

Maternal and Fetal Acid-Base Chemistry: A Major Determinant of Perinatal Outcome

Omo-Aghoja L

Department of Obstetrics & Gynecology, Faculty of Clinical Medicine, Delta State University, Abraka, Nigeria

Address for correspondence:

Dr. Omo-Aghoja L,
Department of Obstetrics &
Gynecology, Faculty of Clinical
Medicine, Delta State University,
Abraka, Nigeria.
E-mail: eguono_2000@yahoo.com

Abstract

Very small changes in pH may significantly affect the function of various fetal organ systems, such as the central nervous system, and the cardiovascular system with associated fetal distress and poor Apgar score. Review of existing data on maternal-fetal acid-base balance in pregnancy highlight the factors that are associated with derangements of the acid-base status and the impact of the derangements on fetal outcome. Extensive search of electronic databases and manual search of journals for relevant literature on maternal and fetal acid chemistry, clinical studies and case studies were undertaken. There is a substantial reduction in the partial pressure of carbon dioxide (pCO₂) in pregnancy. Adequate buffering prevents significant changes in maternal arterial pH. Normal fetal metabolism results in the production of acids which are buffered to maintain extracellular pH within a critical range. Fetal hypoxia can occur when maternal oxygenation is compromised, maternal perfusion of the placenta is reduced, or delivery of oxygenated blood from the placenta to the fetus is impeded. When adequate fetal oxygenation does not occur, metabolisms proceed along with an anaerobic pathway with production of organic acids, such as lactic acid. Accumulation of lactic acid can deplete the buffer system and result in metabolic acidosis with associated low fetal pH, fetal distress and poor Apgar score. There is a significant reduction in pCO₂ in pregnancy. This change, however, does not result in a corresponding significant reduction in maternal arterial pH, because of adequate buffering. Very small changes in pH may cause significant derangement in fetal function and outcome.

Keywords: Acid-base balance, Determinants, Maternal and fetal, Perinatal outcome, Pregnancy

Introduction

Available evidence indicates that pregnancy is associated with a very substantial reduction in the maternal partial pressure of carbon dioxide (pCO₂).^[1,2] The diffusion of blood gases between the fetal and maternal circulations is probably thought to be due to this maternal change. However, because of the adequate buffering that is occurring within the blood system, there is relatively marginal change in maternal arterial pH. The consequence of this chronic reduction in pCO₂ is a state of compensated respiratory alkalosis with enhanced renal excretion and therefore, decreased circulating concentrations

of bicarbonate. The circulatory changes may possibly include intracellular acidosis in the erythrocytes, in which the predominant buffer is hemoglobin. This finding may signify that there is a greater potential for oxygen-hemoglobin dissociation during pregnancy, thus facilitating oxygen delivery across the placenta.^[1] Hyperventilation is a primary factor in the alteration in maternal acid-base balance in pregnancy.^[3]

Existing data suggests that normal fetal metabolism results in the production of acids (carbonic and organic), and despite this, the extracellular pH is kept within a critical range due to the efficient buffer mechanisms of the blood system. This is because the functions of the various fetal organ systems, such as the central nervous system and the cardiovascular system may be significantly affected by very small changes in pH.^[4] The major buffers utilized by the fetus for neutralizing hydrogen ion production are plasma bicarbonate and hemoglobin. Inorganic phosphates and erythrocyte bicarbonate are also potential buffers, although they play a lesser role in fetal acid-base hemostasis.^[1]

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Fetal hypoxia can occur when maternal oxygenation is compromised, maternal perfusion of the placenta is reduced, or delivery of oxygenated blood from the placenta to the fetus is impeded.^[1] When adequate fetal oxygenation does not occur, complete oxidative metabolism of carbohydrates to carbon dioxide (CO₂) and water is impaired and metabolism proceeds along an anaerobic pathway with production of organic acids, such as lactic acid, which are not readily excreted or metabolized. Accumulation of lactic acid can deplete the buffer system and result in metabolic acidosis.^[1] Maternal acidosis is associated with lower fetal pH and poor Apgar score.^[4-7]

The Apgar score is the very first test given to the newborn, immediately after the birth of the baby in the delivery or birthing suite.^[8,9] The test was designed to quickly evaluate a newborn's physical condition and to determine any immediate need for extra medical or emergency care. The Apgar score is usually assessed twice: Once at 1 min after birth and again at 5 min after birth. Sometimes, if there are concerns about the baby's condition or the score at 5 min is low, the test may be scored for a 3rd time at 10 min after birth.^[8,9] Five criteria are used to evaluate the baby's condition and each criterion is scored on a scale of 0-2, with 2 being the best score. The Apgar scoring is summarized in Table 1.

