitation in perinatal asphyxia. Lack of oxygen causes anaerobic glycolysis and metabolic acidosis that result in primary energy failure or deprivation of high energy phosphate, causing cellular damage and multi-organ failure with renal failure, hypoxic myocarditis and neurological damages etc. Also severe hypoxia causes interference with the production of clotting factors from the liver and may initiate DIC also a strong association between hypoxia and intraventricular hemorrhage as cause of death in preterm as increase in intravascular pressure ruptures vulnerable vessels in
the germinal matrix. Hypoxia is also a major factor in necrotizing enterocolitis with interference of blood to the gut [61,62].

The longer hypoxemia, the more severe the sequelae, combating with oxygen supplementation results in prompt increase in heart rate with circulation of oxygenated blood throughout the body improving cellular function by conversion of anaerobic metabolism to aerobic with utilization glucose and generation of 38 mols of Adenosine Triphosphate (ATP) instead of 2 mols of ATP with the removal of lactic acid from tissues [63,64]. Thus Lalana Neonatal Resuscitation (LNR) with oxygenation is a safe resuscitative method physiologically and scientifically proven utilizing continuous positive pressure ventilation by sustained nasal oxygen inflation with higher fraction of inspired oxygen (FiO2), determined by Pulse oximetry SpO2 score, quickly reverses hypoxic injury while initiating rhythmic respiration with circulation of oxygenated blood throughout the body, as well as reducing adverse hypoxic neurological or organ deficits so that children should be normal serves to achieve the aim of effective resuscitation.

When oxygen/air enters the lungs, the normal fetal partial pressure of oxygen (PAO2) levels of 25mmHg rises sharply to above 60 mmHg, resulting in dilation of pulmonary vasculature at birth facilitated by development of surface tension forces in the alveoli that exert radial traction on blood vessels with increase in blood flow through the lungs and pressure in left atrium rises, along with cessation of umbilical circulation, the right atrial pressure falls slightly resulting in closure of foramen ovale and ductus arteriosus constricts in response to increasing PO2 once breathing has started with the entire cardiac output must flow through the lungs allows for full oxygenation of blood [65-67].

Hypoxia is a potent inhibitor of spontaneous respiration and lack of oxygen causes anaerobic glycolysis and metabolic acidosis due to accumulation of lactic acid, hypoxia and acidosis therefore impairs cardiac function and increases pulmonary vascular resistance. The low pH worsens pulmonary vasoconstriction with right to left shunting through foramen ovale and ductus arteriosus and venous blood bypasses lungs to enter aorta with serious consequences causing life threatening hypoxic injury in newborns [63,65,67]. Continuous positive pressure ventilation with sustained nasal oxygen inflation facilitates lung fluid reabsorption at birth, enabling smooth transition from fetal to extra uterine life. Thus oxygen therapy in hypoxic newborns is the only specific treatment to prevent or mitigate the effects of hypoxia to decrease central apnoea and promote regular breathing pattern that is the key to successful resuscitation [38-40]. Oxygen flow rate is determined by grading of hypoxic newborns into Grade I-V, varying from 4 L/min up to 15 L/min with approximate FiO2 36% to 75% respectively, creates continuous distending pressure to achieve optimal gas exchange that stimulates the central respiratory centre to initiate rhythmic respiration, avoiding hypoxemia and hypercapnia that is associated with rise in arterial carbon dioxide causing reduced blood flow to the brain and ischemia with altered mental status [40,53,54].

Some newborns who remain short of breath or have transient tachypnoea (wet lung) for a few hours or occasionally one to two days later after birth due to delayed removal of fetal lung fluid as IPPV with bag and mask provides insufficient transpulmonary pressure for clearance of lung fluid that remains in the alveolar walls and adequate oxygenation is required for reversal of
hypoxia being the only specific treatment [68]. Randomized controlled trials show sustained oxygen inflation decreases need for intubation and mechanical ventilation [69,70]. Animal studies have suggested that a longer sustained inflation may be beneficial for establishing residual capacity during transition from fluid filled to air filled lungs after birth and randomized controlled trials have also demonstrated benefit of sustained inflation decreases need for intubation and mechanical ventilation as well, because lungs are filled so fluid, high pressure 25-30 cm H$_{2}$O is needed for the first inflation applied for five seconds so whole lung becomes inflated and foetal lung fluid has been displaced from the alveoli then lungs can be inflated at lower 10-15 cm H$_{2}$O [39,66].

In LNR despite oxygen FiO$_{2}$ 1.0 or 100% blown through the oxygen tube to baby’s nostril, first breath requires a peak inspiratory flow of around 20-30 L/min or 8 L/kg/min, for e.g. a baby weighing 3500 g, requires approximately 28 L/min, to meet inspiratory flow in addition to oxygen at flow rate of 10 L/min, therefore another 18 L/min of air is sucked in from surrounding atmosphere with FiO$_{2}$ of 21%, hence (10 x 100) + (18 x 21) =1378%, 1378 divided by 28 = gives FiO$_{2}$ 49%. Therefore the air/oxygen mixture inhaled has a FiO$_{2}$ 0.49 or 5% obviating both hyperoxia and mitigating hypoxia [53,54,60].

In contrast NRP with tight fitting mask or endotracheal intubation increases FiO$_{2}$, to 1.0 or 100% predisposes to hyperoxia with its deleterious effect of slowing cerebral blood flow in both term and preterm infants, as also even brief periods of supplemental, uncontrolled exposure of 100% oxygen results in generation of oxygen free radicals, which have a role in reperfusion injury, contributing to eye (ROP), causing blindness, lung injury and altered mental status in preterm [70-73]. In addition intermittent inflation with bag and face mask does not generate adequate intrapulmonary pressure to displace alveolar fluid and also because gastric distension occurs and satisfactory oxygenation in fetal fluid filled lungs is not possible, studies have detected un-even alveolar ventilation during a single breath even with oxygen resulting in decreased pulmonary perfusion, V/Q mismatch further perpetuating hypoxia, hypercarbia and acidosis since pulmonary arterioles remain constricted with right to left shunt through foramen ovale and ductus arteriousus interfering in transition of fetal to neonatal cardiopulmonary circulation [32,35-37]. Newborns remain extremely vulnerable to reopening of fetal right to left shunts for several days to even weeks after birth due to pulmonary vasoconstriction and if PO$_{2}$ of lung tissue falls, further compounded by low pH, that worsens pulmonary vasoconstriction has serious consequences with bypass of venous blood into the aorta being probably the single most life threatening result of hypoxia in the neonatal period as anatomical closure usually takes place by about two weeks of age [34,67]. As such the peripheral oxygen saturation stated by NRP with IPPV seems unacceptable with long delay in hypoxic new-borns to achieve normal SpO$_{2}$ 96%, advocating oxygen saturation at 1 min with SpO$_{2}$ 40-45%, 2 min 65-75%, 3 min 70-75%, 4 min 75-85%, 5 min 80-85% and at 10 min SpO$_{2}$ 85-95% [29,30].

In the fetal lungs surfactant is secreted by the 7th month of gestation and Type II pneumocytes in neonatal lungs, secrete a thin lining of alveolar fluid that combines with surfactant to form an aqueous protein containing hypophase with overlying phospholipid film composed mainly of dipalmitoyl phosphatidylcholine to create a moist surface conducive to gas exchange by lowering surface tension, open alveoli and prevent atelectasis, gases first dissolve in the
alveolar lining fluid and then diffuse across type I, extremely thin squamous alveolar cells and pulmonary arteriolar capillary membrane to combine with haemoglobin [34,74]. Thus oxygenation is the process of taking oxygen from inspired air that diffuses passively from the alveoli to pulmonary capillaries where it binds to haemoglobin forming oxyhaemoglobin and a small amount dissolves in plasma. In the newborn gas exchange occurs in the lungs by two mechanisms for oxygen delivery to the body, 98.5% oxygen is bound to haemoglobin, which is assessed by Pulse oximetry SpO₂, being almost similar to SaO₂ measured by Arterial Blood Gas (ABG) analysis, while some oxygen is dissolved in the plasma, accounts for only 1.5% transport to tissues.

Each haemoglobin molecule carries four molecules of oxygen bound to the iron of the heme prosthetic group. There are about 270 to 300 million haemoglobin molecules present in one-third of erythrocyte cytoplasm which are relatively short lived about 100 to 220 days. As the first oxygen molecule binds to haemoglobin tetramer, it induces a change in shape of haemoglobin that increases its ability to bind to three other molecules of oxygen, reflecting cooperative interaction between haemoglobin and oxygen molecules, thus each haemoglobin tetramer binds to four molecules of oxygen and a gram of haemoglobin can combine with 1.34 ml of oxygen. Hence blood with normal haemoglobin concentration of 15g/dl. 100 ml carries approximately 20 ml of oxygen in addition a small quantity of oxygen is dissolved in blood. If haemoglobin tetramer binds to only three molecules of oxygen instead of four, it leads to hypoxia and deoxyhaemoglobin. However if the partial pressure of oxygen in the alveoli is high, then four molecules of oxygen binds haemoglobin binds to form oxyhaemoglobin [74].

However a lack of oxygen in the blood means that body tissues will not be oxygenated properly causing damage to the organs is an indication of serious pulmonary tissues [74]. While oxygen delivery is the rate of oxygen transported from the lungs to the peripheral tissue and oxygen consumption is the rate at which oxygen is removed from the blood for use by the tissues. Oxygenated blood sustains aerobic cellular metabolism throughout the body, wherein oxygen is used to convert glucose to Adenosine Triphosphate (ATP). Insufficient oxygenation is termed hypoxemia, causes low partial oxygen tension that refers to abnormally low oxygen content in tissue or organ with residual neurological and organ deficits. Arterial blood flows from the heart to parts of the body laden with oxygen where it diffuses to the surrounding tissues with low partial pressure of oxygen and oxyhaemoglobin releases oxygen to cells to form deoxyhaemoglobin. Diffusion of oxygen is related to partial pressure of oxygen (PAO₂) from the alveoli into the pulmonary capillaries (PaO₂), depends on the Alveolar-arterial (A-a) gradient, normal range of difference between PAO₂ PaO₂ being 5-10 mmHg, but collapsed, fluid filled or unventilated alveoli with VQ mismatch shunt, reflects a rising A-a gradient, that impairs oxygen diffusion across the alveolar - pulmonary arteriolar capillary membrane into the blood stream [74].

