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Prediction of Neonatal Acidosis Based on the Type of Fetal Hypoxia Observed on the Cardiotocograph (CTG)

Shehara Amanthi Gunaratne, Siromi Dilhara Panditharatne, Edwin Chandraharan

ABSTRACT

Cardiotocograph (CTG) was introduced into clinical practice to promptly recognize the features of intrapartum fetal hypoxic stress, so that timely action could be taken to avoid hypoxic-ischaemic encephalopathy (HIE) and perinatal deaths. However, the current systematic evidence suggests that the introduction of CTG into clinical practice over 50 years has not resulted in improvement in the rates of cerebral palsy or perinatal deaths. This is because most fetuses are able to withstand intrapartum hypoxic stresses without sustaining damage, and if the features of fetal compensatory responses are erroneously considered as "pathological", "Abnormal" or "Category III" CTG tracing, it would lead to an exponential increase in unnecessary operative interventions without any improvement in perinatal outcomes. Neonatal acidosis at birth, determined by the estimation of pH in the umbilical artery has been considered as a surrogate marker of poor perinatal outcome. This is because significant intrapartum fetal hypoxic stress which leads to fetal decompensation, would lead to the onset of anaerobic metabolism and production of lactic acid in fetal tissues and organs. Entry of lactic acid into the fetal systemic circulation may cause damage to fetal central organs resulting in organ damage and death, and this lactate may lower the pH in the umbilical artery. Understanding the different types of fetal hypoxia on the CTG trace may help practicing clinicians to predict the rate of fall in fetal pH, and therefore, predict the umbilical cord pH at birth. It is important to appreciate that non-hypoxic pathways of fetal compromise such as chorioamnionitis may not be associated with low umbilical arterial pH at birth. Fetal pathophysiological approach to CTG interpretation based on deeper understanding of types of intrapartum hypoxia and features of non-hypoxic pathways of injury may help avoid the onset of neonatal metabolic acidosis and improve perinatal outcomes.

Keywords: Acute Hypoxia, Chorioamnionitis, Chronic Hypoxia, Gradually Evolving Hypoxia, Hypoxic ischaemic encephalopathy (HIE), Neonatal acidosis, Subacute Hypoxia.

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I. Introduction

It has been long recognized that the onset of regular and progressive uterine contractions may increase the risk of intrapartum fetal hypoxic-ischemic injury as a result of repetitive and sustained compression of the umbilical cord and/ or progressive reduction in utero-placental gas exchange. Any interruption in fetal oxygenation via the umbilical cord, if it is profound and / or sustained, can lead to a reduction in oxygen saturation in fetal arterial blood (hypoxaemia), leading to reduced oxygen delivery to tissues and organs (hypoxia), triggering anaerobic metabolism. The production of lactic acid in tissues and organs not only increases the risks of denaturation of proteins and resultant organ failure, but lactate is also a very poor energy source, and therefore, leads to a reduction of energy essential for vital cellular functions, hastening cell death. If anaerobic metabolism and production of lactate commences in fetal essential central organs (i.e. the brain, myocardium and adrenal glands), it is termed "asphyxia", and lead to hypoxic ischaemic encephalopathy (HIE) and its sequalae (e.g. neurological damage culminating in cerebral palsy or learning difficulties) and /or perinatal death.

In reality, neonatal metabolic acidosis secondary to an intrapartum hypoxic insult leading to HIE and neurological damage is very rare. Recently, [1] analyzed 29,787 births and concluded that neonatal metabolic acidaemia was not only rare, but it had a weak to absent association even with short term poor perinatal outcomes. Similar results were reported by [2] who analyzed 51,519 births and concluded that neonatal acidaemia was only weakly associated with adverse perinatal outcomes. They further concluded that most neonates with neurological morbidity had normal pH in the umbilical artery at birth [2]. There are three main reasons for this apparent lack of association between neonatal metabolic acidosis and poor perinatal outcomes. Firstly, human fetus

has Fetal Intelligent, Responsive Adaptation (FIRA) from early gestation not only to avoid damage from the hypoxic intrauterine environment during the antenatal period, but also during labour (Table I). Secondly, intrapartum hypoxia is relatively a small pathway of fetal neurological damage, and the hunan fetus is exposed to several non-hypoxic pathways (Fig. 1) which operate without causing metabolic acidosis. Thirdly, most guidelines on fetal heart rate interpretation during labour are purely based on "pattern-recognition" with parameters grouped under different "categories" with arbitrary time limits without considering the fetal responses to hypoxic and inflammatory stresses during labour [3]- [5]. This has resulted in systematic reviews highlighting an absence of any correlation between electronic fetal heart rate monitoring using a cardiotocograph (CTG) and improvement of long-term perinatal outcomes [6], and several authors recently questioning the role of CTG in preventing neonatal metabolic acidosis [7].

This review aims to help predict neonatal metabolic acidosis based on the types of fetal hypoxia observed on the CTG trace based on the International Consensus Guidelines on Physiological Interpretation of CTG, produced by 34 CTG Experts from 14 countries in 2018 [8].

II. Pathways of Fetal Damage and Types of Fetal Acidosis

Most guidelines developed to aid fetal heart rate interpretation during labour are based on identifying hypoxic or mechanical stresses, by determining the morphology and duration of fetal heart rate decelerations. However, this simplistic approach fails not only to appreciate multiple pathways of fetal compromise during labour (Fig. 1), but also the intensity of hypoxic stress (i.e. different types of fetal hypoxia), and most importantly, fetal responses to ongoing hypoxic and non-hypoxic stresses on the CTG trace.

A. Maternal Environment

Unlike adults, a fetus is not exposed to the external environment. Therefore, the fetus depends on normal maternal environment not only to obtain oxygen and nutrients, but also to excrete metabolic waste products to avoid injury and death. Any derangements in the maternal environment (infection, hypoxia, acidosis, organ failure) would have a direct effect on the fetus, threatening both fetal well-being and survival (Fig. 1). Passive transfer of metabolic acids (e.g. diabetic ketoacidosis) may result in low pH in both the umbilical vein and the artery, whereas in acidosis arising in the fetal compartment would lead to a low pH in the umbilical artery and not the umbilical vein which reflects the pH of the maternal venous sinuses. Similarly, severe maternal sepsis with metabolic acidosis or hepatic or renal acidosis may cause a lower pH in both the umbilical vein and umbilical artery. If maternal condition is not rapidly corrected, persistent passive transfer of acid may lead to fetal compromise. Recently, it has been shown that maternal anaemia is associated with increased significantly higher partial pressures of oxygen in the umbilical artery, and umbilical venous hyperoxaemia, which suggest initial fetal compensation [9]. However, if adverse maternal environment is not rapidly corrected, fetal compensatory responses are likely to fail, resulting in the onset of fetal anaerobic metabolism, and acidosis.