Newborns with scores of 7 and above are generally normal. A score of 4-6 is considered fairly low and 3 and below are generally regarded as critically low.^[8,9]

The fetus produces both volatile carbonic acid (H₂CO₃) and non-volatile acids (non-carbonic or organic acids). The fetus produces H₂CO₃ during oxidative metabolism (aerobic glycolysis). Since H₂CO₃ is formed primarily from CO₂ via hydration in the presence of erythrocyte carbonic anhydrase, the formation of H₂CO₃ is equivalent to CO₂ generation. The rate of CO₂ production, in turn, is equivalent to fetal oxygen

consumption.^[1,2] The non-carbonic (organic) acids in the fetus include uric acid (from the metabolism of non-sulfur-containing amino acids), lactate, and keto acids (from the metabolism of carbohydrates and fatty acids). These non-carbonic acids are eliminated through the maternal kidneys, after diffusing slowly across the placenta. The maternal kidney regenerates bicarbonate from the excretion of the non-carbonic acids.^[10]

Materials and Methods

The articles used for this review covered the period of 1953 to 2012, and in all 127 articles were retrieved following extensive literature search and of these, 65 were adapted for this article. Others were excluded either because they were extremely old publications, the full texts of the articles were not retrievable or unavailable, or where the articles were case reports. Most of the papers adapted for this review article were randomized controlled studies, cohort studies, case control studies, clinical studies, case studies and cross sectional studies. The articles were gotten following extensive literature search using the following search engines or databases: Medline, Elsevier, Medscape, eMedicine, google and PubMed. The literature search was done using the following keywords as a guide: Maternal and fetal, acid-base balance, pregnancy, determinants and perinatal outcome. Additionally, challenges of diagnosis and treatment, fetal hypoxia were also utilized. Literature on the subject was also researched using manual library search from relevant cited textbooks and articles in journals. The key and relevant aspects of maternal acid-base balance in pregnancy, the correlation between the maternal acid-base status, fetal clinical status and Apgar score were explored. Additionally, relevant aspects of fetal acid-base balance and the correlation between the fetal acid-base status and fetal clinical status were also reviewed. Also reviewed and highlighted were the challenges of diagnosis and treatment of fetal hypoxia.

Maternal acid-base balance in pregnancy

Background

During pregnancy the respiratory component of the maternal acid-base system shows a progressive fall in arterial CO₂ tension and a rise in oxygen tension and in the metabolic element, there is a parallel reduction in plasma bicarbonate.^[2,11] This results in a primary respiratory alkalosis and a secondary and compensatory metabolic acidosis and thus normal pH, usually on the alkaline side of the normal range. There is no true "acidosis of pregnancy" but a reduction of total acid and total base; the primary fall in the pCO₂ is buffered by the action of the renal mechanism, which controls loss or conservation of bicarbonate.^[2,11]

The progressive fall in the pCO₂ of maternal capillary blood during pregnancy reaches a nadir at a mean level of 31.3 mmHg and an increase in base deficit to -3.5 mEq/l with a fall in

Table 1: The APGAR scoring system				
Criteria	Score of 0	Score of 1	Score of 2	Component of acronym
Skin color/complexion	Blue or pale all over	Blue at extremities, body pink (acrocyanosis)	No cyanosis, body and extremities pink	Appearance
Pulse rate	Absent	<100	≥ 100	Pulse
Reflex irritability	No response to stimulation	Grimace/feeble cry when stimulated	Cry or pull away when stimulated	Grimace
Muscle tone	None	Some flexion	Flexed arms and legs that resist extension	Activity
Breathing	Absent	Weak, irregular, gasping	Strong, lusty cry	Respiration

standard bicarbonate to 21.3 mEq/l by the last trimester; the pH maintains an even level.^[2,11]

This lowering of maternal CO₂ tension increases its transplacental gradient to about 8-10 mmHg enabling it to be more readily transported from the fetus. The fetus develops, therefore, in an environment of CO₂ tension similar to or even slightly lower than that of the adult.^[2,11]

In labor, there is an increase in metabolic acidosis, with a base deficit of -4.8 mEq/l and a standard bicarbonate of 20.3 mEq/l, due to maternal fixed acids from uteroplacental metabolism and from ketone bodies which appear with stress; in fetal acidosis the umbilical artery has been shown to contain high levels of lactic and pyruvic acids.^[12-16] Huckabee *et al.*^[17] (1962) stated that the placenta and mother serve as large hydrogen depositories for the fetus and help it to withstand anaerobic metabolism. Whilst, however, CO₂ molecules diffuse readily through the placenta, there is experimental evidence^[18] of varying degree of permeability to bicarbonate ions and hence some fetal independence in regard to bicarbonate concentration. Any antacid action of substances with a high degree of dissociation, like sodium bicarbonate, or of low lipid solubility and poor placental penetration, like tromethamine, is likely to be of benefit in lowering a maternal metabolic acidosis.