The normal partial pressure of oxygen in the alveoli (PAO₂) is FiO₂ 0.21 or 21% at atmospheric pressure of 760mmHg, breathing in room air at sea level is around 80 to 100 mmHg, therefore about 90% of oxygen in healthy lungs makes it to the blood. However when PAO₂ is >90%, the increase in PAO₂ has relatively little impact on oxygen saturation by haemoglobin, as there can be no further increase in saturation however high the PAO₂ rises with supplemental oxygen. If however the alveolar partial pressure (PAO₂) falls to 60 mmHg, less oxygen binds to
haemoglobin with rapid fall of oxygen in red blood cells. Hence alveolar partial pressure of oxygen at 100mmHg is much better than the alveolar partial pressure of oxygen of 80 mm Hg even though oxygen saturation of haemoglobin in blood will not change very much despite increments in oxygen supplement [74].

The relationship between the partial pressure of oxygen and oxygen saturation is shown by the oxygen disassociation curve. The sigmoid shape of the disassociation curve reflects the cooperative interaction between haemoglobin and oxygen molecules is initially steep and then flattens out, is a graphical representation of haemoglobin affinity to oxygen or the percentage of saturation of oxyhemoglobin at various alveolar partial pressures (PAO₂) of oxygen. The X axis of the oxygen disassociation curve represents the dissolved oxygen in linear relationship to its partial pressure resulting in a straight line on the horizontal axis and the proportion of haemoglobin in its saturated (oxygen-laden) forms the vertical Y axis against the prevailing oxygen tension.

Oxygen at high alveolar partial pressure (PAO₂) 100 mmHg drives oxygen on to the haemoglobin until 95-100% saturated. Haemoglobin releases oxygen as the blood passes through the tissues and partial pressure of oxygen (PvO₂) returning from the tissues (mixed venous blood) 40 mmHg is much lower than arterial blood. The most important aspect of the oxygen disassociation curve is that if the Pulse oximeter reading falls below 90%, the partial pressure of oxygen in the blood (PaO₂ or SaO₂) drops very rapidly and oxygen delivery to tissues is reduced that may lead to cardiac arrest, requiring quick resuscitative intervention. Pulse Oximeter provides a rapid tool in assessing adequate peripheral oxygenation or percentage of hemoglobin that is saturated with oxygen. In addition the plethysmograph indicates cardiac function by pulsatile changes as prompt increase in heart rate being a sign of adequate lung aeration is based on the concept that a low heart rate is due to vagal-induced bradycardia in response to perinatal asphyxia. Continuous Pulse Oximetry therefore empowers one to respond quickly and confidently to abnormal readings to determine supplemental nasal oxygen flow if SpO₂ falls < 96% [41,42,74].

Various factors affect haemoglobin’s affinity for oxygen. Right shift with decrease in oxygen affinity is influenced by lower pH, higher temperature, PCO₂ as well as high concentration of 2,3 diphosphoglycerate (2,3 DPG) produced from phosphoglyceraldehyde in response to hypoxia in red blood cells, an intermediate metabolite in the glycolytic pathway that binds to the beta chains of deoxyhaemoglobin and rearranges it into the T state by decreasing affinity for oxygen, hence more oxygen is released into tissue, indicating that haemoglobin allows more oxygen to be available to tissues but is also more difficult for oxygen to bind with haemoglobin in lungs. Fetal haemoglobin is the main oxygen transport protein in the human fetus during the last seven months of development and persists in newborn until six months of age to later form adult haemoglobin which has two alpha and two beta subunits, while fetal haemoglobin is composed or two alpha and two gamma subunits which shifts oxygen disassociation curve to the left compared to that of adult haemoglobin, resulting in greater affinity for oxygen, allowing the fetus to extract oxygen from maternal circulation, however oxygen disassociation curve in relation to partial pressure of oxygen is lower than normal adult haemoglobin based on lower P50 value or 6-8 mm Hg (Torr), difference due to decrease affinity for 2,3 Diphosphoglycerate
in that oxygen released from red blood cells requires a lower PaO₂ with left shift when compared to adult Hb [74,75].

Also hypoxia with anaerobic metabolism produces lactic acid causing metabolic acidosis that decreases pH and shifts the curve to the right, referred as Bohr effect, as the higher hydrogen ion concentration causes an alteration in amino acid residues that stabilises deoxyhaemoglobin in a T (taunt or tense) state that has lower affinity for oxygen, thus further promotes hypoxia. While left shift indicates increase affinity of haemoglobin for oxygen binding at any given PAO₂ with increase oxygen transport to tissues, as blood passing through the lungs gives CO₂ and H⁺ ions in the form of carbonic acid that increases oxygen binding to haemoglobin. Tissues have low oxygen concentration and oxyhemoglobin releases oxygen to form deoxyhaemoglobin, thus diffusion of oxygen from haemoglobin to tissue cells is enhanced by this process and corresponds to the steep portion of the ‘S’ shaped curve [74,75].

Oxygenation in LNR is from high pressure sources such as cylinder or piped wall supply that first passes through a pressure regulator to a lower pressure which then flows through the flow meter, controlled by a valve for litre flow per minute. Sustained positive pressure is maintained according to the flow rate of oxygen dialled on flow meter usually between 1-15 Litres per minute (L/min) while FiO₂ is defined as the percentage concentration of oxygen inhaled or fraction of inspired oxygen. Air gives 21% oxygen equivalent to FiO₂ 0.21 and flow rate of 1 L/min gives an oxygen increment of approximately 4% or FiO₂ 0.04 for each increased in litre/min flow i.e. FiO₂ 24% when 1 L/min oxygen flow is mixed with air. Thus flow rate of 6 L/min gives oxygen concentration of 45% or FiO₂ 0.45 or volumetric fraction of oxygen that mixes with air during inhalation. Therefore even though 100% oxygen or FiO₂ 1.0 through flow meter which is connected to either medical wall supply or oxygen cylinder at varying flow rates between 1-15 L/min dialled on flow meter, is bubbled through a bottle containing 5 cm water for humidification, passes through the wide bore oxygen tube, mixes with room air on inspiration resulting in FiO₂ of 0.24 up to 0.72 i.e. 24% to 72% oxygen but never 100% oxygen on inspiration by the neonate. In addition a wide bore oxygen tube proves advantageous in allowing for quick adjustment of varying oxygen flow rates between 2 L/min to 15 L/min without the requirement for changing from low to high flow oxygen delivery devices [53,54,60,69].

Low flow oxygen delivery devices allows oxygenation of FiO₂ <35%, while moderate oxygen flow delivery devices allows FiO₂ 35% -60% and high oxygen flow delivery devices allows FiO₂ >60. Low flow oxygen delivery devices includes paediatric nasal cannula consisting of a thin tube with two small nozzles that inserts into the nostrils and allows oxygen at flow rate of 2-4 L/min with approximate FiO₂ 0.28-0.36. Simple face mask allows oxygen flow of 5-6 L/min with FiO₂ 0.32-0.36. Higher oxygen flow rate require humidification with minimum 5 L/min to flush carbon dioxide (CO₂) from mask in breathing patients and to protect mucosa of nostrils from drying. Partial rebreather allows oxygen flow of 6-8 L/min sufficient to keep reservoir bag from deflating during inspiration, does not have a one way valve [69].

High oxygen flow device, the Venturi mask has a one way valve over port that limit entrainment of room air with humidified oxygen flow rate of 6 L/min upto 15 L/min and approximate FiO₂ 0.44 to 0.78. The non-breather mask is high flow device with one-way valves to exit exhaled air and draw oxygen from attached reservoir bag with oxygen flow rates of 10
L/min to 15 L/min, delivers approximate FiO₂ 0.70 up to 1.0, if mask is properly fitted to 100% oxygen as with endotracheal intubation. An aerosol generating device will deliver FiO₂ anywhere from 0.21 to 1.0, depending on the set up usually at 10 L/min and desired FiO₂ is selected by adjusting an entrainment collar located on the top of the aerosol container with humidity device connected to the flow meter through wide bore tubing that connects to patient’s mask [53,54,69].

While Continuous Positive Airway Pressure (CPAP) is a non-invasive nasal type of respiratory support in spontaneously breathing preterm newborns, CPAP with blender to maintain <30% FiO₂ in delivery room is recommended for early rescue of preterm babies <32 weeks and <1250g for respiratory acidosis, respiratory distress syndrome, recurrent apnoea, atelectasis etc. [76-80]. Bubble CPAP with blender allows for increase in FiO₂ with increasing oxygen saturation in newborn but not in oxygen flow rate, preterm < 32 weeks have periodic breathing and may have short attacks of apnea due to immaturity and inadequate control of breathing. Prolonged apnea results in hypoxia, so instead of breathing air by CPAP, increasing PaO₂ by 23%-25% or 50 mmHg raises PAO₂ to about 70-80 mmHg. Oxygen bubbled through 5 cm water in a bottle with FiO₂ <0.3 or <30% produces small airway pressure oscillations that improves gas exchange and lung function to maintain oxygen saturation between 90%-96% avoids routine intubation in management of respiratory distress syndrome, as well as decreases surfactant need by 50% and provides post extubation respiratory support effectively reducing broncho-pulmonary dysplasia [76-81]. However in low income Asian countries with limited resources, oxygen hood may also be used instead of CPAP machine, the oxygen flow rate adjusted to maintain preterm SpO₂ around 95% managed with parenteral fluids and treatment of any complications.

CPAP titrated pressure is prescribed pressure of steady oxygen flow rate between 4-8 L/min ensures bubbling through 5 cm H₂O to deliver constant air pressure into the baby’s nose through nasal prongs, enabling air sacs to stay open by increasing Functional Residual Capacity (FRC) and maintaining lung volume during expiration, prevents atelectasis by building up Positive End Expiratory Pressure (PEEP) or alveolar pressure above atmospheric pressure that exists till the end of expiration preventing alveolar collapse and apnea, making it easier for the baby to breathe independently. Also any decrease in lung volume (FRC) decreases surface area for gas exchange with intrapulmonary shunting or V/Q mismatch perpetuating hypoxia [76-80].