TABLE I: "EVEREST-IN-UTERO": FETAL INTELLIGENT, RESPONSIVE, ADAPTATION (FIRA) TO HYPOXIC INTRAUTERINE ENVIRONMENT

Parameters		Maternal	Fetal
Blood Flow Oxygen carrying capacity	Intrauterine Fetal Adaptation	Uterine = 800-1000 ml / min Hb = 110-140 g/L	Fetal = 300 ml/min (significantly more per Kg body weight) Hb = 180-220 g/L
Affinity for Oxygen		Adult haemoglobin with lower affinity for oxygen and a lower P_{50},	Fetal haemoglobin with increased affinity for oxygen and higher P_{50}
Baseline Heart Rate		60 – 90 bpm	110-160 bpm – increased perfusion to vital organs and increased rate of oxygenation from the placenta
Ability to maintain myocardium in positive aerobic balance when exposed to hypoxic stress		Increased rate and depth of respiration to increase the supply of oxygen to prevent anaerobic metabolism	A reflex reduction in the myocardial workload (i.e. deceleration) when oxygenation is interrupted to reduce the myocardial oxygen demand to avoid anaerobic metabolism.
Ability to redistribute Using catecholamines		Moderate – need to perfuse vital organs including the lungs	Excellent – can shut off all fetal organs to protect the brain, heart and the adrenal glands
SO_2 –Uterine artery	Oxygen saturations and partial pressures	98 %	45%
SO_2 – Uterine Vein		75%	70%
PO_2 Uterine Artery		100 mmHg	18 mmHg
PO_2 Uterine Vein		40 mmHg	28 mmHg

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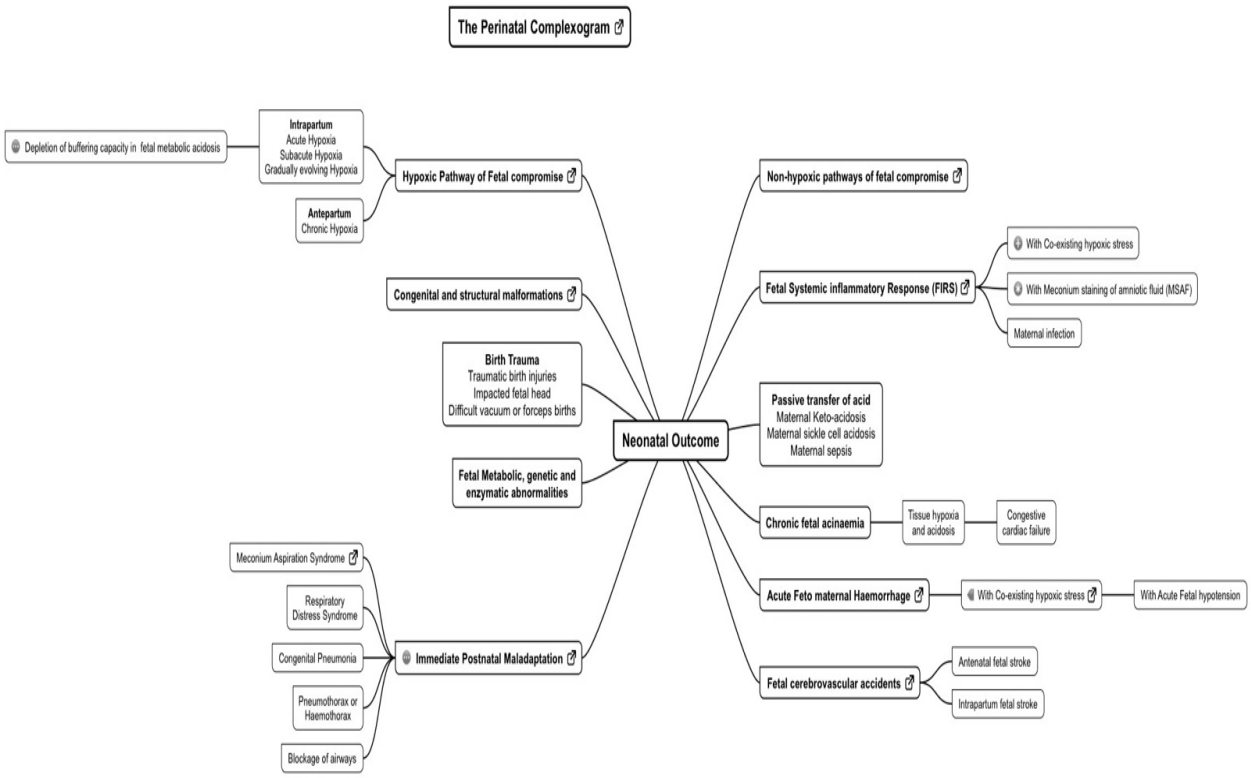

Fig. 1. The "Perinatal Complexogram": Multiple pathways of potential fetal compromise.

B. Intrauterine Hypoxic Environment

The intrauterine environment is profoundly hypoxic during the antenatal period, as it reflects the oxygen saturation of the uterine vein which is 70 % (Table I). An adult would require intubation and positive pressure ventilation if oxygen falls to 70%. However, due to the presence of fetal haemoglobin with higher affinity and presence of larger haemoglobin concentration, the human fetus avoids hypoxic-ischaemic injury during the antenatal period. However, with the onset of uterine contraction in labour, which progressively become longer, stronger and more frequent as the labour advances, the fetal oxygen saturation may fall down to even 30% [10]. At the summit of the Mount Everest, the estimated oxygen saturation is 33%, and therefore, during labour, the human fetus is exposed to an "Everest-in-Utero". Fetal compensatory responses which include decelerations to protect the myocardium from acidosis, loss of accelerations (to conserve energy by restricting unnecessary somatic body movements), catecholamine surge to increase the heartrate (i.e. cardiac output), and effective redistribution and centralization to protect the essential central organs would help avoid hypoxic ischaemic injury [11]-[13]. However, if these compensatory responses fail or if the fetus is unable to mount effective compensatory responses due to antenatal compromise or previous injury or insult, then evidence of metabolic acidosis will be seen in the umbilical artery.