The change in the dynamics of respiration in pregnancy as manifested by hyperventilation and the accompanying progressive fall in alveolar pCO₂ accounts for the respiratory alkalosis of pregnancy. This fall is found to reach a mean level of 30-32 mmHg and is associated with a 21% increase in oxygen uptake. The physiological hyperventilation of pregnancy is due to the hormonal effect of progesterone on the respiratory center.^[11]

In labor, the mother may exhibit forced hyperventilation and similarly under anesthesia for surgery the lungs may be excessively inflated which is akin to forced hyperventilation; both situations can cause fetal acidosis and depression of the new born.^[4,11,16,19,20] However, it should be noted that moderate hyperventilation could be beneficial as it can improve fetomaternal gradients at placental sites, but may rapidly become associated with adverse maternal and fetal consequences as it gets more pronounced. Usually when a maternal pCO₂ of 15 mmHg and pH of 7.650 is approached there is a fall in fetal blood oxygen saturation; maternal muscle cramps and fetal heart irregularities in rate and rhythm appear. Experimental studies in animals have shown that excessive hyperventilation causes spasm of placental vessels and slowing of the umbilical circulation with fetal acidosis.^[19]

There have been inconsistent results following attempts to oxygenate the fetus in labor by giving the mother 100% oxygen to breathe.^[11] It has been demonstrated that in cases of obstruction to uteroplacental flow and fetal circulation,

maternal oxygen is unlikely to be of value, and in some cases there is increased acidosis. Even with high levels of maternal pO₂, the fetal pO₂ is only increased approximately 12 mmHg. Experiments with animals^[21] and placental perfusion^[22] have demonstrated a decrease in umbilical blood flow and vasoconstriction in the placental vessels in the presence of high oxygen tensions.

Correlation between the maternal acid-base status, fetal clinical status and Apgar score

Certain pregnancies are considered high-risk cases if there are maternal conditions that put the fetus, the mother or both at an increased risk of perinatal and maternal morbidity and mortality. Some clinical parameters have been used as criteria to separate pregnant women into normal and high-risk groups.^[23] Some of the leading conditions based on which pregnancies are categorized as high risk are presented in Table 2 and these listed conditions are the indications for elective fetal blood sampling (FBS) in labor.^[24] Additionally, it should be noted that there are also clinical parameters for which fetuses of normal pregnancies are subjected to FBS in labor and these are equally presented in Table 2. Biochemical monitoring revealed that during labor all patients showed a gradual fall in fetal pH and an increase in pCO₂ and base deficit, especially in the second stage of labor and during delivery.^[16] These biochemical changes were more marked in high-risk fetuses. At birth and during the 1st h of life the neonates of high-risk mothers were more acidotic and recovered more slowly than neonates of normal mothers. It therefore implies that the fetuses of high-risk pregnancies are less able to tolerate the stress of labor as compared to the fetuses of normal pregnancies. Hence biochemical and biophysical surveillance of the high-risk fetus may provide early warning of the impending difficulties so that during labor timely intervention may be instituted.^[25,26]

Overall, maternal acidosis is associated with lower fetal pH and poor Apgar score. The newborns that had low Apgar scores were significantly more acidotic during labor and delivery and during the 1st h of life than babies born with high Apgar scores.^[24,26,27]

Table 2: Indications for fetal blood sampling

Categories

High-risk cases

- Pre-eclampsia/eclampsia syndrome
- Uterine inertia
- Elderly primigravida
- Postmaturity
- Prolonged second stage
- Diabetes mellitus
- Fetal growth restriction

Normal

- Clinical fetal distress
- Meconium alone
- Fetal tachycardia
- Meconium and abnormal fetal heart rate