While extrinsic PEEP is applied by ventilator, intrinsic PEEP is facilitated by sustained nasal oxygen flow with higher FiO₂ as well as by incomplete expiration. Pressure support PEEP or pressure applied during inspiration causes progressive air trapping (hyperinflation). This accumulation of air increases alveolar pressure at the end of expiration. Alveolar gas equation used to calculate alveolar pressure with any given FiO₂ is PAO₂=FiO₂ × PBAR-PH₂O - PACO₂/RQ. If PH₂O at 37°C = 47 mm Hg, PBAR or barometric pressure at sea level varies from 745 to 765mmHg or 747mmHg, PACO₂ = arterial PaCO₂ = 40 mmHg and RQ = 1, then PAO₂= PAO₂ (700)-PaCO₂. Infant breathing 30% O₂, (FiO₂= 0.3) has arterial CO₂ of 40 mmHg then Alveolar oxygen tension: PAO₂ = 0.3(700)-40mmHg = 170mmHg [53,54,69].
Pre-oxygenation is dangerous and an ineffective practice [81]. Effective oxygen therapy is delivering the lowest FiO₂ to achieve normal oxygen saturation based and heart rate assessed according to Grade II -V, based on Pulse oximetry SpO₂ thus preventing hypoxia and hyperoxia, LNR with sustained positive pressure ventilation establishes an ideal approach in resuscitating hypoxic/asphyxiated newborns, transiting from fluid filled fetal lungs to uniformly well aerated neonatal lungs by avoiding inappropriate supplemental oxygen therapy based on Pulse oximeter SpO₂, oxygen flow discontinued at zero score SpO₂ >96% [60]. The dangers of Neonatal Resuscitation Program (NRP) in that tight fitting face mask or endotracheal intubation predisposes to hyperoxia with FiO₂ up to 0.8-1.0 has deleterious effect of slowing cerebral blood in both term and preterm infants and reperfusion injury with generation of oxygen free radicals, may cause injury to eye (ROP) and lungs in preterm, high regional cerebral oxygen saturation may predispose to periventricular haemorrhage with increased incidence of necrotizing enterocolitis [29,30,71-73]. However randomized trials (SUPPORT) and benefits of oxygen saturation targeting (BBOT), the best oxygen profiles to reduce ROP while optimizing the health of preterm and their development remain unknown [71,72,82-86].

Neurodevelopmental impairment may be observed among extremely premature infants at 18-22 months of age [82]. However SpO₂ 85-89% in extremely preterm was associated with increased mortality at the time of discharge compared to higher 91-95% (19.9% vs 16.2%; p=0.045), preferably preterm newborns should not be exposed to either damaging hyperoxia with SpO₂ 100% or hypoxia SpO₂ <95% [71-73,85,89].

Initiation with room air remains controversial as current Neonatal Resuscitation Program (NRP) guidelines suggest using air or blended oxygen to titrate oxygen to meet preductal saturation SpO₂ at 85-94%, but there are no studies to justify any particular starting oxygen concentration [86-90]. In LNR maximum FiO₂ of upto 68% id administered through sustained nasal inflation and at no time is 100% oxygen administered except with endotracheal intubation in Grade V preterm with poor circulation and low arterial oxygen saturation in asphyxiated babies, who are subject to high mortality rates [60]. Though to date no randomized trials of strategies to achieve the NRP recommended interquarteli range of preductal saturations have been conducted in preterm neonates, perhaps maintaining SpO₂ around 95-96% would be ideal in preventing both hypoxia and hyperoxia [86-90].

Pulse oximetry SpO₂ readings follow the Gaussian curve of normal distribution and equipment bias, within ± 1 Standard Deviation (S.D.) of true arterial oxygen saturation 68% of the time, then SpO₂ 90% is 1% on equipment bias then true arterial saturation will be 89%, 90% or 91%. If monitor has 3% bias then SpO₂ 90% will be between 87% and 93% for 68% of the time and as such, a difference of 1-2% may be inconsequential. The alarm limits should preferably be set at 1% or 2% above or below the chosen target range, high alarm should be set at 95% to avoid PaO₂ of >80 mmHg and lower limits should be set at ≥85% when breathing supplemental oxygen with FiO₂ > 0.21 with careful attention on averaging and sensitivity of monitors. Since there is no definite conclusive evidence for ideal oxygen saturation in extremely premature newborns, it is perhaps best to avoid both hypoxia as well as hyperoxia by maintaining oxygen saturation of SpO₂ around 95% to 96% [87-91].
The assessment of peripheral oxygen saturation specifically in peripheral arterial blood by Pulse Oximeter was developed by Takuo Aoyagi in 1935, is a small non-invasive portable device is of particular value in neonatal units to prevent hypoxia and hyperoxia, is also known as the fifth vital sign, the first four being Temperature, Pulse, Respiratory rate and blood pressure (TPR and +BP) [41]. The Pulse oximeter probe consists of two parts, Light Emitting Diodes (LEDs) and light detector called photo-detector which notes how much light at each red and infrared wave length has been absorbed and determines the ratio of the two wave lengths.

Light emitted from light source passes through the body part to a photo detector that measures amount of light absorbed according to Beer’s law that states that the amount of light absorbed is proportional to the concentration of light absorbing substance and Lambert’s law, which states that the amount of light absorbed is proportional to the length of the path light has to travel in the absorbing substance. Red light is absorbed by deoxyhemoglobin and infrared light by oxyhemoglobin. The ratio of the absorbed red light and infrared light differs and the microprocessor calculates a value for the oxygen saturation in the pulsing arterial blood excluding venous blood, skin, bone, muscle fat etc. providing percentage of haemoglobin saturated with oxygen within seconds, being almost similar to arterial oxygen saturation (SaO2) measured by Arterial Blood Gases (ABG) analysis [41,42].

Pulse oximeter also provides reading of heart rate, the increase in heart rate indicating adequate lung aeration and circulation of oxygenated blood. Also pulsatile change in absorbance due to pressure changes in arteriolar blood volume in the skin represented in graphical form is called plethysmography trace. The variation of pulsatile changes in transmission of light signal received by the sensor indicates cardiac function and how well the heart is pumping oxygenated blood through the body. The perfusion index quantifies the amplitude of the peripheral plethysmography waveform and helps to predict early adverse respiratory outcome in neonates, also any irregularity of cardiac rhythm improves detection of critical congenital heart disease in newborns, is implemented as screening test for critical congenital heart diseases [91,92]. Pulse oximetry Photoplethysmogram (PPG) is measurement of respiratory rate by application of digital band filters to allow the removal of cardiac component on the PPG waveform. PPG signal should have two distinct peaks, one low frequency corresponding to respiratory rate and another higher frequency corresponding to heart rate. A recent method titled ‘ARspec’ (Acute Regressive speceral median) yielded most reliable respiratory rate estimation [93,94].

Apgar’s simple clinical practical score at 1, 5 and 10 minutes of birth, 0-3 severe asphyxia, 4-7 as moderate asphyxia and 8-10 in normal healthy newborns in terms of cardio-respiratory status, reflex irritability, muscle tone and colour of newborn, is now rendered redundant and obsolete as it is subjective and poorly reproducible and as such the need for active resuscitation being a specific sign of delayed onset of respiration could therefore indicate recent cerebral injury especially hypoxic-ischemic [95-97]. Also umbilical blood gases for metabolic acidosis is difficult, as pH below 7.18 and a base excess more negative than -8 despite being indications of oxygen deprivation in newborn is a poor predictor of significant perinatal brain injury [98]. While Pulse oximetry automatically provides condition or status of newborns within seconds, significantly detecting more cases of hypoxia requiring immediate resuscitative measures [41].
Pulse oximeter also guides the flow rate of supplemental oxygen based on grading I-V among hypoxic newly borns [60].

Hence birth asphyxia is best defined as lack of oxygen during antepartum, more so intrapartum period or just before birth, Graded I-V as mild, moderate, severe birth asphyxia, secondary apnea and terminal apnea respectively assessed within 20-60 seconds of birth, as delayed onset of respiration indicate recent cerebral injury especially hypoxic-ischemic. Pulse oximetry scoring of SpO2 <96% is also an accurate indicator of hypoxia in newborns. Resuscitation best achieved by sustained positive airway pressure with nasal oxygen inflation at flow rates 1-15 L/min, results in uniform aeration and increased pulmonary compliance with prompt increase in heart rate and cardiac output with rhythmic breathing. Alternatively birth asphyxia maybe defined as Pulse oximetry score +1 to +5 with SpO2 <96% due to lack of oxygen in newborns causing failure to initiate or sustain rhythmic breathing at birth necessitating immediate resuscitative intervention by LNR.

The practice of resuscitation IPPV with bag and mask or endotracheal intubation was undertaken at Christian Medical College and Hospital, (CMCH), Vellore, South India, the then, premier institution in South East Asia, decades earlier to my post graduate residency in early eighties at the neonatal unit, that was later implemented world-wide with the introduction of ‘Neonatal Resuscitation Program’ (NRP) published in 1988 [29,30]. I immediately resuscitated severely asphyxiated newborns with endotracheal intubation and intermittent positive pressure ventilation with adjunct therapy of epinephrine as well as sodium bicarbonate administered in ventilated breathing newborns for severe perinatal asphyxia with Apgar score of 0-3 at 1 min to 5-10 min. However if newborn is properly oxygenated, metabolic acidosis due to anaerobic glycolysis will rapidly resolve, precluding use of hypertonic bicarbonate solution that may overload circulation causing increase risk of cerebral haemorrhage [99]. It wasn’t until 2016 that I discovered the application of continuous positive pressure ventilation by sustained nasal oxygen inflation at flow at rates of 8-15 litres/min resulted in almost immediate revival of the central respiratory centre in initiating rhythmic respiration with no residual adverse sequelae in hypoxic newborns who on observation for four hours in Neonatal Intensive Care Unit (NICU) fared well, were then shifted to mothers side, breast feeding initiated and discharged 3-5 days later. I have since used LNR with supplemental nasal oxygen flow successfully in all asphyxiated newborns till date with success, without the resort to IPPV with bag and mask ventilation or endotracheal intubation with good neonatal outcome.

