

INTRAPARTUM FETAL MONITORING: PATHOPHYSIOLOGY AND EVOLUTION OF VARIOUS TECHNIQUES



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ABSTRACT

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Perinatal hypoxia has been a source of major concern for the pregnant woman and her obstetrician alike. The former was plagued by constant worries of neonatal morbidity and mortality and the latter, by constant threat of medical litigations. Intrapartum fetal monitoring (IPFM) played an important role in the attempt to establish equilibrium. Initially, intermittent auscultation was the only method of monitoring the well-being of fetus during labor. Further research led to the evolution of electronic fetal monitoring, scalp blood sampling, fetal pulse oximetry, ST-analysis of the fetal ECG and the use of sophisticated magnetism and infra-red optics. A trial using artificial intelligence in IPFM has recently reached its final phase. Even as more novel methods of monitoring continue to emerge, the perfect monitoring technique still remains to be discovered. Analysis made it evident that no single method was capable of distinguishing true cases of fetal distress from false one, sufficiently accurately. A combination of two or more methods is required for a reliable diagnosis to be obtained, and current treatment protocols should reflect this. The concurrent use of two or more monitoring methods in an algorithmic manner will go a long way in reducing the incidence of perinatal morbidity especially in high risk obstetric cases.

Contribution/ Originality: The study documents the challenges faced by obstetrician during the intrapartum fetal monitoring (IPFM). Various methods of IPFM have been critically analyzed. The conclusion is that a single method is not optimum but a combination of methods in an algorithmic manner should be the current method of choice.

1. INTRODUCTION

Perinatal asphyxia accounts for 23% of global neonatal mortality.(1) In the mid eighteenth century, the relationship between asphyxia neonatorum and cerebral palsy (CP) was established [1]. Gurbuz A et al reaffirmed this relationship in their studies and documented the relationship between hypoxia induced encephalopathy (HIE) and neonatal seizures [2]. In 2009, a systematic review revealed that HIE was associated with 25 per 10000 live births and perinatal asphyxia accounted for 14.5% of cerebral palsy cases [3]. In the year 2002 alone, payouts for hypoxia-induced CP exceeded £3 million in the UK, increasing to £107.6 million in 2007-08 [4]. Considering this huge socioeconomic burden and the disability meted out to countless children, the need for the best possible methods for intrapartum fetal monitoring (IPFM) is warranted. The aim of IPFM is to identify abnormal variations in biological parameters which reflect fetal hypoxia, allowing for a prompt decision on further

management in order to minimize or prevent adverse perinatal outcomes. IPFM has evolved with modern technology, utilizing numerous methods over time. The objective of this review is to critically analyze the evolution, advantages, drawbacks, specificity and sensitivity of IPFM and its role in modern obstetrics. An enhanced knowledge of IPFM will ensure that evidence-based decisions are made in routine clinical practice.

2. PATHOPHYSIOLOGY OF INTRAPARTUM FETAL HYPOXIA

The physiological fetal cardiac output is 480ml/min/kg of fetal weight. This output is distributed between the placenta (45%), and the fetal body (55%). Table 1 shows the fetal body blood flow (55% of total fetal cardiac output), which is variably redistributed in conditions of fetal hypoxia [5]. Prolonged hypoxia causes HIE – the devastating outcome of perinatal asphyxia as shown in Figure 1.

Table-1. Fetal Blood flow Redistribution in Hypoxia

	Normal O ₂ delivery	70% of Normoxia	50% of Normoxia
Musculoskeletal system and skin	29.7%	24.5%	21.9%
Viscera	Lungs	11.8%	5.1%
	Brain	3.0%	6.3%
	Heart	2.6%	4.5%
	Gut	2.9%	2.3%
	Kidneys	2.3%	2.0%
	Adrenals	0.06%	0.2%

Source: Jensen [6]