Apart from the scenarios mentioned above that cause derangement in fetal acid-base status, other predisposing conditions that may result in this are either acute or chronic clinical conditions of the mother, placental and/or fetus.^[4] Acute maternal conditions may include any clinical situation that causes hypotension or hypovolaemia such as hemorrhage, a vasovagal attack, or epidural anesthesia, with a resultant reduction of maternal blood supply and therefore oxygen delivery to the uterus. Uterine contractions can also interrupt uterine blood flow by a pressure rise and if prolonged, as in hypertonus, may cause hypoxia and acidosis.^[4] Acute placental factors on the other hand, include conditions such as abruption that usually result in disruption of the utero-placental circulation by separating and tearing the uterine spiral arteries from the placenta.^[4] Similarly, the blood flow from the placenta to the fetus is often affected during labor and delivery by the umbilical cord compression; this can sometimes happen before labor if there is reduced liquor or a true knot in the cord. Animal experiments have shown that there is significant reserve because the fetus can compensate by increased oxygen extraction,^[28] meaning blood flow to the fetus must be reduced by at least 50% to cause hypoxia.^[29]

Chronic clinical conditions that have been associated with fetal acid-base derangement on the other hand may also be maternal, placental or fetal.^[4] Maternal causes of chronic fetal acidosis include reduced oxygenation of maternal blood, such as in severe respiratory or cardiac disease, or reduced blood flow to the placenta, as in connective tissue diseases – for example, systemic lupus erythematosus – and preeclampsia.^[4] Chronic placental factors usually result from impairment of placental transfer of oxygen.^[30] This is thought to result from inadequate trophoblast invasion of the myometrium in early pregnancy,^[31] leading to reduced perfusion of the intervillous spaces. In animal experiments, like acute cord compression studies, utero-placental blood flow also needs to be reduced by at least 50% to produce fetal hypoxia.^[32] This indicates that the reduction in placental transfer seen in human fetal growth restriction must be substantial to produce the hypoxia and acidosis found at cordocentesis in such cases. Finally, even with normal placental function, chronic conditions within the fetus can cause acidosis.^[4] Anemia from rhesus disease, parvovirus infection, thalassaemia or fetomaternal hemorrhage, when severe enough to reduce fetal hemoglobin concentrations below 40 g/l (equivalent to an oxygen content below 2 mmol/l), can lead to a fall in pH.^[33,34] Arterio-venous shunting in fetal tumors, serious cardiac structural abnormalities, or arrhythmias are other conditions, which can lead to chronic acidosis by decreased oxygenation as a result of reduced fetoplacental blood flow.^[4]

Fetal acid-base balance

Background

Hypoxia in fetuses is potentially very hazardous with an adverse outcome for the neonate because the fetus normally has a very low PaO₂ (approximately 35 mmHg in the

umbilical vein) and high PaCO₂ (approximately 42 mmHg in the umbilical vein).^[35] The inherent response therefore is preferential redistribution of blood to vital organs, and hence in acute severe fetal hypoxemia there is associated and sustained maintenance of blood flow to the brain, adrenal gland and the heart at the expense of other tissues. This result in activation of peripheral chemoreceptors, with an increase in sympathetic tone, and in later gestation there is also an increase in concentrations of circulating cortisol, catecholamines, angiotensin II and vasopressin, with a resultant increase in peripheral resistance. Following severe hypoxia there is a shift to anaerobic pathways of metabolism as the “deprived” tissues may not be able to maintain oxidative phosphorylation.^[35] Since the fetus has a lesser ability to cope with acid-base disturbances, lactic acidemia can rapidly develop.^[35,36] This shifts the oxyhemoglobin dissociation curve to the right, with a further reduction in blood O₂ content. Thus, the resulting vicious circle can quickly result in fetal death. Less severe, but chronic hypoxemia is associated with increased erythropoietin concentrations, a slowing of fetal growth, and reduced glycogen stores because of their utilization. Such children have a higher than usual incidence of neurological deficits.^[6,26,37-39] The fetal oxyhemoglobin dissociation curve is left-shifted in comparison with the mother’s [Figure 1] because fetal hemoglobin has a lower binding affinity for 2,3-diphosphoglycerate.^[2,35] The fetus has a high hemoglobin concentration (16 g/dl), which also contributes to the relatively high oxygen content. The low umbilical PaO₂ and fetal vasculature pO₂ means that although umbilical venous blood is approximately 85% saturated (compared with approximately 95% in the adult) and has a relatively high oxygen content, the steep dissociation curve allows adequate oxygen unloading to the tissues. The high fetal blood flow allows equivalent or higher oxygen deliveries compared with adults to most tissue beds. However, it appears that fetal PaO₂ varies inversely with oxygen consumption, as the capacity to increase oxygen uptake from the lungs is absent.^[2,35]