I earlier published a study from CMCH, Vellore, that reported high perinatal mortality rate (PMR) of 40.7/1000 among 21,585 consecutive total live-borns births during 1979-1983, being one-half contemporary national PMR of around 80/1000 total births, in spite of CMCH being a tertiary referral centre for high-risk cases. The Stillbirth Rate (SBR) 23.6, featured one and a half times higher than Early Neonatal Mortality Rate (ENMR) of 17.5 per 1000 live births. There were 509 stillbirths accounting for 58% of 878 perinatal deaths with 369 Early Neonatal Deaths (ENDs), indicating that most asphyxiated babies died before birth as fresh stillbirths and nearly half 48% (n=119/369) as early neonatal deaths dying within two hours of life from severe perinatal asphyxia instead as fresh term stillbirth as a result of obstetric intervention and skilled resuscitation with IPPV using bag and mask or endotracheal intubation etc. could therefore constitute a total 72% stillbirths of perinatal deaths [21]. The adage “masterful
inactivity and watchful expectancy” proves detrimental in ethnic Asian-Indian population with high perinatal mortality rates, hence active management of labour with quick obstetric intervention is important to rescue endangered foetuses, which has however resulted in a sharp increase of LSCS from 14% in the eighties to 42% in twenties, as fetal distress was the commonest indication for emergency LSCS indicating undetected CPD with prolonged labor [100,101].

Among 369 early neonatal deaths within the first seven days of life, birth asphyxia in 116 (31.4%) was the leading cause during 1979-1983 at CMCH Vellore. However majority 41.7% (154/369) severely asphyxiated newborns had Apgar scores 0-3 at 1 min of birth, most 38 of whom had lethal congenital malformations, constituting an absolutely unavoidable cause of perinatal deaths, 10 died later of intracranial haemorrhage, 9 hyaline membrane disease, 5 fulminant sepsis, 2 massive meconium aspiration syndrome and 1 second birth, infant had hydrops fetalis [8].

Nearly two-thirds 67.2% (n=248/369) of ENDs, took place within the first 24 hours of life. The main cause of death was severe birth asphyxia 30% (n=74/248), lethal malformation (LM) 24% (n=59/248) and Respiratory Distress Syndrome (RDS) 21% (n=52/248) ranked as second and third causes respectively, followed by intracranial haemorrhage (ICH) 7.6% (n=19/248), neonatal infections 3.2% (n=8/248) and ‘miscellaneous’ 14.5% (n=36/248) which included extreme prematurity, pulmonary haemorrhage, liquor aspiration and Rh iso immunization, constituted the remaining first day deaths [9].

Time of death among 248 first day deaths, nearly half 48% (n=119/248) took place within two hours of birth and 29% (n=72/248) >2-12 hours with less than a quarter 23% (n=57/248) within 12-24 hours [9]. Other studies have noted that more than half, 57 % of neonatal mortality occurred within 24 hours [102]. Seven out of every eight stillbirths is due to severe birth asphyxia, with stillbirth rate figuring one and a half times that of early neonatal mortality rate, reveals the magnitude of asphyxiated stillbirths [21,103]. Emphasizing that birth asphyxia continues to be a major cause of preventable proportion perinatal and neonatal and that the neonatal period, more so the first one week, especially within the first 24 hours of life being critical for survival in the life of a child with prevailing high mortality rates predominately in developing Asian countries [5-10].

I also observed during my neonatal residency at CMCH, Vellore that more babies born by normal vaginal delivery were hypoxic when compared to those delivered by LSCS, though those delivered by outlet forceps delivery, cutting short second stage had least perinatal mortality rate [100]. However during 1982 increased sensitization of obstetrician to fetal hypoxial injury by avoiding prolonged labor with active management and judicious obstetric intervention, reduced incidence of birth asphyxia which ranked fourth with lethal congenital malformations ranked as the first cause, being an absolutely unavoidable proportion of perinatal mortality, followed by respiratory distress syndrome and Intracranial haemorrhage as second and third cause of early neonatal deaths an increase in outlet forceps deliveries cutting short second stage of labor was also noted with least PMRs [8,9,100].
The low ethnic Asian mean birth weight in the 1983 cohort was 2881 g, compared to three decades later was almost similar to 2873 g, in 2015-'17 cohort. The decrease of -8 g is attributed to a shift in demography with small family norm and over 50% young primigravida mothers having lower birth weight babies [101,104]. The distribution of birth weight between Asian and Caucasian newborns is remarkable. Caucasian newborns have higher mean birth weight of 3470g reported in a British study, most 82.7% weighed above 3000 g with only 17.3% weighing below 3000 gm that contrasted to low Asian mean birth weight of 2874 g with around one-fourth 27.7 % weighing more than 3000 g and a high 72.3 % weighing 3000 g and below [105]. In fact almost two thirds 65.6% of Asian Indian births weighed between 2000-3000g, while almost similar 68% Caucasian births weighed higher 3000-4000 g, indicates why ethnic Asian population have to set standards and perinatal definitions of their own for international comparison [101,105,106].

Norway reported highest mean birth weight of 3575 g being statistically significant (p=0.001) when compared to other Asian countries such as D.R. Congo, Egypt and Thailand with 400g less birth weight median, while Argentina, Brazil and France had birth weight less than 200g and Denmark, Germany with mean birth weights approximately 100 g less. WHO has also observed that differences in birth weight when adjusted to gestational age at birth between other countries is highly significant for all percentiles at birth, p=0.0018 at 5th percentile to p<0.001 for 10th, 25th, 50th, 75th, 90th and 95th percentiles, reveals the wide variation in human fetal growth across ethnic Asian and Caucasian population, indicating that Asian and Caucasian perinatal definitions are mandated, taking into consideration the wide variation in mean birth weight gestation at birth and intrauterine growth pattern based on ethnicity that will result in improved perinatal and neonatal outcome among ethnic Asian population, presently comprising a majority four-fifths of world’s nearly 8 billion population [106-109].

The Asian Indian peak births 32.6 % in 1983 cohort occurred at 39 weeks gestation with mean gestation of 38.86 weeks S.D. ± 1.29 weeks while peak births 27.4% among 2015-'17 cohort took place at 38 weeks with mean gestation of 38.2 S.D. ± 2 weeks, contrasted with Caucasian births which peaked 31% at 41 weeks gestation, mean gestation of 41.03 weeks S.D. ± 1.32 weeks, with a highly statistically significant difference of 3-4 weeks (p=0.001), while Norway reported mean gestation of 40 weeks 3 days [101,104,105,108]. The shortened gestation of 38 weeks at peak births among Asian-Indian babies results in smaller babies with lower average birth weight 2881g when compared to Caucasian newborns who with a longer gestation upto 42-44 weeks continue to gain weight by deposition of subcutaneous fat have birth weight around 3500g [101,105,106,108,110].

The early peak births at 38 weeks gestation in 2015-17 study compared to 39 weeks in 1983 study is due to judicious quick surgical obstetric intervention in rescuing jeopardized foetuses that resulted in increased incidence of LSCS deliveries 41.6 %, when compared to low 14.8% during the 1979-1983 [100,101]. Not only shortened gestation but also decreased intrauterine fetal growth potential contributes to the low mean birth weight in ethnic Asians as intrauterine growth curves for Asian- South Indian newborns, constructed for 1983 cohort when compared three decades later to 2015-'17 cohort revealed almost similar low growth potential for 10th, 25th, 50th, 75th and 90th percentile curves till 32 weeks gestation, thereafter the 2015-'17 study gained 100-300 g weight from 32 to 37 weeks, following which there was catch-up growth by the 1983 cohort at 40 weeks with 200-300 g growth spurt 40-42 weeks gestation and thereafter.
500 g in 2015-’17 study demonstrating an inherent genetic predisposition at play rather than environmental factors despite vast increase of socioeconomic reforms and technological advances in the country [101,104].

The comparison of national and international intrauterine growth chart revealed that the 10th percentile in the 2015-’17 South Indian cohort and the All India National Neonatal Perinatal Data base (NNPD) study with Lubchenco’s were closely related, thereafter the Lubencho curve diverged from 32-33 weeks gestation with rapid weight gain of around 500 g at 37 weeks, then decreased by 200- 300g weight gain at 40 weeks gestation. However the 50th percentile curve in 2015-’17 study and 50th percentile NNPD study revealed low growth potential corresponded to the 10th percentile International WHO curve [104,111,112].

However though the 90th percentile growth curve in 2016-’17 Indian study was similar only till 32 weeks gestation to 90th percentile World Health Organization (WHO) curve, it thereafter declined to below the 50th percentile WHO curve at 40 weeks in contrast the 90th percentile WHO curve continued to gain more than 1000g at 40 weeks gestation [104,108]. Also the 90th percentile all India NNPD had the least growth potential corresponding to 50th percentile WHO curve up till 37 weeks gestation and thereafter fell by over 250 g less but had a catch-up growth to the 90th percentile South Indian 2015-17 curve at 40 weeks gestation [104,108,111].

Comparison of the 10th percentile intrauterine growth curve reported in UK study corresponded to the 50th percentile of 2015-’17 South Indian curve till 36 weeks, which thereafter flattened by almost 800 g to meet the 10th percentile of 2015-’17 South Indian curve at 41-42 weeks gestation. However the 50th percentile South Indian curve was lower by around 200 g compared to 50th percentile UK curve at all gestation, though the 90th percentile South Indian curve corresponded to 90th percentile UK curve till 38 weeks, the UK curve thereafter increased by almost 500 g greater weight gain by 41-42 weeks gestation [104,113]. The 50th percentile US curve though similar to the 50th percentile South Indian curve till 30 weeks, thereafter diverged with rapid intrauterine fetal growth up to 34 weeks corresponding to 90th percentile Indian growth curve and gaining more than 1000 g at 40 weeks gestation [104,114].

Birth weight for gestational age is a commonly assessed perinatal outcome parameter and Small for Gestational Age (SGA) defined as weighing less than 10th percentile of birth weight for that gestation is also an indicator for Intrauterine Fetal Growth Restriction (IUGR), its importance is due to high associated perinatal and infant morbidity and mortality as well as future adult chronic non-communicable diseases such as cardiovascular disease, stroke, type II diabetes, obesity, other endocrine and metabolic disorders prominently linked to Small for Gestational Age (SGA) [115,116]. Invalidating international reference WHO percentile intrauterine growth curves which differs from the Indian intrauterine growth curves such that the 10th percentile is almost 800 g below WHO 10th percentile curve, while 50th percentile South Indian curve corresponds to 10th percentile WHO curve, that would mistakenly identify a large proportion of Appropriate for Gestational Age (AGA) Indian babies as small for dates after birth feed avidly and gain weight [104,107,108,112].
Pooling of data as in the international WHO intrauterine growth curves do not represent variations among populations in a single intrauterine growth chart but only partially reflect the individual population included, hence ideally two separate ethnic Asian and Caucasian intrauterine growth charts are recommended [104,107,108,113,114].