C. Intrauterine Inflammatory Environment

Intrauterine environment is exposed to the entry of bacteria and other microbes from the maternal environment via the transplacental spread (less common) or as an ascending infection from the maternal birth passage (more common). In adult systemic inflammatory response (SIRS), metabolic acidosis occurs very late in the disease process as a result of increased oxygen extraction as a result of increased metabolic demands and reduced tissue perfusion due to vasoparalysis and hypotension. Similarly, in fetal inflammatory response syndrome (FIRS), fetal metabolic acidosis and resultant changes on the CTG are very late signs. It has been shown that in chorioamnionitis one should be vigilant for features of neuroinflammation and not decelerations on the CTG trace [14]-[15]. Fetuses exposed to severe inflammatory response are more likely to lose their active and quiet sleep-activity cycle, a phenomenon called "cycling" most likely as a result of increased neuronal metabolism as a result of inflammation [16], [17]. Therefore, babies with chorioamnionitis unlikely to show evidence of neonatal acidosis at birth, unless there was a co-exiting hypoxic stress, especially with injudicious use of oxytocin. Presence of meconium within the uterine cavity may increase the likelihood of intrauterine infection [14], [18]-[19], and infection may increase the likelihood of meconium aspiration syndrome [19]-[20]. In such cases, the umbilical arterial pH may be normal at birth, but there may be rapid development of neonatal hypoxia and acidosis *after* birth as the neonate may not be able to oxygenate the lungs due to the presence of meconium within the airways and the alveoli leading to the damage to the alveolar membrane, irritation of the pulmonary blood vessels and primary pulmonary hypertension (PPHN), after clamping the umbilical cord [19].

D. Impact of Aerobic and Anaerobic Fetal Metabolism

In aerobic metabolism, the pyruvate which is formed from a molecule of glucose after glycolysis, is able to enter the mitochondria and the Tricarboxylic Acid (TCA) or the "Kreb's Cycle. This process of oxidative phosphorylation and activation of the electron transport chain results in the production of 38 Adenosine Triphosphate (ATP) molecules

to maintain membrane stability and cellular functions (Fig. 2). In contrast, in the absence of oxygen, the pyruvate is unable to enter the mitochondria, leading to the production of lactate, which generates only 2 ATPs, resulting in membrane instability and loss of energy to maintain essential cellular functions leading to cell damage and cell death (Fig. 2).

E. Normal Acid-Base Balance in the Umbilical Blood Vessels in Aerobic Conditions

In the absence of ongoing hypoxic stress, the umbilical vein carries oxygenated blood from the placental sinuses to the fetus, whereas the umbilical artery brings the fetal blood with metabolic by-products. Therefore, one would expect to see a lower pH, high PCO_2 and higher lactate concentration in the umbilical artery as compared to the umbilical vein.

F. Types of Fetal Acidosis and Changes in the Umbilical Arterial and Venous pH

Respiratory acidosis occurs as a result of the inability of the fetus to expel carbon dioxide, usually occurs due to the repetitive compression of the umbilical artery immediately prior to birth. The retained carbon dioxide combines with water to produce a weak acid (carbonic acid), which easily dissociates to produce hydrogen ions (H^+) and bicarbonate (HCO_3^-), which is a reversible reaction (Fig. 3). Therefore, when the carbon dioxide is able to be expelled (i.e. when the transient cord compression is relieved or with crying at birth), the equation rapidly reverses leading to the combination of H^+ and HCO_3^- to form carbonic acid, which h rapidly dissociates to form CO_2 and H_2O. Therefore, respiratory acidosis appears fast and disappears fast and is seldom associated with fetal damage. Moreover, for each H^+ produced due to the breakdown of carbonic acid (H_2CO_3) there is a simultaneous production of HCO_3^-, resulting in absence of any base deficit. The umbilical artery is likely to show a mild lowering in the pH with no increase in base excess.

Metabolic acidosis occurs due to oxygen deprivation leading to the production of lactate, without simultaneous production of any bases or buffers (Fig. 3). This results in rapid depletion of buffers as the fetus attempts to "mop-up" the lactate to maintain the pH to ensure continuation of enzymatic function and to avoid denaturation of cellular and membrane proteins. Therefore, the umbilical artery is likely to show a low pH and an increased base deficit because of depletion of bases to "buffer" the lactic acid.

It is important to appreciate there may an overlap resulting in a mixed acidosis, and it is vital to determine the lactate level when analyzing the umbilical artery and the vein at birth because estimation of pH may mask the severity of ongoing mixed acidosis. Moreover, the increased levels of fetal haemoglobin not only carries more oxygen to avoid fetal acidosis, it can also act as a good buffer when needed. The drop in the fetal pH is not linear, but *"curvilinear"* because in the initial phase, due to the presence of sufficient bases, addition of large amount of H^+ would lead to a smaller drop in the pH in the umbilical artery. However, as the acidosis worsens and the buffers are progressively depleted, even addition smaller amount of H^+ may lead to a significant fall in the pH.

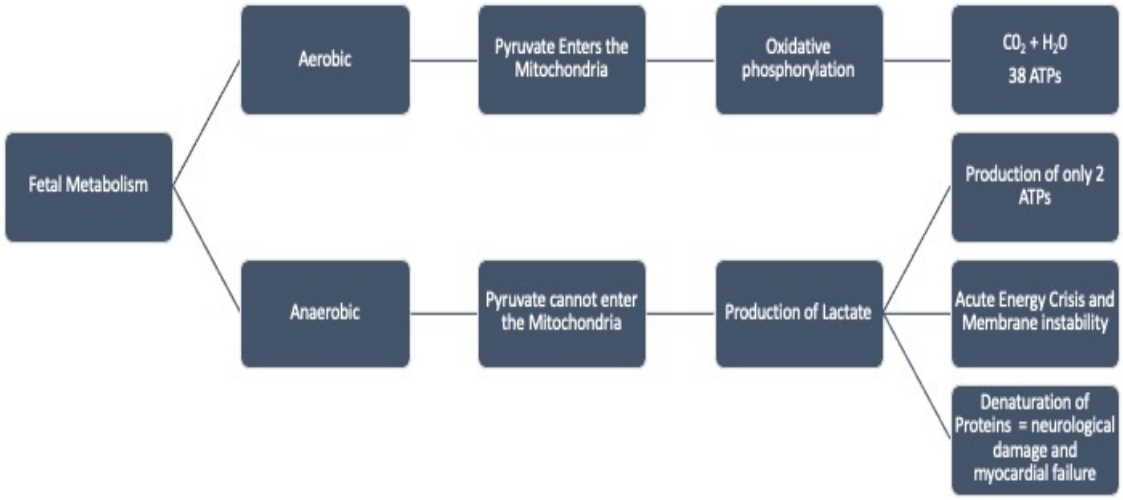

Fig. 2. Mechanisms and effects of respiratory and metabolic acidosis.