Fetal PaCO₂ is high with approximately 60% being carried as bicarbonate. As fetal blood is oxygenated, it releases hydrogen ions, which combine with bicarbonate and push the equilibrium towards CO₂ and H₂O which diffuse across the placenta, down the concentration gradient for CO₂.^[2,35] In the maternal circulation, the reaction proceeds in the opposite direction. Maternal pH in the placental blood thus falls slightly while that in the fetal placenta rises slightly. This small rise increases the oxygen affinity of fetal hemoglobin, shifting the oxyhemoglobin dissociation curve further to the left while the maternal curve is shifted right (the “double Bohr shift”). This enhances maternal to fetal oxygen transfer.^[2,35]

Fetal and neonatal plasma bicarbonate concentrations are low because of the immaturity of the proximal tubular bicarbonate reabsorption.^[25] Buffering via the regulation of bicarbonate is slower than in the adult.

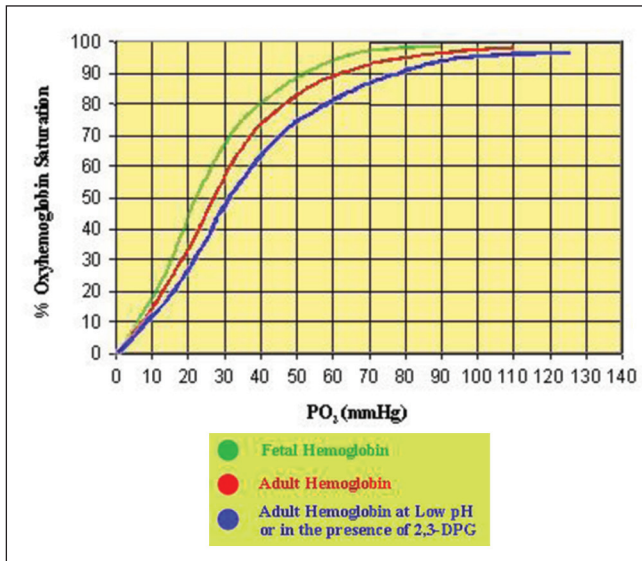


Figure 1: Fetal-maternal oxyhemoglobin dissociation curve

The literature is replete with reports that indicate that asphyxia remains a common cause of intrapartum fetal death.^[40] Whilst prematurity and lethal congenital abnormalities accounted for 36% of these and the remaining are due to asphyxia.^[40] Many of these deaths might have been avoided by the routine use of continuous fetal heart rate (FHR) monitoring had it been available. However, abnormalities in the FHR pattern are only suggestive of fetal asphyxia, and it has become generally accepted that the pH of a fetal scalp blood sample offers the most reliable indicator of fetal asphyxia in present-day use.^[5,6,41-44]

During hypoxia, the fetal pCO₂ rises, increasing the level of H₂CO₃ in the fetal blood and giving rise to a respiratory acidosis and a fall in the blood pH. The combination of hypoxia, hypercapnia and metabolic acidosis constitute asphyxia. At any given level of oxygen depletion, the survival time of the hypoxic fetus will depend primarily on its glycogen reserve. Thus, the well-nourished fetus can be expected to withstand a standard hypoxic insult better than the growth retarded fetus.^[14]

The introduction of FBS by Saling (1963),^[40,45,46] whereby arterialized capillary blood could be obtained from the fetus during labor, revolutionized the diagnosis of intrapartum fetal asphyxia. Saling (1966) showed that a scalp blood pH <7.20 was associated with poor clinical condition of the infant and he designated values below 7.20 as “acidosis”; he also suggested that a fetal scalp blood pH of between 7.20 and 7.25 were indicative of early fetal deterioration and he designated values within this range as “preacidosis”.^[40]

Correlation between the fetal acid-base status and fetal clinical status

Fetal acid-base status in clinical fetal distress and high-risk cases

The classical features of fetal distress which includes meconium staining of the liquor amnii and alteration in the

FHR pattern, have been shown not to be sufficiently reliable as an indicator for accurate assessment of the fetus.^[12,24] For confirmatory interpretation of the findings, it may have to be combined with fetal blood gas analysis. However, FBS still remains superior to cardiotocography (CTG) alone as it provides direct information about the fetal acid-base balance and gives a more accurate picture of the state of the fetus. Therefore, fetal scalp blood has been found to be suitable for the purpose of predicting the fetal status.^[12,24] Good correlation has been established between the fetal pH and the condition of the infant at birth:

- i. Fetal distress: It is well evidenced^[4,15,24] that in clinical fetal distress, there is a significantly lower fetal pH than that in normal fetuses.
- ii. Post-maturity: Cases of post-maturity also gave a lower fetal pH than normal.^[24]
- iii. Uterine inertia: In labors associated with uterine inertia, it has been consistently demonstrated that the fetal pH is lower than normal. A lower pH in cases of uterine inertia is not unexpected as progressive retraction of the uterus would jeopardize the placental circulation.^[16,24]