Therefore despite the vast technological and economic revolution that has influenced all sections of society in India including improved obstetric care, ethnic Asian foetuses will continue to have low intrauterine growth velocity with low average birth weight as a result of asymmetrical intrauterine growth retardation as well as shortened gestation when compared to Caucasian counterparts is primarily due to inherent genetic predisposition [105,114]. Hence ethnic Asian specific intrauterine growth curves is mandated for accurate identification of small for dates for institution of early management of treatment of complication for SGA as well as LGA newborns as well as ethnic specific Asian and Caucasians perinatal guidelines [104,107,114].

I have also reported 21.2% incidence of birth asphyxia comprising 583 cases among 2750 singleton live births who required resuscitation at birth to establish rhythmic respiration, majority delivered at 39 weeks by emergency LSCS births OR 4.91, [CI 95%] 3.94-6.10 times compared to normal delivery being highly statistically significant P=0.0001. In contrast elective LSCS deliveries was associated with low risk 9.1% of birth asphyxia with OR 1.67 [CI 95%] 0.84-1.63, not statistically insignificant P=0.358. Though vacuum extraction comprised 11% of births, it was associated with a significantly higher risk of birth asphyxia, OR 8 [CI 95%] 5.58-11.69, being highly statistically significant P=0.0001 [10].

Also, Meconium Staining Of Amniotic Fluid (MSAF) was associated with 84% asphyxiated newborns, OR 8.42 [CI95%] 5.1-14 being 30 times higher compared to newborns with clear liquor (P=0.0001) (117). One-fifth 21% newborns with MSAF develop MAS, one-third requiring intubation and mechanical ventilation. MSAF is usually present in 8-20% of all deliveries increasing to 23-52% by 42-44 weeks of gestation but rarely found in amniotic fluid before 34 weeks gestation. MSAF with increasing gestation beyond 39weeks, predisposes to maternal complications such as meconium laden amniotic fluid embolism, intra-partum chorio-amnionitis, puerperal endometritis, wound infection etc. with increasing morbidity and mortality in both the newborns and their mothers. Peak delivery 38% of newborns with thick MSAF, 35% MAS, and 32% newborns with thin MSAF occurred at 39 weeks delivered mainly by emergency LSCS [117-122].

WHO has stated that LSCS performed when necessary can effectively reduce maternal and neonatal mortality, the ideal rate of LSCS being 10% for a given population with a rise towards is 10-15%. However if LSCS rates go above 10% there is no evidence to indicate that mortality rates will improve. Though emergency LSCS is a boon for mothers and babies, there is no similar evidence for elective LSCS, which in fact could become life threatening. However the benefits of elective LSCS in high risk cases is associated with improved neonatal and maternal outcome and other benefits such as decreased perineal pain and urinary incontinence at three months [123]. In India, the National Family Health Surveys (NFHS) 4 and 5 in 2015 and 2019 respectively reported an overall incidence of 17.5% LSCS, being higher than WHO
recommended limits with a high 60.7% in Telengana followed by 42.2% in Andhra Pradesh, 41.7% in Jammu and Kashmir, 39.5% in Goa and 37.6% in Ladakh [124,125]. I reported LSCS of 42% in Bangalore in 2015-’17 with up to 80% in some centres [101,126]. In fact Turkey has the highest caesarean section rate of 54.9% followed by Korea 45%, Poland 38.9%, US 32%, UK 28.5%, Canada 27.7% [127]. Thus it may be observed that caesarean section rates are highest in Asian countries as compared to western countries due to the increased vulnerability of ethnic Asian foetuses to asphyxial birth injury with prolonged labor due to undetected CPD during vaginal delivery as compared to Caucasian foetuses who have remarkably low perinatal mortality rates, having almost eliminated birth asphyxia with low incidence of around 1% [18,19,101,128].

Planned elective LSCS or active management labor and cutting short second stage of labor with outlet or low perineal forceps delivery in high risk cases at 38 weeks gestation will obviate complications of later delivery by 39 weeks and beyond by decreased resort to emergency surgical intervention, could not only envision reduction in incidence of emergency LSCS but also improvement in outcome of both mother and baby with resultant significant fall in perinatal, neonatal and maternal mortality and morbidity [101,104,107].

Intrapartum events with placental insufficiency during labour contractions results in maximum decrease in fetal oxygen saturation especially during the latter part of the second stage of labour as fetal blood supply is diminished by uterine contractions or terminated by cord compression, resulting in asphyxia [129]. Thus intrapartum events have more impact than antepartum factors as various studies show placental insufficiency with decrease in oxygen supply to the fetus during contractions, assessed by scalp electrode, an intrauterine pressure catheter and a specially designed fetal pulse oximetry sensor, that records maximum drop in fetal oxygen saturation 92 seconds after the peak of a contraction with recovery 1 minute 30 seconds later, is statistically significant (P=0.036). Also intravascular oxygen electrode measuring continuous fetal arterial PO$_2$ showed transient fetal hypoxemia following uterine contractions [130]. Fetal infrared spectroscopy demonstrated a fall in cerebral oxygenated hemoglobin after a contraction, as well as angiographic studies reveal blocked circulation through the intervillous space during uterine contractions decreasing oxygen transfer to the fetus with lower oxygen levels and pH, noted more so, at the end of labor than at the beginning, compounded by maternal pain, breath holding and maternal metabolic acidosis further reducing oxygen delivery to the fetus [131-133].

In the fetus deoxygenated blood with low oxygen saturation of 25-40% passes through umbilical arteries to the placenta which is the organ of gas exchange returns to fetus through umbilical vein with high oxygen saturation of 80-90% is first delivered to brain and myocardium as circulation is ‘shunt dependent’, also fetal haemoglobin (HbF) helps to maintain oxygen delivery due to shift in left of oxygen disassociation curve which after birth proves disadvantageous with impairment of oxygen extraction at tissue level [63,74,75].

During labor the mean fetal SpO$_2$ decrease to around 45-50%, and during last one hour of delivery if SpO$_2$ falls below <30% for more than 30% correlates highly with fetal acidosis in cases of non-reassuring fetal heart rate [133,134]. However after birth, gas exchange shifts to lungs with 8-10 fold increase in pulmonary blood flow and fall in pulmonary vascular
resistance as better oxygenation of neonatal blood increases pulmonary compliance by reversing pulmonary vasoconstriction caused by hypoxia [34,63]. Therefore a low SpO₂ below 50% may be expected if the asphyxiated newborn fails to establish breathing soon after birth mandating immediate resuscitation with oxygen to quickly reverse hypoxial injury and its sequelae or death [135].

Bradycardia with weak, irregular beats is indicative of fetal anoxia, usually observed a few minutes to a few days before delivery associated with sudden increase in fetal activity followed by diminished activity. Scalp blood analysis may show acidosis with a pH of less than 7.20, comprising both of respiratory and metabolic components [131,134,136]. Fetal heart rate monitoring reveals variable late (type II dips) deceleration pattern without any variability in response to fetal movements or uterine contractions. Consistent slowing or late deceleration of the fetal heart rate following termination of each uterine contraction is indicative of uteroplacental insufficiency also considered as positive oxytocin challenge test requires supplemental oxygen to mother before delivery [134,136]. If fetus is at high risk for asphyxia due to inadequate supply of oxygen from the placenta detected during labor presenting with fetal distress, then emergency delivery may be attempted preferably by caesarean section or alternatively by outlet forceps delivery if head is in perineum.

The longer the hypoxic episode the more severe the sequelae with secondary and terminal apnea requiring immediate effective resuscitation to avoid death with supplemental oxygen administration at 16 to 20 cm H2O for 1 to 2 seconds to counteract hypoxia or up to 1-3 minutes by nasal oxygen inflation at flow rates between 12-15 L/min [38-40]. Due to hypoxemia and acidosis, the impaired cellular function results in failure of mitochondrial ATP pump and energy reserves are depleted. Among all sources of energy, glucose alone is capable of sustaining energy metabolism in the brain under conditions of total cerebral ischemia, because of its capacity for consumption via anaerobic glycolysis with the production of lactic acid and ATP. However, during anaerobic conditions, one molecule of glucose yields only 2 mols of ATP as opposed to 38 molecules of ATP during aerobic metabolism. Production of lactic acid due to the anaerobic metabolism remains in the tissue because of poor perfusion. The concomitant acidosis leads to decreased heart rate and cardiac output with decreasing blood pressure leading to cell damage and functional abnormality-such as renal failure in the kidneys, necrotizing enterocolitis in the gut, hypoxic myocarditis, decreased pulmonary perfusion, abnormalities of gas exchange and persistent pulmonary hypertension in the lungs [34,63,64,74].

Birth asphyxia initiates diving reflex; causing shunting of blood to the brain; heart and adrenals with reduce flow or hypo perfusion in organ system of lungs, gut, liver, kidney, spleen and skin. In mild hypoxia there is increase in blood pressure and heart rate to maintain cerebral perfusion-the brain sparing effect [34,35]. In the initial stage of primary apnea, the fetus gasps in utero, for a short period, heart rate and blood pressure may remain constant or become slightly elevated, following which, after an interval of a few minutes the fetus commences a second period of gasping and enters terminal stage or secondary apnea wherein the heart rate and blood pressure fall quickly and if not immediately resuscitated, will die at birth [135]. Apnea is defined as cessation of breathing greater than 20 seconds and most asphyxiated infants born with primary apnea will commence spontaneous respiration if given air or supplemental
oxygen to breathe, while secondary or terminal apnea requires immediate resuscitative measures best achieved by LNR to establish rhythmic respiration [34,60,135].

Asphyxia has been demonstrated to cause two patterns of brain damage in animals, firstly acute total asphyxia produce neuronal necrosis of the brain stem nuclei and secondly partial prolonged asphyxia results in necrosis of cerebral hemisphere [137]. However pathogenesis of intrapartum asphyxia in a full term neonate with redistribution of organ blood flow, result in oxygen debt to brain cells, impaired auto regulation of cerebral blood flow, intracellular swelling, leading to focal ischemia, generalized brain swelling, increased intracranial pressure, causing cerebral necrosis and atrophic cortical sclerosis [138]. Autopsy study in preterms with repeated prolonged apnea more than 20 seconds and cyanosis revealed diffuse neuronal loss in cerebral cortex, leukomalacia in periventricular watershed zones while full terms with hypoxic episodes between 2 to 52 weeks of age noted subcortical leukomalacia related to border zones with tenuous arterial blood supply from anterior, middle and posterior cerebral arteries and in preterm as auto regulation of smooth muscle tone in vessel is not present is mainly dependant on systemic blood pressure hence these areas are extremely susceptible to hypoxic injury [139]. The mechanism of intraventricular haemorrhage is probably that an asphyxial episode causes vascular constriction followed by vascular dilation with increased intravascular pressure which ruptures vulnerable vessels in the germinal matrix especially in the periventricular area in the immature-brain [140].