TABLE II: NORMAL UMBILICAL ARTERIAL AND VENOUS PH, LACTATE AND BASE DEFICIT

	Umbilical Artery (UA)	Umbilical Vein (UV)	Expected A-V Difference
pH	7.27 (7.00-7.35)	7.35 7.23-7.44)	<0.02 in UA (fetal blood contains more metabolic waste products)
PCO_2 (kPa)	7.3 (5.6– 9.8)	5.4 (3.8 – 7.1)	> 1 kPa in UA (Fetal blood has more carbon dioxide from metabolism)
B Def (mmol/l)	-3.0 (-2.5 to - 10.0)	-3.0 (-1.0 to– 9.0)	~ = (in the absence of acidosis, there is no depletion of buffers)
Lactate (mmol/l)	3.7 (2.0 – 6.7)	0	Lactate is a by-product of anaerobic metabolism and therefore, should be absent in the umbilical vein which brings oxygenated blood

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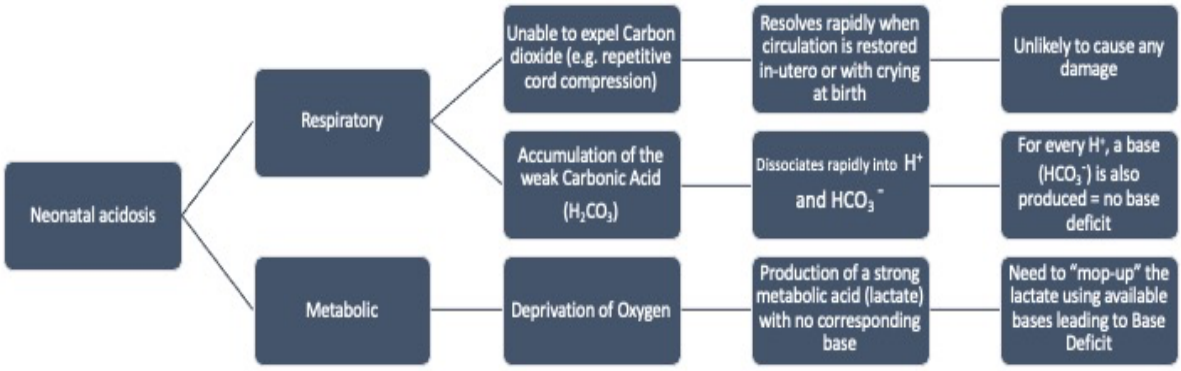

Fig. 3. Mechanisms and effects of respiratory and metabolic acidosis.

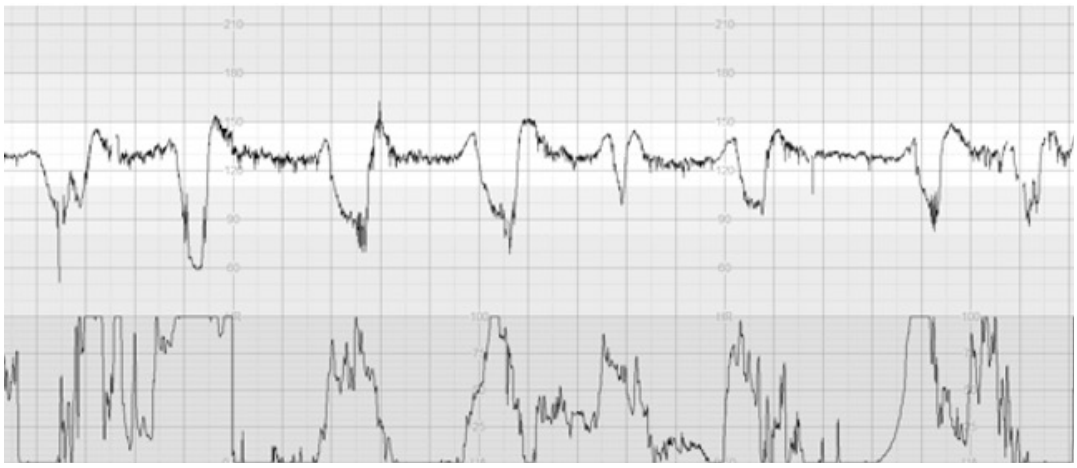

Fig. 4. Gradually evolving Hypoxia with evidence of normal variability and cycling.

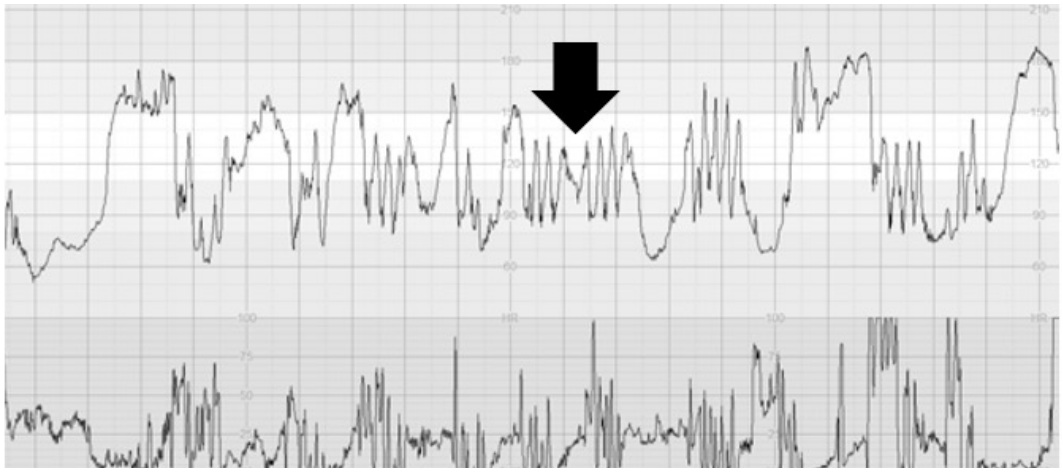

Fig. 5. Subacute Hypoxic pattern with reduced time spent at the baseline as compared to the time spent during the decelerations Note the presence of the "ZigZag" pattern (Arrow) due to autonomic instability.

III. Types of Fetal Hypoxia and Umbilical Arterial Acidosis

The rate of fall in the fetal pH during labour will depend on the intensity and duration of the hypoxic stress, the individual reserve of the index fetus, and any pre-existing or co-existing fetal pathology such as chorioamnionitis [21]. A fetus with a reduced placental reserve may rapidly develop acidosis when exposed to the same intensity of hypoxic stress as compared to a fetus with a normal placental reserve. Similarly, a fetus with intrauterine growth restriction with smaller "non-essential" organs may not be able effectively redistribute oxygenated blood by the release of catecholamines to protect the central organs. Conversely, a macrocosmic fetus with relative utero-placental insufficiency (RUPI), also may not be able withstand ongoing hypoxic stress due to increased tissue metabolic demand. Therefore, in such cases, fetal acidosis may develop rapidly.