It must be noted that of the different signs of clinical fetal distress, meconium is the least important and fetal tachycardia is more significant than others.^[24] A cautionary note must be added here that some fetuses have transient abnormal acid-base balance (a check within 30 min was normal), and the FHR trace (obtained immediately after the sampling) showed no ominous changes in these cases. Therefore, an abnormal fetal acid-base balance is not uncommon in a low-risk population in the labor. However, a critical evaluation of the acid-base balance is necessary since in most cases, the abnormal acid-base balance is transient and of a respiratory, innocuous type without concomitant fetal distress.^[44]

Fetal acid-base balance in labor

Intrapartum scalp blood sampling

Decelerations occur in at least 50% of labors where electronic fetal monitoring (EFM) is used.^[46] Even with the worst pattern of tachycardia, reduced variability and decelerations, only 50-60% of fetuses are acidotic. Acidosis is a function of time with ongoing insult. CTG has high sensitivity but low specificity. Meta-analysis of three trials comparing Intermittent Auscultation with EFM used without FBS showed a fourfold increase in caesarean section rate. This increase was limited to twofold where FBS was used in conjunction with CTG, with no improvement in outcome measures in either group Table 3.

Decelerations indicate “stress” to the fetus. The addition of a rise in baseline along with reduction in baseline variability indicate a “stress” to “distress” period, but the duration of the “distress” period to the development of metabolic acidosis is unpredictable.^[4,23,27,46,47] If FHR develops a “distress” pattern, FBS may be indicated and this may need to be repeated if

Table 3: Main learning points

Clinical techniques have been used to separate pregnant patients into normal and high-risk groups
Pregnancy is associated with substantial reduction in the partial pressure of CO ₂
This change favors diffusion between maternal and fetal circulations
Adequate buffering prevents significant changes in maternal arterial pH
Very small changes in pH may significantly affect function of various fetal organ systems, such as the central nervous system and the cardiovascular system
Fetal hypoxia can occur when maternal oxygenation is compromised, maternal perfusion of the placenta is reduced, or delivery of oxygenated blood from the placenta to the fetus is impeded
In presence of hypoxia, complete oxidative metabolism of carbohydrates to CO ₂ and water is impaired and metabolism proceeds along an anaerobic pathway with production of organic acids, such as lactic acid, which are not readily excreted or metabolized
During labor of all patients, a gradual fall in fetal pH and an increase in pCO ₂ and base deficit were noted, especially in the second stage of labor and during delivery. This acidosis was more marked in high-risk fetuses
The high-risk fetus does not tolerate the stresses of labor as well as the normal
At birth and during the 1 st h of life the neonates born to high-risk mothers were more acidotic and recovered more slowly than neonates born to mothers with normal pregnancies
Apgar scores of high-risk babies were statistically significantly lower than babies of normal pregnancies
Biophysical and biochemical surveillance of the high-risk fetus may provide early warning of impending difficulties so that timely intervention during labor may be instituted
Scalp blood pH is useful to increase specificity of CTG (i.e., to verify the CTG reading) while cord blood pH is useful to differentiate the depressed baby due to hypoxemia/acidosis from other causes

CTG: Cardiotocography, pCO₂: Pressure of carbon dioxide, CO₂: Carbon dioxide

delivery is not imminent. During the development of subacute hypoxia, a rapid deterioration of pH is possible with no increase in FHR if decelerations involve drop in FHR >60 bpm lasting for 90 s or with less than 60 s of recovery in between. A decline in pH at the rate of 0.01/2-4 min may occur – the decline being more rapid in situations with intrauterine growth restriction, infection, and thick meconium with scanty liquor.^[46] It may thus not be appropriate to do FBS if delivery is not likely in a reasonable time.^[4]

Alternatives to FBS include scalp stimulation or acoustic stimulation.^[46] If accelerations occur in response to stimulation, the fetus is unlikely to have an acidotic pH. In the absence of accelerations in response to stimulation, 50% of fetuses may be acidotic. Other options include fetal electrocardiography ST waveform analysis and fetal pulse oximetry.^[46,48]

Umbilical cord blood acid-base assessment

The 26th Royal College of Obstetricians and Gynecologists study group on Intrapartum Fetal Surveillance (1993)^[12] recommended measurement of umbilical artery and vein blood pH and base deficit as a measure of fetal condition at birth.^[46]