Various other criteria recommended by AAP and ACOG for severe birth asphyxia include: (I) Profound metabolic or mixed academia, with an umbilical artery pH <7.00, (II) Apgar score of 0-3 beyond 5 minutes, (III) Neurological involvement such as convulsions, unconsciousness and hypotonia, (IV) Multi organ system dysfunction involving various systems such as CVS, GI, kidneys, lungs etc [141]. Hypoxic Ischemic Encephalopathy (HIE) mild, moderate or severe, classified by Sarnat and Sarnat as stages I, II, or III is based on level of consciousness, neuromuscular control, tendon and complex reflexes, gastrointestinal motility, presence or absence of myoclonus, electrography findings and autonomic functions, however these parameters have no predictive value for long-term neurologic injury after mild to moderate asphyxia is no longer validated as accurate assessment of birth asphyxia can be monitored by pulse oximeter [142].

Nearly 20-40 percent of perinatal deaths are attributed to birth asphyxia especially in Asian countries [5-12,16,17]. Strictly speaking stillbirths are fetal deaths nevertheless even live born neonate who is apneic and cyanotic with pulse is set aside after birth and left to initiate respiration, or are inadequately resuscitated and die are classified as stillbirths as unskilled birth attendants may not be able to distinguish between the two conditions with inaccuracy of recording these fatalities, often termed stillbirth with high stillbirth rates. Hence misclassification of stillbirths has significant implications of national health policies and global strategies for reducing perinatal mortality is actually a poorly resuscitated viable newborn, would lower stillbirths rate as also a large number are unregistered [16,17]. The disadvantages of effective neonatal resuscitation by Neonatal Resuscitation Program (NRP) include highly trained skilled birth attendants and well outfitted resuscitation teams and as such is not universally applicable in many parts of low income Asian countries with limited resource
settings who lack essential resuscitation equipment and in addition bulb syringes, bag and mask devices may be substandard and unskilled birth attendants [29,30].

Lalana Newborn Resuscitation is a new novel non-invasive approach in management of all cases of birth asphyxia, requires minimal infrastructure for oxygen supply from either piped oxygen of cylinder with flow meter and wide bore oxygen tube, requires minimal training of even unskilled birth attendants, help improve individual outcome of newborns suffering from lack of oxygen resulting from perinatal asphyxia will prove to be of vital importance as quick oxygenation of tissues, reversing hypoxic insult in initiating regular breathing pattern will save millions of lives by reducing asphyxial neonatal deaths with minimal residual sequelae or ill effects as well as reviving viable apneic newborns who otherwise would be termed as stillbirths [60].

In India current neonatal mortality rate is 28/1,000 live births, with 40 and 49 per 1000 live births being infant and child mortality rates being 70% of total infant deaths and more than half of under five deaths and ENMR of 22 per 1000 live births account for 45% of total under five deaths. Of 25 million global births of children each year, India contributes to one-fifth of total global live births and more than a quarter of neonatal deaths [12,51,52]. Almost all asphyxia deaths (97.8%) occur within the first week with 70% within the first 24 hours of life [51]. In fact India leads with 522 neonatal deaths per 1000 live births followed by Nigeria at 270, Next Pakistan 248, Ethiopia 99, Democratic Republic of the Congo 97, China 64, Indonesia 60, Bangladesh 56, Afghanistan 43 and United Republic of Tanzania 43 per 1000 live births [51,52,143]. However NMR is not uniform across the country with Kerala and Tamil nadu with low NMRs of below 20/1000, Odisha, Madhya Pradesh and Uttar Pradesh have high NMRs of more than 35/1000, though Haryana and Gujarat have similar or higher per capita GDP than Tamil Nadu but almost double NMR. In fact four states, Uttar Pradesh, Madhya Pradesh, Bihar and Rajasthan alone contribute to 55% of total neonatal deaths in India and up to 15% of global neonatal deaths occur every year [51,52].

Thus Birth asphyxia is leading preventable cause compounded by the high stillbirth rate, who would have had a good chance of healthy life on survival with effective resuscitation, however essential newborn care recommended by WHO reveals inadequacies in mother and child with only around four antenatal visits and skilled birth attendants is about 50% in 68 count down countries and neonatal mortality comprising 52% of under five-year mortality [143]. Effective newborn resuscitation by LNR in many low to middle income Asian countries with limited resources would require minimal set up with availability of humidified oxygen regulated with flow meter and pulse oximeter to monitor peripheral tissue oxygenation (SpO₂), in fact portable oxygen cylinders even allows for effective domiciliary resuscitation, equipping even unskilled birth attendant, who may easily be taught detection of hypoxia/asphyxia of newborn based on pulse oximetry SpO₂ and recording of heart beats per minute obviating the need for a stethoscope. Simple classification of newborns as ‘Normal’ and hypoxic as Grade I-V determines sustained nasal oxygen flow rate varying from 2-15 L/min, oxygen flow to be discontinued with Pulse oximetry, zero score SpO₂ 96%, while drying the baby, suctioning nose and mouth to clear the airway passage aided by tactile stimulation in initiating rhythmic respiration, maintaining body temperature, under asepsis precautions and initiating early breast feeding practices. In the present study LNR proved eminently effective in all 178 asphyxiated
newborns resuscitated among 830 deliveries attended, three of whom had secondary apnea Grade IV and one newborn with terminal apnea Grade V initiated rhythmic respiration, smoothly transiting from fetal fluid filled lungs to well aerated neonatal lungs with vital cardiovascular transition to neonatal life.

**Advantages of Lalana Newborn Resuscitation (LNR) with Continuous Positive Pressure Ventilation by sustained nasal oxygen inflation at flow rates varying from 2-15 litres per minute assessed by Pulse oximetry score of SpO₂**

1. Resuscitation of the newly born is unique as the presence of fetal lung fluid prevents exchange of gases.
2. Sustained nasal oxygen inflatory flow provides continuous distending pressure that generates hydrostatic pressure to effectively overcome the high resistance of moving fetal lung fluid through the airways and across the alveolar wall into the interstitial tissue as well as opposes elevated interstitial pressure during expiration, preventing lung fluid from re-entering the airways promoting enhanced reabsorption of lung fluid.
3. Lalana Newborn Resuscitation (LNR) is safe and quick resuscitation of newborn by non-invasive technique based on CPPV by sustained nasal oxygen inflation meets the aim of effective resuscitation preventing neonatal death or adverse long term neurodevelopmental sequelae in survivors, ensuring that children should be normal.
4. Continuous positive pressure ventilation results in uniform lung aeration, improved oxygenation with increased pulmonary compliance that increases Functional Residual Capacity (FRC), prevents atelectasis and maintains lung volume.
5. Stabilizing newborns with low fraction of inspired oxygen at birth is difficult since hypoxia is a potent inhibitor of spontaneous breathing; therefore increase in oxygen flow rate with higher FiO₂ determined by Pulse oximetry reading of SpO₂, help to overcome hypoxial insult with quick onset of respiration.
6. Oxygen is the only treatment for hypoxia that facilitates aerobic metabolic glycolysis and mitigates vagal-induced bradycardia resulting from perinatal asphyxia that perpetuates hypoxemia with hypercapnia or rise in arterial carbon dioxide, reducing blood flow to the brain with ischemia causing altered mental status.
7. The prompt increase in heart rate with improved cardiac output indicate adequate lung aeration and function resulting in left to right shunting triggering reflex physiological mechanism that converts fetal circulation to adult type.
8. Continuous Pulse oximetry monitoring gives real time assessment of newborns in maintaining SpO₂ at 96%-98%, mitigates hypoxial injury and cell damage causing multi-organ failure, neurological deficits or death.
9. LNR prevents both deleterious effects of hypoxia and detrimental hyperoxia especially in preterms with sustained nasal oxygen inflatory flow rate determined by Pulse oximeter SpO\textsubscript{2} and discontinued at SpO\textsubscript{2} 96%.

10. LNR Protocol require minimal infrastructure for supply of humidified oxygen with flow meter as well as minimal training of even unskilled birth attendants, proves advantageous more so in low to middle income Asian countries with limited resources wherein majority of the world’s population reside accounting for 98% of global perinatal mortality rates.

11. Indications of successful ventilation by LNR is achieved with Zero Pulse oximetry score, SpO\textsubscript{2} >96%, rhythmic pattern of respiration, rate of 30-60/min, heart rate 120-160 bpm and regular pulsatile changes on plethysmograph with adequate circulation of oxygenated blood throughout the body.

**Disadvantages of Neonatal Resuscitation Program (NRP) with Intermittent Positive Pressure Ventilation, using bag and simple mask or invasive endotracheal intubation**

1. Short Intermittent Positive Pressure Ventilation (IPPV) is potentially harmful, causing un-even alveolar ventilation with increased susceptibility to lung injury as the entire tidal volume will only enter previously aerated regions which has important implications because during subsequent inflation air will first rapidly flow into and expand previously aerated lung regions due to much lower airway resistance.

2. IPPV is proven both scientifically and physiologically weak in effectively clearing lung fluid due to impaired generation of hydrostatic pressure while also permitting fluid to re-enter the airways with rising A-a gradient, poor oxygenation and circulation of deoxygenated blood to peripheral tissues.

3. Hypoxia is perpetuated due to increased pulmonary compliance with intermittent alveolar collapse during IPPV causing V/Q mismatch and right to left shunting of deoxygenated blood to peripheral tissues.

4. Peripheral oxygen saturation stated by NRP protocol by IPPV seems unacceptable advocating SpO\textsubscript{2} 40-45% at 1 min, SpO\textsubscript{2} 65-75%, at 2 min, SpO\textsubscript{2} 70-75%, at 3 min, SpO\textsubscript{2} 75-85%, at 4 min, SpO\textsubscript{2} 80-85% at 5 min, SpO\textsubscript{2} 85-95% at 10 min with long delay for hypoxic newborns to achieve SpO\textsubscript{2} 96%. Longer hypoxic episode result in more severe sequelae often leaving of survivors with permanent lifelong neurological deficits or multi-organ complications or death within the first few days.