A. Gradually Evolving Hypoxia

Fetus responds to a gradually evolving intrapartum hypoxic stress by decelerations to protect the myocardial workload, loss of accelerations to conserve energy and then releases catecholamines to increase the cardiac output, evidenced by an increase in the baseline fetal heart rate on the CTG trace [11]-[13]. Reference [22] reported that even if there are repetitive variable or late decelerations suggestive of a gradually evolving hypoxia (Fig. 4), if the baseline variability remains normal, there was no acidosis. It has been shown that even if the baseline FHR increases due to fetal

catecholamine surge, there was no acidosis if the baseline variability continued to remain normal, and only when the baseline variability reduced, approximately 30% of neonates had evidence of acidosis in the umbilical cord [22]. Therefore, in a gradually evolving hypoxia, if the baseline FHR remains stable and the variability remains normal in between the decelerations (Fig. 4), then, there is very low risk of acidosis in the umbilical cord at birth. In a gradually evolving hypoxia with increased baseline FHR and reduced variability, one would expect to find similar pH in both the umbilical artery and the umbilical vein as there would be sufficient time for the acidotic fetal blood to reach the placental sinuses and then return via the umbilical vein.

B. Subacute Hypoxia

Subacute hypoxia occurs when the intensity of hypoxic stress increases, with reduced time available for the fetus to mobilize resources to protect the fetal organs, [11]-[13], [21]. Subacute hypoxia is recognized on the CTG trace when the time spent on the baseline to perfuse central organs is less than then time spent during the decelerations (Fig. 5). It usually occurs during the second stage of labour with active maternal pushing or injudicious use of uterotonic agents. It is estimated that the fetal pH drops at the rate of 0.01 every minute or 0.1 in 20-30 minutes. Therefore, clinicians should be able to predict the umbilical arterial pH at birth by calculating the duration of ongoing subacute hypoxic pattern. Reference [23] reported that an abrupt increase in variability, called the "ZigZag Patterrn" (Fig. 5) secondary to fetal autonomic instability in subacute hypoxia is associated with poor perinatal outcomes. If subacute hypoxia is continues for less than 60 minutes, it is likely that pH of the umbilical artery may be approximately 0.2 -0.3 units lower than the umbilical vein. However, if it is allowed to persist for more than 90 minutes, then the pH in umbilical artery and the vein may be similar as there would be sufficient time for the acidotic blood from the fetus to contaminate the placental sinuses and then return back to the fetus via the umbilical vein.

C. Acute Hypoxia

A sudden and profound disruption to fetal oxygenation can occur either due to an irreversible cause (e.g. placental abruption, uterine rupture or umbilical cord prolapse) or due to a reversible cause (e.g. maternal hypotension, uterine hyperstimulation or a sustained umbilical cord compression), and is characterized by acute hypoxia on the CTG trace (Fig. 5). The fetus immediately drops the heart rate, and then sustains it to prevent the myocardium from shifting to an anaerobic metabolism which may result in myocardial acidosis [11]-[13], [21]. Reference [13] emphasized the importance of having a systematic approach to the management of Acute Hypoxia to optimize perinatal outcomes. A sudden and sustained reduction in the fetal heart rate would lead to a reduction in fetal perfusion pressure, increasing the likelihood of fetal metabolic acidosis [21]. It has been estimated that the pH in the umbilical artery drops at the rate of 0.01 every minute or 0.1 in every 10 minutes [11], [13], [24]. Therefore, it is based on the duration of acute hypoxia, it is possible to predict the umbilical arterial pH at birth. Recently, it has been reported that if the nadir of the prolonged deceleration observed on the CTG trace during an acute hypoxic insult is below 80 bpm, then, it was associated with increased risk of neonatal metabolic acidosis [25]. This is not surprising because the fetal myocardium operates at almost at the maximum Frank-Starling Law, and therefore, it is not possible to increase the cardiac output by increasing the force of contraction of the ventricles. The only way to for any fetus to increase the cardiac output is to increase the baseline heart rate, and if the nadir of the baseline FHR falls below 80 bpm, it would not only reduce the central organ perfusion due to the sudden drop in the cardiac output and systemic blood pressure, but, it would also reduce the perfusion of the placenta, leading to rapid development of hypoxia and acidosis. It is also important to appreciate the fact that in placental abruption and uterine blood pressure, in addition to a sudden and profound reduction of fetal cardiac output during the prolonged deceleration and fetal bradycardia, there may be concomitant loss of fetal blood volume. This would lead to an acute fetal hypovolemia and hypotension, leading to severe acidosis. Therefore, unlike acute hypoxia due to reversible causes, in conditions where there is a co-existing fetal hypovolemia, the umbilical arterial pH may be worse than what would be normally anticipated. It is essential to accomplish an urgent birth in all cases of acute hypoxia due to an irreversible cause to avoid severe neonatal metabolic acidosis and poor perinatal outcome. Reference [11] emphasized the importance of "3, 6, 9, 12, 15" Rule to avoid hypoxic ischaemic insult in acute hypoxia. In acute hypoxia, if delivery is accomplished immediately, one would expect to have a large difference between the pH of the umbilical artery and the vein, with severe acidosis in the umbilical artery but near normal pH in the umbilical vein.

D. Chronic Hypoxia

Chronic utero-placental insufficiency leading to fetal decompensation results in chronic hypoxia on the CTG trace [11]-[13], [21], [26]-[27], charactered by higher than expected baseline FHR, reduced variability and shallow decelerations (Fig. 7). Reference [26] Chandraharan have published a "Chronic Hypoxia Checklist" to ensure timely delivery to avoid poor perinatal outcomes in fetuses with pre-existing compromise. In chronic hypoxia, the pH in the umbilical artery is expected to be between 7.0 -7.15 (i.e. mild acidosis), with similar pH in the umbilical vein [26], [27]. Avoidance of further hypoxic stress is essential by ensuring timely recognition of chronic hypoxia and immediate delivery without subjecting the fetus to ongoing uterine contractions.

E. Chronic Fetal Anaemia and Acidosis

In chronic fetal anaemia and acidosis, one would expect to see a smooth, undulating "sine wave" pattern with reduced variability, and absence of accelerations on the CTG trace, referred to as a "Typical sinusoidal pattern" [26], [28]. The pH in the umbilical artery is likely to show a mild acidosis (7.0 -7.15), however, if the fetus is exposed to further hypoxic stress, severe metabolic acidosis can occur. Therefore, continuation of uterine contractions should be avoided if a typical sinusoidal pattern is observed on the CTG Trace (Fig. 8).