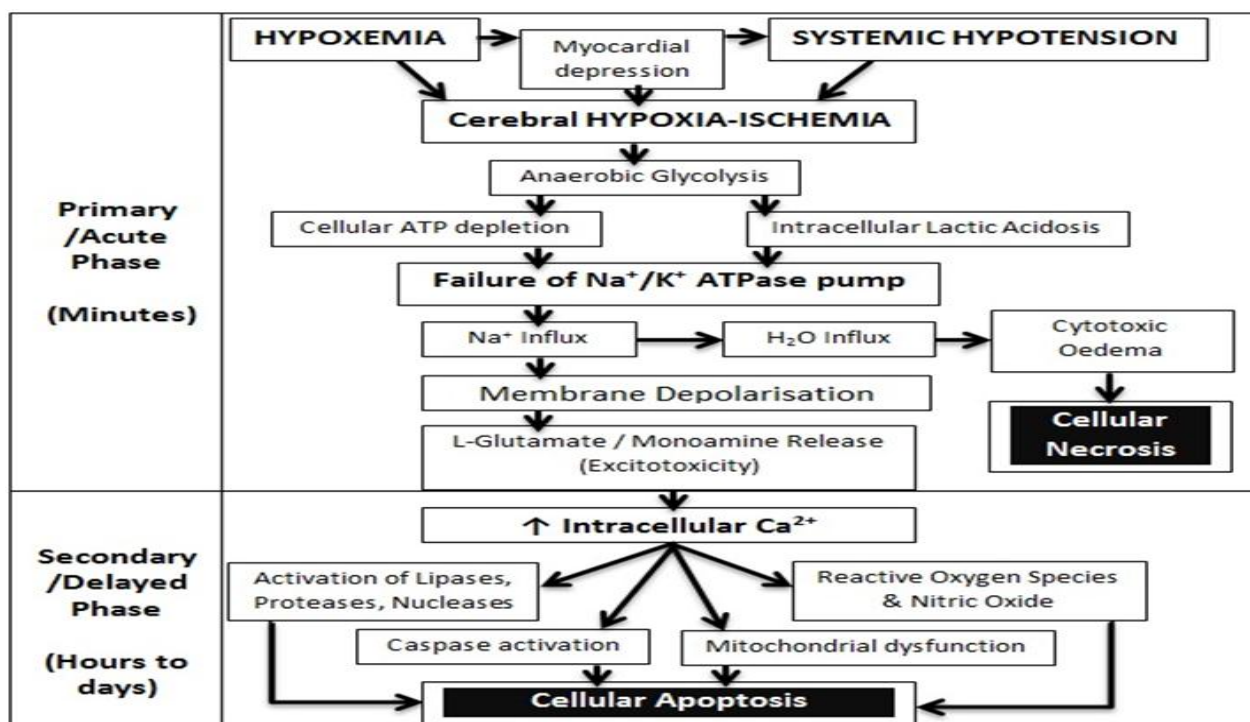


Figure-1. Pathophysiology of fetal hypoxia

Source: Jensen [5]

The sudden insult of hypoxia initiates vital compensatory mechanisms, as follows:

- 1) Vagal-mediated bradycardia; Fahey and King [6]
- 2) Peripheral vasoconstriction triggered by the release of catecholamines, resulting in a redistribution of blood flow prioritizing perfusion of vital organs namely heart, brain and adrenal glands, at the expense of the peripheral organs like lungs, kidneys, gastrointestinal tract and musculoskeletal structure; [7, 8]
- 3) Shunting of glucose to anerobic metabolism in response to reduced partial pressure of oxygen [7].

Fetal hypoxia also leads to redistribution of umbilical venous blood flow with more blood bypassing the liver via the ductus venosus (55% to 65%), Reuss and Rudolph [9] and an increase in preferential streaming of the 'venous' blood through the foramen ovale to maintain oxygenation of the heart and brain [10]. The detailed visceral distribution is further depicted in Figure 2 (illustration of data from Table 1) [5].