5. Prolonged hypoxia predisposes to anaerobic metabolism and acidosis, impairs cardiac function resulting in bradycardia and poor peripheral circulation hindering smooth transition of fetal to neonatal circulation.

6. IPPV with bag and face mask or mouth-to-mouth breathing is not effective as adequate trans-pulmonary pressure for adequate displacement of lung fluid is difficult to achieve as also because gastric distension occurs.

7. Also simple tight fitting of face mask or endotracheal intubation with FiO\textsubscript{2}, up to 1.0 or 100% predisposes to hyperoxia with generation of oxygen free radicals, which have a
deleterious role causing reperfusion injury contributing to eye (ROP), neurological and lung injury in preterm.

8. NRP requires the presence of a team of highly trained skilled birth attendants for bag and mask or invasive endotracheal intubation for Intermittent Positive Pressure Ventilation, as more severely asphyxiated newborns require cardiopulmonary resuscitation or medication such as epinephrine or saline volume expanders etc.

9. NRP protocol is best adapted for resuscitation in cardiopulmonary arrest of infants, children and adults with previously well aerated lungs.

10. Neonatal Resuscitation Program (NRP) has been associated with remarkable decline in asphyxial deaths worldwide, however the degree of morbidity remains high affecting quality of life in nearly half of survivors as the rate of Hypoxic Ischemic Encephalopathy (HIE) has remained the same over the past decades [4,7,11,29,30,31,48,49].

Thus in spite of vast advances in perinatal care, obstetric management with improved technology in fetal monitoring etc. birth asphyxia continues to be the leading cause of the preventable high prevailing perinatal and neonatal morbidity and mortality in most Asian countries in spite of world-wide reduction in asphyxial deaths following the introduction of Neonatal Resuscitation Program but with high morbidity with up to 40% of survivors suffering from ill effects of hypoxial sequelae ranging from mild to severe permanent neurological deficits etc with incidence of HIE has shown no decrease over the past decades [7,11,16,17,29,30,49].

I have reported average duration of pregnancy in ethnic Asian-Indian population is 38.2 weeks and that peak births of healthy, non-asphyxiated newborns born normally with clear liquor took place at 38 weeks, while most asphyxiated births, majority delivered by emergency LSCS occurred at 39 weeks (10). In fact 84% of asphyxiated newborns developed complications of Meconium Staining of Amniotic Fluid (MSAF) and Meconium Aspiration Syndrome (MAS) [101,117]. This has important significance as increased in emergency surgical intervention at mean gestation of 39.1 ± S.D. 1.2 weeks, occurring in more mature, high birthweights newborns weighing around 4000g indicating fetal distress usually after prolonged labor due to undetected CPD more so in young primigavida mothers, who are at higher risk of dying from perinatal asphyxia [10,101,104].

Thus the small Asian neonate with average low birth weight around 2800 -3000 g attributed to asymmetrical intrauterine growth retardation due to inherent genetic predisposition rather than environmental factors with low energy reserves are less well equipped to cope with any asphyxial insults resulting from uterine contractions especially when labor is prolonged with increased mortality and morbidity with adverse long term sequelae [101,104,115,129]. However healthy small for dates, shortly after birth, will feed avidly and gain weight indicating effective preventive strategies now takes on priority in saving the small Asian babies, that mandates institution of new ethnic Asian specific guidelines for well-being of Asian newborns by clinical implementation of peak ethnic Asian births with Asian Due Date (ADD) for delivery at 38+6 weeks gestation, thus preventing hypoxial birth injury and colossal asphyxial deaths which are totally preventable [101,104,107].
Other clinical studies from the west report low digit figures perinatal, neonatal and maternal mortality rates having almost eliminated birth asphyxia with low 1% incidence, yet demonstrate delivery at 38 weeks by planned or elective LSCS in high risk groups have least risk of perinatal deaths and that prolonging pregnancy to 39 weeks up to 43 weeks note increased perinatal risk index due to obstetric events more so in primigravidas with greater risk of antepartum stillbirth [18,19,144-147]. Also, non-laboring women delivered by caesarean section before 39 weeks, obviates intrapartum events, reported 83% reduction in moderate to severe encephalopathy, being one of the leading causes of HIE as well as late fetal death, signifying that early planned delivery preferably at 38 weeks more so by elective section in high risk cases before intrapartum events was associated, not only with reduction in birth asphyxia cases but also fresh stillbirths due to anoxia and neonatal complications such as respiratory disorders etc, being the most effective strategy than any other so far implemented, yet still others estimate the lowest cumulative risk of perinatal deaths and advocate delivery by 37 weeks gestation [49,107,144-151].

Thus prolonging pregnancy to 39 weeks and beyond increases the risk of stillbirth, neonatal and maternal morbidity and mortality with adverse increase in neonatal risk predisposing to high risk of perinatal asphyxia and higher risk of stillbirth as well as other outcomes such as PIH that rises with each additional week of gestation [10,49,144-151]. Postdate induction is typically not recommended prior to 41st week, a dictum followed also by Asian obstetricians in management of pregnancy in ethnic Asian women, who often experience uterine contractions by 38 weeks of gestation, labelled as ‘false labor pains’ and instead of attempting delivery with amniotomy, which is now well accepted in acceleration of labour, or use of prostaglandin E2, for cervical ripening, instead opt to prolong pregnancy to 40 weeks or Expected Date for Delivery (EDD) with tocolytic medication to suppress uterine contractions and/or bed rest increasing risk of neonatal and maternal morbidity and mortality.

Also the later delivery at term questions management of pregnancy at 39-43 weeks associated with increase obstetric intervention by emergency LSCS more so in ethnic Asian population [101,104,107,146]. In fact a substantial number of newborns could have perinatal asphyxia attenuated or removed given timely obstetric intervention and as such elective section at 38 weeks more so in high risk cases would remove the risk of intrapartum asphyxia and reduction of HIE with improved perinatal outcome and lower term stillbirth rates [10,21,101,107]. Hence the lowest risk of perinatal deaths was noted at 38 weeks, sharply increased among primigravida women beyond 39 weeks, because of greater risk of shoulder dystocia, foetal trauma, meconium staining of liquor, neonatal encephalopathy and intrauterine demise with higher incidence of HIE [10,49,145,147]. Hence majority of ethnic Asian women who do experience uterine contractions before 40 weeks EDD, should be allowed to progress even from 36 weeks of gestation onwards, though a blanket policy for induction of labour at 38 weeks would certainly be associated with an unacceptable general increase in rate of obstetric intervention, it is important to take into consideration the unique ethnic diversity or genetic predisposition by implementing ethnic due dates for the two main ethnic races, Asians and Caucasians [107,146]. Thus implementation of ethnic Asian Due Date at 38+6 weeks gestation will result in improved perinatal outcome as opposed to a common EDD at 40 weeks well adapted to Caucasian population [152].
The existing perinatal definitions and guidelines established by World Health Organization stated in standard medical text books have not taken into consideration ethnic difference that exists between the two main Asian and Caucasian races [153]. It is this inability to address the unique ethnic inherent genetic predisposition in Asian population, that resulted in failure of MDGs - 4 goals with the specific aim of reducing under five child mortality rates by two-thirds, despite addressing determinants of human health and welfare including poverty, hunger and disease between 1990 to 2015 that was adopted by United Nations (UN) globally, as majority under-five child mortality occurs predominantly in ethnic Asian population residing mainly in low to middle income Asian countries [154-156].

Following years of research and in-depth analysis, I outlined up-to-date ethnic Asian perinatal standards and definitions, providing appropriate guidelines for ethnic Asian Obstetricians, Paediatricians/Neonatologists, if implemented will result in improved neonatal and maternal outcome with reduction in perinatal, neonatal and maternal morbidity and mortality, consequently infant and under-five years child mortality rates to reach targets set by SDG goals [152,153]. While extended perinatal team includes radiologists, paediatric surgeons, genetic/prenatal councillors etc in the event of fetal anomalies for advice or if surgically correctable with in utero or immediate post-natal surgical intervention.

Hospital based study suggests that 25-62 % of intrapartum stillbirths can be avoided with better obstetric care and more rapid response to intrapartum complications and the question can intrapartum-related deaths be reduced as well as disability and can the health system deliver? as well as reducing the global rate in caesarean section, which is alarmingly increasing [128,156]. The answer is ‘No’ as so far, all strategies in maternal and child care implemented all over world has not seen any dramatic reduction in perinatal mortality rates (stillbirths and early neonatal deaths) due mainly to birth asphyxia which is a preventable cause including maternal mortality rates as well as reduction of emergency LSCS be envisioned, unless a simple perinatal guideline of ethnic specific Asian Due Date (ADD) at 38+6 weeks by planned or spontaneous delivery gestation is implemented by eliminating a common E.D.D at 40+6 weeks gestation, stated in all standard western text books, best suited for Caucasian population, by avoiding intrapartum events at 39 weeks and beyond, ensures not only reduction in stillbirths but also early neonatal deaths due to perinatal asphyxia by decreasing impact of shoulder dystocia, foetal trauma, neonatal encephalopathy and intrauterine demise and other complications of labour that occurs more common at delivery by 39 weeks and beyond, circumventing the problem by delivery in ethnic Asians by 38 weeks gestation [144-152].

In fact only 1.7 percent of Asian women gave birth after 40 weeks EDD, while 90.3% Asian-Indian women delivered before EDD i.e. 40 completed weeks or 280 days gestation (105). The Asian Due date at 38+6 weeks is most appropriate for ethnic Asians, most accurately calculated if menstrual cycles were regular and 28 days interval with ovulation occurring on Day 14, estimated by Lalana’s rule, Step 1: Determine the first day of last menstrual period, Step 2: Subtract 1 week, Step 3: Subtract 3 months, Step 4: Add 1 year to arrive at 38+6 weeks or 266 days of gestation, for e.g. if LMP was 15th November, 2021, then ADD is August 8th , 2022 approximately at an interval of 38+6 weeks (or 266 days) from LMP [107].