Reference [28] emphasized the importance of differentiating the "Typical" sinusoidal pattern due to chronic hypoxia and acidosis from the "Atypical" sinusoidal pattern or the "Poole Shark Teeth" pattern (Fig. 9) seen in an acute

feto-maternal haemorrghage. Poole Shark Teeth Pattern is an acute obstetric emergency which may occur in placental abruption, uterine rupture, rupture of vasa praevia or an acute feto-maternal haemorrhage which warrants an immediate birth to avoid poor perinatal outcomes. Similar to an acute postpartum haemorrhage, the umbilical arterial pH may be normal with very low haemoglobin level, unless there was a delay in accomplishing delivery.

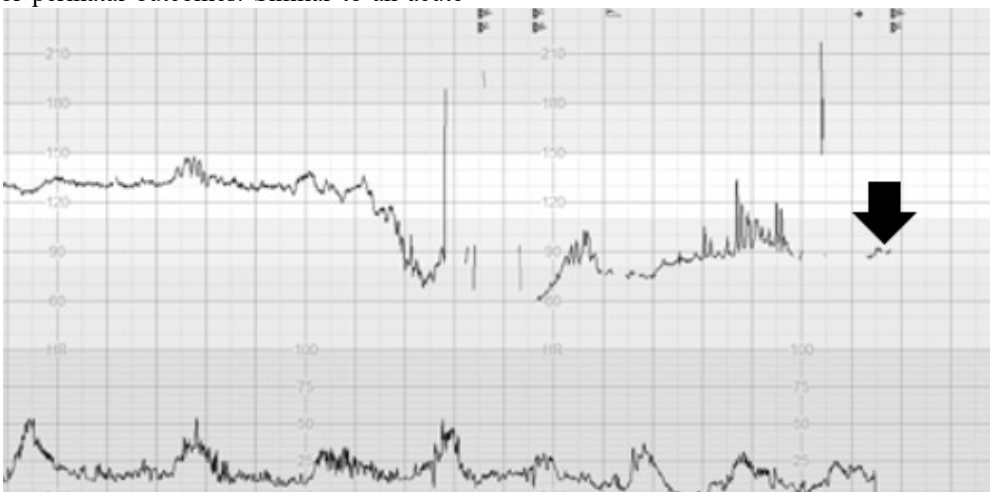

Fig. 6. Acute hypoxia due to an irreversible cause. Note the inability of the fetus to restore normal baseline with the onset of reduced baseline FHR variability (Arrow).

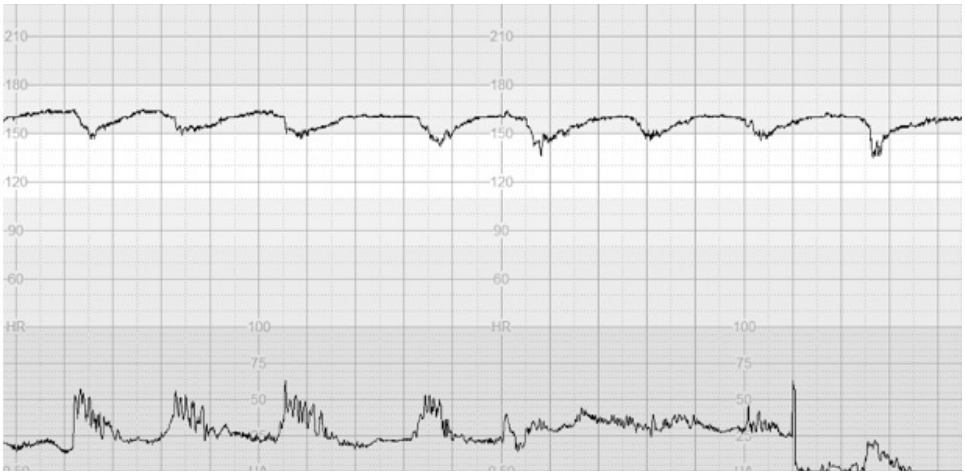

Fig. 7. Chronic Hypoxia: note higher than expected baseline FHR for gestational age (41 weeks), reduced baseline variability, and repetitive shallow decelerations.

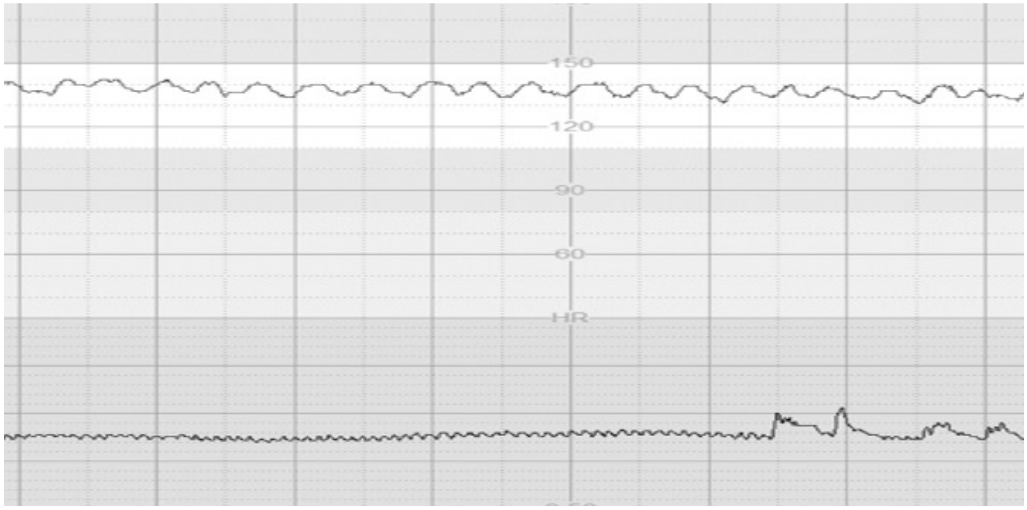

Fig. 8. Typical sinusoidal pattern with smooth, undulating, sinus wave-form pattern.