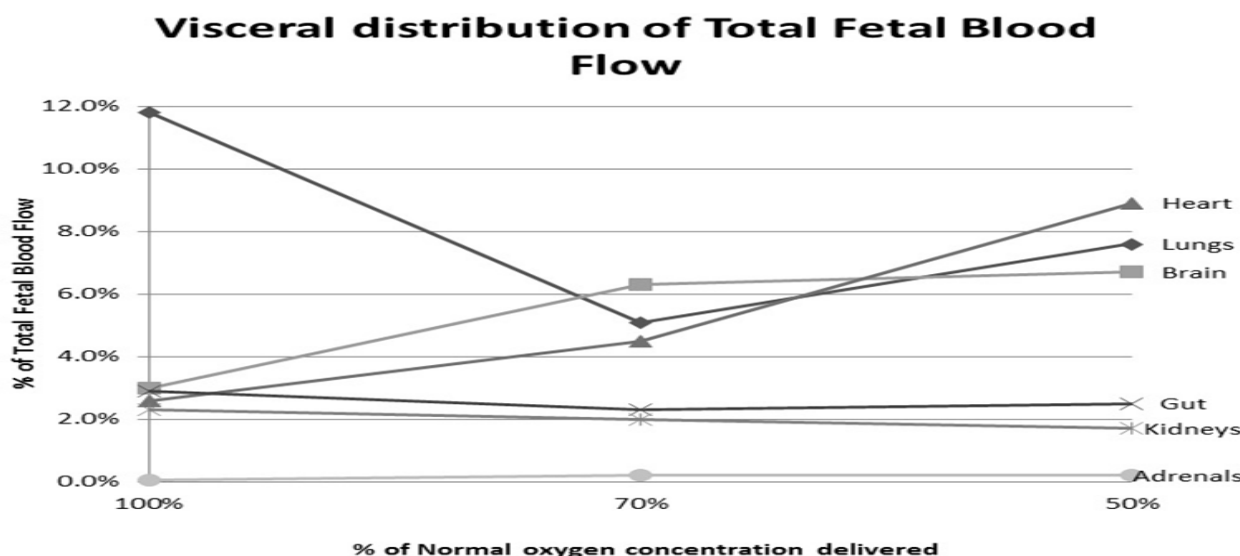


Figure-2. Visceral distribution of fetal blood flow*

Source: Jensen [5]

3. CLINICAL SIGNIFICANCE OF FETAL HYPOXIA

Fetal hypoxia may lead to a rise or fall in fetal heart rate, with an increase in arterial blood pressure [11]. However the cardiac output remains maintained in hypoxia until acidosis occurs; then the cardiac output drops by 20%, leading to a 40% decrease in flow to the fetal body [12]. Acidosis is evidenced by a base deficit of 12-16mmol/L and is an indicator of poor prognosis [13]. Fetal acidosis further predisposes to irreversible tissue damage, leading to perinatal morbidity or fetal demise. Therefore, perinatal outcome hugely depends on the fetal adaptation to hypoxia and the resulting metabolic acidosis.

4. TECHNIQUES OF INTRAPARTUM FETAL MONITORING

4.1. Fetal Heart Rate Monitoring

The fetal heart rate (FHR) is regulated by the central and autonomic nervous system. Hypoxia stimulates peripheral chemoreceptors, Bennet, et al. [14] coordinating a cardiovascular response mediated by the neural chemoreflex system which is augmented by endocrine, local and behavioral factors [15]. These changes carefully balance out the severity of hypoxic insult with the cellular adaptability of the fetus. The changes also produce variable responses which are noted as decelerations [16]. Slower onsets of mild to moderate hypoxia cause a mere rise in FHR. However an acute onset of severe hypoxia usually results in the following:

- A primary response of fetal bradycardia and hypertension (due to increased vagal tone) are seen on Cardiotocography (CTG) as rapid decelerations, (the depth of which are proportional to the degree of hypoxia) [17]. Bradycardia reduces myocardial oxygen demand thus preserving myocytes.
- The secondary response is determined by the duration and severity of hypoxia. In severe hypoxia, the bradycardia deepens and cause late decelerations which unlike other decelerations, are not abolished by atropine. This indicates a depletion of myocardial glycogen and overall decline in myocardial conductivity and excitability [18].

The resilience of the fetal chemoreflex system allows the fetus to maintain visceral oxygenation in moderate hypoxemia [19]. Late decelerations can persist for up to 100 minutes without acidosis [20]. However, FHR

variability is blunted in the presence of chronic hypoxia. This complex physiology of cardiovascular response to hypoxia warrants the need for fetal heart monitoring during the intrapartum phase.

4.1.1. Intermittent Auscultation (IA)

The pioneer approach to FHR monitoring involves the structured, intermittent auscultation of the fetal heart either with a fetoscope or with a hand-held Doppler ultrasound at defined temporal intervals for a full minute, noting the rate, rhythm and variability. The main advantages of IA are its simplicity and mobility. It allowed time for patient support and 1:1 staffing ratio predicting a better perinatal outcome. However, by using IA, one cannot record FHR variability and types of decelerations. The added patient factors like obesity and polyhydramnios may impede its use. Lastly, its inability to produce reliable documentation poses a major drawback in the face of medicolegal litigation. Conclusively, intermittent auscultation may be used as a screening technique at admission and for patients having a low risk of developing fetal compromise [21].

4.1.2. Electronic Fetal Heart Monitoring (EFM)

IA gave way to the breakthrough of EFM better known as Cardiotocography (CTG) in 1958, which has since become a routine part of maternity care and currently the most widely used method of fetal surveillance [22]. It involves the monitoring of the following:

- a. Fetal heart rate (by an abdominal Doppler ultrasound transducer or a fetal scalp electrode)
- b. Uterine contractions, (by a pressure gauge transducer placed between the uterine fundus and umbilicus).

Standardized recommendations for the use and record-keeping of EFM have been devised by the Royal College of Obstetricians and Gynecologists (RCOG), National Institute for Health and Care Excellence (NICE) and Clinical Negligence Scheme for Trusts (CNST) and included in their practice guidelines.