Despite the fact that a wide pH range of 7.00-7.16 is quoted in the literature for acidemia, there is a general consensus that a cord artery pH <7.00 is more significantly correlated with adverse neonatal outcome.^[26,34,49,50] The babies with pH <7.00, are more likely to suffer complications in the short term, while long term outcome is correlated to neonatal encephalopathy rather than pH.^[46] Also, base deficit is now used as a surrogate to assess metabolic acidemia-the commonest cut off values to indicate abnormality include BD >8 mmol as moderate and >12 as severe metabolic acidosis.^[46]

The principal contributor to metabolic acidosis is lactic acid, which at times of oxygen deficiency is mainly produced by anaerobic glycogenolysis.^[12,40] Metabolic acidosis reflects tissue oxygen debt and therefore is of greater prognostic significance than respiratory acidosis. Accumulation of lactic acid together with hypoxia leads to tissue edema and cellular damage.^[4,47,51,52] Lactate can be measured in a 5 µl blood sample using an electrochemical strip method with results available by the bedside in 60 s. It is easier to measure than a full blood gas analysis using maintenance free, battery operated pocket size devices like the Lactate Pro (Oxford Sonicaid Ltd.). Lactate is comparable to pH and base deficit with respect to sensitivity, specificity and predictive values of various perinatal complications.^[4]

In conclusion, scalp blood pH is useful to increase specificity of CTG (i.e., to verify the CTG reading) while cord blood pH is useful to differentiate the depressed baby due to hypoxemia/acidosis from other causes.

Correlation between the fetal acid-base status and the Apgar score

With a well-defined setting of a critical pH, the fetal acid-base status correlates well with the Apgar score of the newborn irrespective of the sampling delivery interval. With the criterion of the critical pH set at 7.13, there would be no false results and the error of prediction would be reduced to insignificant values.^[5,25,49,50,53]

Challenges in the diagnosis and management of fetal hypoxia (intrapartum asphyxia) in developing countries

Intrauterine fetal hypoxia occurs when the fetus is deprived of an adequate supply of oxygen.^[53-55] During hypoxia the fetal pCO₂ rises, increasing the level of H₂CO₃ in the fetal blood

and gives rise to a respiratory acidosis and a fall in the blood pH. The combination of hypoxia, hypercapnia and metabolic acidosis constitute asphyxia. At any given level of oxygen depletion, the survival time of the hypoxic fetus will depend primarily on its glycogen reserve. Thus, the well-nourished fetus can be expected to withstand a standard hypoxic insult better than the growth retarded fetus.^[14]

Asphyxia remains a common cause of intrapartum fetal death. Whilst prematurity and lethal congenital abnormalities accounted for 36% of these, the remaining are due to asphyxia.^[40] The World Health Organization (WHO) estimates that globally, between four and nine million newborns suffer birth asphyxia each year leading to an estimated 1.2 million deaths and about the same number of infants who develop severe disability. WHO estimates for global neonatal deaths caused by birth asphyxia are 29%.^[56,57] In Nigeria like most other developing countries, intrauterine hypoxia and birth asphyxia are leading causes of perinatal death.^[58-60] And existing data reveals that approximately 4 million fetal deaths occur each year, 98% of them in developing countries.^[58-60] These are rough estimates as fetal deaths are infrequently acknowledged or recorded in developing countries.

Intrauterine hypoxia and or birth asphyxia was the ninth most expensive medical condition treated in U.S. hospitals by average hospital cost and resultant hospital charge.^[61,62] Though the situation has not been systematically documented in most developing countries like Nigeria; the burden is certainly enormous and probably worse in the developing countries against the backdrop of the poor socioeconomic status of the citizenry.

Clearly from the foregoing, it is imperative that appropriate diagnostic and management modalities for fetal hypoxia be available and accessible. This is the only way the burden of perinatal morbidity and mortality can be reduced with a view to achieving the millennium development goal of improved perinatal outcome. The modalities that can be used for diagnosis include clinical observation of meconium staining of liquor in labor, FHR abnormalities on auscultation or from CTG, as well as FBS for pH assessment and blood gas analysis.^[63,64] Very recently, fetal pulse oximetry has gained importance in the intrapartum assessment of the fetus and seems to compare favorably with fetal blood gas analysis.^[48] Other assessments are biophysical profile assessment and Doppler studies.^[63,64] For the management to be effective, efficient and adequate, skilled birth attendants with proficiency in fetomaternal medicine should be available, and the complimentary neonatal unit to handle the neonates that have suffered fetal hypoxia and subsequent birth asphyxia should also be available. Most of the diagnostic modalities enunciated above are high-tech procedures with the paucity of facilities, and expertise for their use in the few health care facilities where they are available in most developing countries. There is also a paucity of facilities

and expertise for neonatal care in most settings in developing nations. Indeed, the public and private primary and secondary health care facilities in most developing nations are devoid of these services. A significant proportion of the tertiary health care facilities also does not have the full complement of diagnostic modalities enumerated above.