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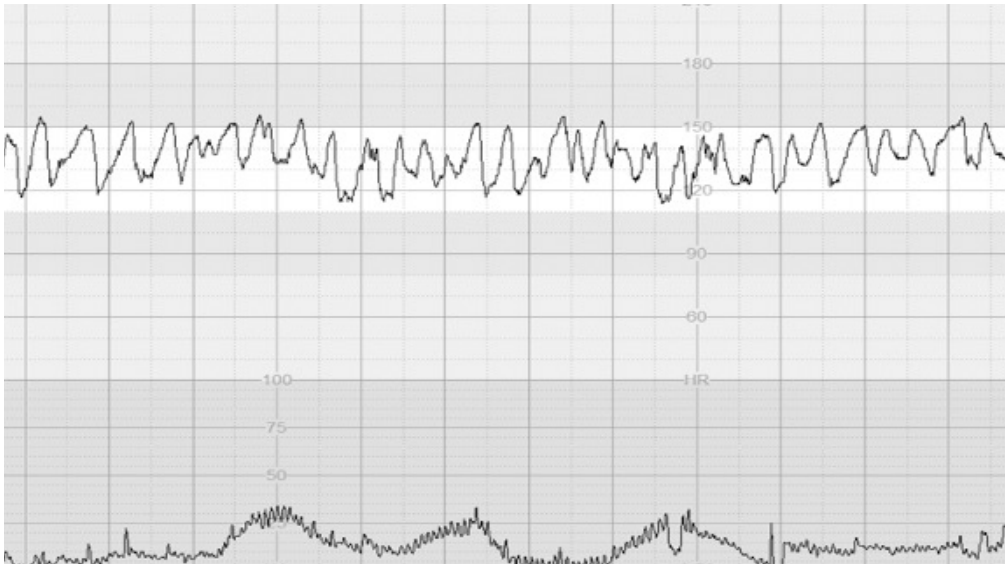

Fig. 9. The Atypical Sinusoidal Pattern (also called the "Poole Shark Teeth" Pattern) seen in acute feto-maternal haemorrhage.

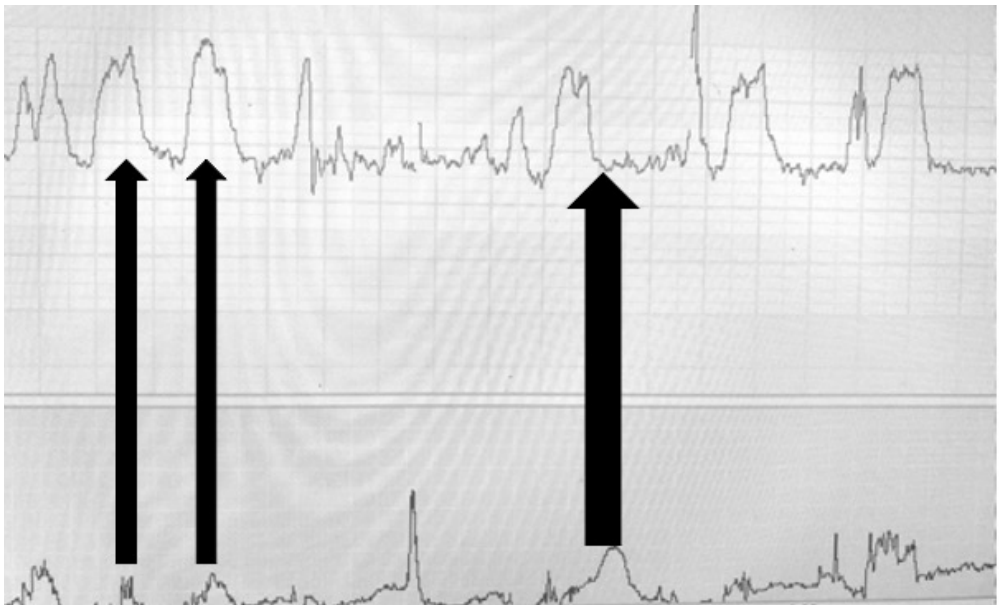

Fig. 10. The "Double Mountain Peak" Sign : Erroneous monitoring the maternal heart rate as fetal heart rate. Note the large amplitude accelerations of the maternal heart rate (second d mountain) coinciding with uterine contractions (first mountain).

IV. Correlation between Types of Fetal Hypoxia and Neurological Injury

Reference [29] reported that there was a correlation of the types of intrapartum hypoxia on the CTG trace and the pattern of neurological injury observed on the Magnetic Resonance Imaging (MRI) scan after birth. More recently, [30] reported that physiological classification of CTG and the detection of types of fetal hypoxia correlated with neonatal MRI scan findings. Moreover, recent evidence appears to suggest that the use of physiological interpretation of CTG and the determination of the types of fetal hypoxia on the CTG trace is associated with a reduction in the rate of hypoxic-ischaemic encephalopathy (HIE) and neonatal metabolic acidosis [31]-[34]. Recently, the use of CTG guidelines which are based on 'pattern-recognition" have been discouraged, and a physiological approach to fetal heart rate interpretation based on the types of fetal hypoxia and fetal responses to stress has been advocated to ensure individualization of care and to improve perinatal outcomes [35], [36]. It is anticipated that understanding the types of fetal hypoxia and recognizing the features of fetal compensatory responses on the CTG trace may help clinicians to predict umbilical artery pH at birth, and ensure timely action including intrauterine resuscitation [37] to avoid neonatal metabolic acidosis at birth.

V. Medico-Legal Pitfalls

A. Recognition of the "Double Mountain Peak" Sign

Erroneous monitoring of the maternal heart rate as the fetal heart rate may result in severe fetal metabolic acidosis if the ongoing fetal bradycardia is missed, leading to severe perinatal neurological injury or fetal death [38]-[40]. It is important to appreciate that due to the repetitive compression of the fetal head, the umbilical cord and reduction in the utero-placental circulation with the onset of maternal active pushing, fetal heart rate often shows repetitive decelerations to protect the myocardial workload. In contrast, due to pain, and muscular activity, the maternal heart rate increases with uterine contractions Recently, [41] emphasized the importance of recognizing the "Double Mountain Peak" sign (Fig. 10), where the large amplitude accelerations coincide

with uterine contractions to avoid severe metabolic acidosis secondary to erroneous monitoring of the maternal heart rate as fetal heart rate during labour.

Similarly, in cases of acute cord compression immediately prior to birth or if there are tight loops of umbilical cord, the umbilical arterial pH may be normal, if the blood sample is taken from the loop of the umbilical cord proximal to the site of obstruction. In this case, the neonatal sample may show evidence of severe metabolic acidosis. Blood sample should always be taken from the segment of the umbilical cord distal to the obstruction to accurately assess fetal acid-base status at birth to avoid medico-legal pitfalls [42].

VI. Predicting Umbilical Arterial pH Based Pathophysiological Approach to CTG Interpretation

Umbilical arterial (UA) pH reflects the oxygenation of the fetal compartment, the onset and severity of fetal respiratory and metabolic acidosis. Therefore, lowering of umbilical arterial pH will be seen only in cases of hypoxic pathways of fetal compromise which result in the shift in the metabolism from aerobic to anaerobic with the production of lactic acid in the fetal compartment. The fetus attempts to maintain the pH within a range that would avoid denaturation of proteins, enzymes and the cell membranes which may cause cellular dysfunction and irreversible cell damage and/ or death. As the bases (bicarbonate, phosphate, ammonia, plasma proteins including fetal haemoglobin) are utilized to "mop-up" the metabolic acids, one would expect to see a gradual depletion of buffers leading to an increased base-deficit. It is important to appreciate the "curvilinear" fall in the umbilical arterial pH in metabolic acidosis due to the presence of sufficient buffers the pH falls slowly despite of the addition of large amount of metabolic acid in the initial period. However, as the acidosis persists or gets worse, all the buffers get depleted, leading to a rapid drop in the pH even when a small amount of acid is added to the fetal circulation.