DOI: http://dx.doi.org/10.46889/JCMR.2021.2305
In contrast only one-third, 32% of Caucasian - British women delivered before Expected Date of Delivery (EDD) or 40+6 weeks gestation, as significantly more British women, 68 percent delivered after 40 weeks EDD during 41-44 weeks of gestation [105]. The importance of addressing inherent genetic or racial differences Asian and Caucasian population cannot be underestimated as this important criterion has not been addressed world-wide so far, in formulating ethnic Caucasian and Asian perinatal definition and guidelines that will go a long way in catering to the well-being of ethnic Asian foetuses and neonates as well as their mothers. UNICEF, WHO, World Bank and UNDESA reports that sixty million under-five years children will die between 2017 and 2030, though only 5.6 million children died in 2016 compared to 9.9 million in 2000. Despite a decline in maternal mortality ratio by 37 percent between 2000 and 2015, globally has dropped from 451,000 in 2000 to 295,000 in 2017, a 38% decrease, that’s around 808 women every day, mostly from preventable causes with aim to reduce global maternal mortality ratio to less than 70 per 100,000 live births. While Finland, Greece, Iceland and Poland have 3 women per 100,000 births, thus nearly 95% reduction is to be envisioned since majority births occur in in Asian countries with nearly two-thirds of maternal deaths with rate of 130/100, 000 live births during 2016-2018 or 26437 maternal deaths in 2018 mainly 50-98% caused by post-partum haemorrhage, sepsis, PIH and complications of delivery which may be reduced just by delivering at optimum 38 weeks gestation [14,15,51,157-160]. However I hope that it will not be too frustratingly too long before we finally change practices in implementing ethnic specific perinatal guidelines and clinically accepted before steep reduction in perinatal, neonatal and maternal mortality and morbidity becomes a reality.

The current world population of 7.8 billion according to recent United Nations estimates, ethnic Asians comprise 60% of world population with 4.5 billion residing in Asian countries report high prevailing perinatal, neonatal, and maternal mortality rates as well as under five years, morbidity and mortality [109,154-156]. The MDG- 4 set out by World Health Organization (WHO) significantly reduced under-five mortality rate by 59% between 2000-2015, WHO in 2013 reported that the number of deaths of children under five years fell from 12.7 million in 1990 to 6.3 million in 2013, almost all, 95% of these occur in developing low to middle income Asian countries [157].

In 2018 WHO reported that over 6 million children and adolescents died globally, of which 5 million died before the age of five, majority of these deaths being preventable occurring mainly in low-middle income Asian countries despite measures for intervention in the care of newborn and their mothers such as infant and young child feeding, expanded programme on immunization with newer vaccines, prevention and case management of pneumonia, diarrhea and sepsis, malaria control and prevention and care of HIV/AIDS by appropriate home care and early treatment of complications of newborn, with integrated management of childhood illnesses in under five years, complimented by interventions for maternal health and nutrition, especially skilled care during pregnancy and childbirth has not shown further significant reduction in perinatal and neonatal mortality [158-160].

As in 2019, 5.4 million children under five died of preventable/treatable causes on an average means 15,000 young children. While infants comprised 1.5 million, 1-4 years accounted for 1.3 million deaths. The remaining 2.4 million deaths occurred among neonates in the first 28 days of life, highlights importance of reducing neonatal deaths and thereby under-five year
mortality rates occurring mainly in ethnic Asian population. Sustainable Development Goals (SDGs) 3.2.1, known also as Global Goals stipulate reduction of 11 million under-five child deaths between 2019-2030, is a huge achievement, currently far away, despite improvement of global health. 4.5 million child deaths will occur by 2030 or 86 million child deaths in SDG era, aimed at reduction of neonatal mortality to at least 12 per 1000 live births, or that 97.5% of all newborns would survive, no matter where they are born and child mortality to at least 2.5% signatory by more than 100 UN Member States as part of the 70th session of UN General Assembly with renewed commitment to children rights who will grow up to become the future leaders and pillars of society in protecting their healthy growth and development with emphasizes shifted to the neonatal period or first 28 days of life as being the most vulnerable time in the life of a child with high mortality rates [14,15,160].

India with growth rate of 1.11% with 1.35 billion is poised to become the most populated country in the world by 2027 according to new UN study of global population trends, just second to China with 1.41 billion, with growth rate 0.39-0.59% (109,161). Thus India could well set ethnic specific perinatal Asian guidelines and definitions to envision improved perinatal, neonatal and maternal outcomes, as well as reference intrauterine growth chart for accurate identification of those at risk neonates SGA and LGA newborns that require special care. Therefore the most vulnerable time in child survival is during the neonatal period, especially the first 24 hours of life and within the first week that is critical in the life of individual and effective strategies are needed to improve outcome by addressing inherent ethnic diversity in Asian and Caucasian population being the need of the hour. In India among 0.386 million cases of newborn asphyxia occur each year, 75% of newborn deaths are preventable, birth asphyxia comprising about 20% and other two causes being prematurity 35% and sepsis 33% with congenital malformation an absolutely unavoidable cause of perinatal mortality being 9% [12,13,51]. Thus India has highest 522 neonatal deaths per 1000 live births with Early Neonatal Mortality Rate (ENMR) 20 per 1000 live births and Neonatal Mortality Rate (NMR) 26 per 1000 live births. Nigeria ranks second with 270 0/00 followed by Pakistan 248 0/00, Ethiopia 99 0/00, and Democratic Republic of the Congo 970/00, China 64 0/00, Indonesia 60 0/00, Bangladesh 56 0/00, Afghanistan 430/00 and United Republic of Tanzania 43 0/00 live births [14,15,20,51].

The projected NMR of 22/1000 live birth for 2020 in India has not been attained and current NMR 28/1000 and ENMR 22/1000 live births accounts for 45% of total under-five year child deaths. This NMR is not uniform across the country, Kerala and Tamil Nadu report low NMR of below 20/1000, Odisha, Madhya Pradesh and Uttar Pradesh have high NMRs of more than 35/1000 total births. Though Haryana and Gujarat have similar or higher per capita GDP than Tamil Nadu but doubles NMR, in fact four states, Uttar Pradesh, Madhya Pradesh, Bihar and Rajasthan alone contribute to 55% of total neonatal deaths and 15% of global neonatal deaths every year. India contributing to one-fifth global live births but more than a quarter of neonatal deaths is concerning, indicating strategies aimed at reduction of early neonatal deaths to substantially reduce under-five child mortality rate depends mainly on India’s progress to meet the world SDG [13,14,51].

Preventive strategies should be aimed at intrapartum period rather than antepartum or post-partum, as it has been reported to have a major impact with adverse outcome especially in
ethnic Asian population, such as active management of labor with judicious obstetric intervention in rescuing endangered foetuses, that presently lies entirely in the domain of the obstetrician will be circumvented by the clinical implementation of Asian Due Date (ADD) for delivery at 38+6 weeks will prove to be the single most eminently suitable guideline for Asian obstetrician in delivering healthy babies and safe guarding their mothers, given that peak Asian births do take place at 38 weeks gestation causing improved perinatal, neonatal and maternal outcome as opposed to a common EDD at 40 weeks gestation [101,104,107].

I am convinced with the aftermath of the covid pandemic affecting all aspects of life, including non-availability of health care facilities with hundreds of thousands more under-five fatality, Sustainable Development Goals (SDGs) 3.2.1, known also as Global Goals for target reduction of under-five child mortality has faced setbacks and requires renewed determination for the stipulated goal of reduction to 11 million under-five child deaths between 2019-2030 that is specifically aimed at reduction of neonatal mortality to at least 12 per 1000 live births and consequently under-five years child mortality to a low 25 per 1000 live births [50,160]. As the given past endeavors and strategies have met with little or no further fall, it is important that we implement new approaches and preventive strategies in management of newborns and their well-being to envision attaining targets by 2030.

WHO is now calling for new sustainable development goals to continue to reduce child mortality rate to a low 2.5% in all countries by 2030, Goal 3.2 would mean more than 97.5% of all newborns should survive the first five years of their life, no matter where they are born, even as UNICEF works to end preventable new-born and maternal deaths. Current trends indicate that accelerated progress is needed to reach target, as 80% of under five years deaths globally occur in Asian countries with nearly half, 45% of under-five child deaths being neonatal deaths, in addition to the colossal stillbirth loss and maternal deaths that occur each year with almost 95% occurring in low to middle income Asian countries [158-160].

Thus the implementation of two important new criteria aimed at improving the outcome of newborns and their mothers, thereby reducing perinatal, neonatal and maternal morbidity and mortality, with focus on intrapartum period precluding events occurring at 39 weeks and beyond with effective resuscitation of hypoxic newborns, impacting early neonatal period, especially life within first 24 hours, being most critical to target global fall in infant and under five mortality rates includes:

Criteria

1. **Asian Due Date (ADD) for delivery at 38+6 weeks, as peak births take place at 38.2 weeks S.D ± 2, will prove to be the single most important strategy in reducing neonatal, perinatal and maternal mortality and morbidity with focus on intrapartum period, also stemming the colossal stillbirth loss.**

2. **‘Lalana Newborn Resuscitation’ will revolutionize resuscitation of asphyxiated newborns by sustained nasal inflatory oxygen flow up to 2-15L/min, monitored continuously by Pulse oximetry for superficial oxygen saturation and successful ventilation is indicated by Zero pulse oximetry score, SpO2 >96%, with rhythmic respiration, rate 30-60/min and heart rate 120-160 bpm, under asepsis and thermo-control with early institution of breastfeeding will**
result in well-being of newborn, so that children should be normal, Thereby ensuring children be normal with healthy growth and development throughout infancy, childhood and adolescence, the right of every individual.

**Conclusion**

Timely delivery of ethnic Asian newborns and effective resuscitation of hypoxic newborns will not only reduce birth asphyxia which constitutes a leading preventable proportion of perinatal and neonatal mortality, almost all occurring in Asian countries with focus on events occurring during intrapartum period having a major impact on mother and child. Therefore the two most important preventive strategies include clinical implementation of Asian Due Date for delivery at 38+6 weeks gestation and effective resuscitation by Lalana Newborn Resuscitation (LNR) based on scientific principle of application of Continuous Positive Pressure Ventilation (CPPV) by sustained nasal oxygen inflation monitored by pulse oximetry, will save lives, thereby reducing perinatal, neonatal mortality and consequently under-five child mortality rate.

**Conflict of Interest**

The authors declare that they have no conflict of interest.

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Christopher GL | Volume 2, Issue 3 (2021) | JCMR-2(3)-042 | Research Article


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