Over the immediate past years, a lot of tertiary health facilities have obtained CTG machines for fetal monitoring. This, in addition to the readily available ultrasonography machines has made it possible to undertake biophysical profile studies. Use of FBS for pH and blood gas analysis is still poorly domesticated in these centers; this is in spite of the fact that abnormalities of the FHR pattern are only suggestive of fetal asphyxia, and it has become generally accepted that the pH and blood gas analysis of a fetal scalp blood sample offers the most reliable indicator of fetal asphyxia in present-day use.^[5,6,39-43] Also only very few centers undertake Doppler studies due to non-availability of the equipment and expertise.

The readily available diagnostic tools to skilled birth attendants attending to parturients in most developing nations including tertiary health care facilities are clinical observation of meconium staining of liquor and the use of FHR abnormalities from auscultation or CTG. Other modalities such as FBS for pH and blood gas analysis as well as Doppler studies are not readily available. Interestingly, the presence of meconium staining of liquor and or FHR abnormalities on auscultation or CTG monitoring are of high sensitivity, but low specificity,^[5] and they have been shown not to be sufficiently reliable for the accurate assessment of the fetus.^[12,24] FBS provides direct information about the fetal acid-base balance as well as the blood gas status and gives a more accurate picture of the state of the fetus.^[63,64] Fetal scalp blood has been found to be suitable for this purpose.^[12,24] Good correlation has been established between the fetal pH and the condition of the infant at birth. It therefore means that the former tests are at best screening tools while the later are diagnostic and confirmatory.

A large proportion of the citizenry in developing nations live in resource poor settings where there are no access to health care facilities, and for those that even live close to the health care facilities, they may not have the economic wherewithal to afford hospital care. Therefore, finance remains yet another major impediment and challenge to accessing requisite diagnostic investigations and the subsequent management of fetal hypoxia in a significant proportion of parturients.

The management of a fetus with established hypoxia includes temporary measures to mitigate the impact of the predisposing conditions if possible such as discontinuing oxytocin infusion in cases of induction or augmentation of labor, displacing the presenting part off the cord in cases of cord prolapse, lying the parturient in the left lateral position and giving oxygen by

face mask.^[62] The decision to deliver is then made, and this may include a caesarean section and/or instrumental delivery depending on the stage and progress of the labor. Following delivery, the neonatologist is expected to receive the baby for full evaluation of the newborn and management in the neonatal intensive care unit. Again, a major challenge is the paucity or non-availability of skilled accouchers, neonatologists and neonatal facilities in most public/private primary and secondary health care facilities. This makes it impossible for fetal hypoxia to be picked up early and where they are picked up, the facilities are often not able to appropriately respond to the clinical situation. Finally, in all these the largely poor financial state of the parturients in developing nations may further compound the already bad situation as the policy of health care delivery in most developing countries is based on a “cash and carry” principle.

Conclusion and Summary

Pregnancy is associated with a substantial reduction in the $p\text{CO}_2$ and this change favors diffusion between maternal and fetal circulations.^[65] Adequate buffering prevents significant changes in maternal arterial pH.

Normal fetal metabolism results in the production of acids which are buffered to maintain extracellular pH within a critical range. Very small changes in pH may significantly affect the function of various organ systems, such as the central nervous system and the cardiovascular system. The major buffers utilized by the fetus for neutralizing hydrogen ion production are plasma bicarbonate and hemoglobin. Inorganic phosphates and erythrocyte bicarbonate are also potential buffers, although they play a lesser role in fetal acid-base hemostasis.

Fetal hypoxia can occur when maternal oxygenation is compromised, maternal perfusion of the placenta is reduced, or delivery of oxygenated blood from the placenta to the fetus is impeded. When adequate fetal oxygenation does not occur, complete oxidative metabolism of carbohydrates to CO_2 and water is impaired and metabolism proceeds along an anaerobic pathway with production of organic acids, such as lactic acid, which are not readily excreted or metabolized. Accumulation of lactic acid can deplete the buffer system and result in metabolic acidosis.

The diagnosis and management of fetal hypoxia remains a major challenge in developing nations due to paucity of facilities and skilled personnel coupled with overriding ravaging effect of poverty.

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