A drop in the umbilical arterial pH from 7.28 to 7.18 occurs with excessive amounts of H^+ because the availability of sufficient amount of buffers prevent a significant fall in the pH ensure enzymatic and cellular functions.

TABLE III: PREDICTING UMBILICAL CORD PH BASED ON THE PATHOPHYSIOLOGICAL APPROACH TO CTG INTERPRETATION

Underlying Pathology	Physiological CTG Interpretation	Predicted Umbilical pH	Interpretation	Suggested Actions to avoid damage due to acidosis
Acute Hypoxia	Sudden and prolonged deceleration lasting for > 3 minutes	Drops at the rate of 0.01 / every minute or 0.1 in 10 minutes	Large arterio-venous difference	If irreversible causes are identified, urgent birth is recommended. In reversible causes, immediate intrauterine resuscitation, including acute tocolysis should be considered.
Subacute Hypoxia	Reduced time spent at the baseline as compared to the time spent during decelerations. Often associated with the ZigZag Pattern (ZZP)	Drops at the rate of 0.01 every 2-3 minutes or 0.1 in 20-30 minutes	If delivery is accomplished within 30-60 minutes, the UA pH will be 0.1-0.2 units lower than the UV. If delivery is not accomplished and fetal oxygenation is not improved for > 90 minutes, then, both the UA and UV will show low pH	Immediate action to improve fetal oxygenation including stopping oxytocin, and stopping active directed pushing. If ZZP is seen and if immediate spontaneous or operative vaginal birth is not imminent, consider tocolytics to rapidly improve oxygenation.
Gradually evolving Hypoxia	Repetitive decelerations, loss of accelerations and increase in the baseline FHR	If the baseline remains stable and the variability remains normal, the likelihood of low pH in the UA is extremely low. If there is a reduction of baseline variability following receding decelerations and an increased baseline FHR, then, the risk of UA pH of < 7.0 is approximately 30%	If the variability is reduced, both the UA and UV are likely to show similar acidotic pH because there was sufficient time for the acidotic fetal blood from the UA to contaminate the placental sinuses and return via the UV	If the variability remains normal despite ongoing decelerations and an increase in the baseline FHR, immediate action to reduce the hypoxic stress. If the variability is reduced, an urgent intrauterine resuscitation including acute tocolysis to restore fetal circulation. If birth is not imminent, and uterotonics are not used, then, the overall clinical picture should be considered, and an emergency caesarean section is recommended
Chronic Hypoxia	Higher than expected baseline for the Gestational age, associated with reduced variability and shallow decelerations	Mild acidosis (7.00-7.15) will be expected in both the UV and the UV because this is a long standing, slowly progressive failure of placental oxygenation.	If additional hypoxic stress is caused either by artificial rupture of membranes or allowing the uterine contractions to continue, then, the UA pH may fall below 7.0	Avoid further hypoxic stress, including administration of tocolytics if repetitive decelerations are observed, and accomplish birth within 60 minutes.
Chorioamnionitis	Increased baseline FHR (> 10%) without preceding decelerations usually associated with features of neuroinflammation (absence of cycling, sinusoidal and the ZZP).	UA pH is usually normal unless additional hypoxic stress is caused. UA lactate level is high in later stages	In late stages, or in the presence of injudicious use of oxytocin, pH will be low in both UA and the UV with increased lactate level.	If spontaneous or operative vaginal delivery is not imminent, emergency caesarean section is recommended in the presence of features of neuroinflammation.

However, once the buffers have been depleted, even a small addition of H^+ may lead to a rapid drop in the pH from 7.18 to 6.8. It is vital to consider this information in clinical practice whilst making decisions regarding the urgency of birth, based on the type of fetal hypoxia observed on the CTG trace and the underlying pathology (Table III).

Hydrogen ions rapidly diffuse across the placenta and therefore, is likely to normally earlier when fetal oxygenation is restored. However, the lactate takes a longer time to clear from the fetal circulation. The base deficit also takes longer to normalize because buffers need to be resynthesized and restored. In non-hypoxic causes of fetal compromise such as chorioamnionitis or acute fetomaternal haemorrhage, the pH in the umbilical artery may remain normal, unless additional hypoxic stress is super-imposed by allowing the uterine contractions to continue. If oxytocin is used in such cases, severe metabolic acidosis may occur leading to lowering of the pH in the umbilical artery. In severe chorioamnionitis, similar to adult sepsis, anaerobic metabolism may occur in fetal tissues and organs due to increased metabolic demand and excessive extraction of oxygen. The onset of anaerobic metabolism may result in increased lactate in the umbilical cord. Therefore, when analysing the umbilical acid-base balance, the pH, base deficit, lactate and the arterio-vernous difference should be scrutinized (Tables II & III) to ensure appropriate management in the neonatal period, and to counsel parents regarding likelihood of long term sequalae.

VII. Conclusion

Physiological interpretation of CTG and determining the type of fetal hypoxia based on the International Consensus Guidelines on Physiological Interpretation of CTG may help determine the rate of fall in the pH in the fetal umbilical artery. Such an approach may help frontline clinicians providing care to predict the umbilical cord pH at birth, therefore, would enable timely and appropriate interventions to optimize fetal oxygenation. Except in cases of acute irreversible intrapartum accidents, the interventions should be aimed at reversing the cause of interruption of fetal hypoxic stress, and considering the use of tocolytics to improve utero-placental circulation. In non-hypoxic causes such as fetal inflammatory response syndrome (FIRS), umbilical artery pH is unlikely to provide information about fetal condition. In such cases features of fetal neuroinflammation and depression of central nervous system (CNS) on the CTG trace may help clinicians to ensure birth without subjecting these fetuses to additional hypoxic stress. Although, a large systematic review which analysed 481,753 neonates has concluded that low umbilical arterial cord pH at birth showed strong, consistent, and temporal associations with clinically important neonatal outcomes, it is important to appreciate that non-hypoxic pathways of fetal compromise may not be associated with low umbilical arterial pH at birth. In such cases, recognition of features of these non hypoxic causes on the CTG trace by deeper understanding of fetal physiology is essential to improve perinatal outcomes.

Conflict of Interest

Authors declare that they do not have any conflict of interest.

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