The distinct advantages of EFM are its ability to record baseline variability and to detect minute variations in FHR, allowing identification of various types of deceleration, thus making it more sensitive than IA. It produces a continuous, documented recording and does not require continuous monitoring thereby overcoming many of the aforementioned difficulties with IA [23]. EFM also bears a prognostic significance as unremitting bradycardia has been associated with the development of ischemic basal ganglia brain injury [24]. A meta-analysis of 12 trials by Thacker SB et al showed that EFM led to a statistically significant decrease in neonatal seizures (RR 0.5 [95%CI: 0.3-0.82]) [25]. Another meta-analysis of 9 randomized trials by Vintzileous AM et al found that if the analyses only included deaths attributed to fetal hypoxia, the reduction of perinatal mortality was found to be significant (7 per 10000 vs 18 per 10000, OR 0.41, P<0.05) [26]. Conversely, the largest RCT of EFM by MacDonald D et al which included 12,964 participants showed no benefit of using EFM in terms of perinatal mortality rates, or incidence of cerebral palsy [27]. Moreover, EFM limits the mobility of the expecting mother and prevents the use of massage, various positioning techniques and water-immersion to improve maternal comfort and coping. Unlike IA, it allows a poorer staffing ratio, which may shift staff focus and resources away from the mother.

The idea of CTG use during admission as a screening technique for all laboring mothers created much interest amongst researchers. However Blix E and Oian P concluded that it has no role in predicting the outcome of labor, especially among low-risk women [28]. Impey L et al concluded that routine admission CTG does not improve neonatal outcome, Impey, et al. [29] and this finding was further corroborated by Devane, et al. [30].

The advantages of EFM come at the expense of spuriously high rates of operative deliveries due to its increased sensitivity and insufficiently specificity for fetal distress. Issues with specificity have led clinicians to turn to additional investigations such as pulse oximetry, fetal scalp blood pH and fetal ECG analysis to avoid excessive numbers of cesarean deliveries [31]. Based on the studies, IA is preferred in monitoring low-risk pregnancies and EFM is deemed the most appropriate choice of fetal surveillance in high-risk pregnancies [32].

4.2. Fetal Scalp Blood Sampling (FBS)

In this technique, a sterile lance and capillary tube are used to withdraw a fetal blood sample (~ 35 µl) from the exposed fetal scalp, under amnioscope guidance. Healthy fetal blood will have pH more than 7.25 with a base excess less than -8 mmol/L. In hypoxic fetus, anerobic glucose metabolism generates lactic acid which accumulates, causing fetal acidemia. Fetal blood lactate may also be measured with increased accuracy than pH as it requires only 5µl of fetal blood sample [33]. Lactate levels of 4.2-4.8mmol/L are considered borderline and any higher should warrant urgent delivery. Studies have shown that acidosis parallels the partial pressure of oxygen in the bloodstream as a direct measure of fetal asphyxia [34]. Hence FBS has been the objective gold standard against which biophysical indicators are compared. The use of FBS as an adjunct to CTG improves the sensitivity of EFM [35]. Many studies have used FBS to determine the exact timing of asphyxia, by correlating fetal heart rate, pH recording, lymphocyte and thrombocyte count. A rise in lymphocyte count occurring 25 minutes following abnormal fetal bradycardia can be considered a reliable sign of fetal brain damage [36]. Thrombocytopenia has also been shown to occur after fetal hypoxia though the cause is not known [37]. Blood lactate concentrations over 9mmol/L at 30 minutes after birth can predict moderate to severe brain damage, Silva, et al. [38] while levels less than 5mmol/L indicate the absence of risk [39].

However, while this test confirms fetal acidemia, it is only recommended as an adjunct to non-reassuring CTG readings since obtaining the blood sample subjects the fetus to certain risks. These include the invasive nature of the procedure (exposing the fetus to an increased risk of infection), the availability and cost of equipment and high level of technical skill required to perform the procedure [40]. Other drawbacks of this test include the discomfort and anxiety the mother is subjected to, the time taken to perform it and the compulsory prerequisite of cervical dilation more than 4cm. Numerous studies have reported that the liberal use of FBS avoided excessive operative deliveries [29]. However, Alfircvic Z et al. investigated this claim and found that FBS may not be able to prevent this completely [23]. Hence the contribution of FBS in obstetric care has been questioned, as its absence has been shown to have no major effect on outcome, Perkins [41] and alternative techniques may help avoid the risks of FBS [42].

4.3. Fetal Pulse Oximetry

Fetal pulse oximetry (FPO) provides an accurate instantaneous measurement of fetal arterial oxygen saturation at a given time, by measuring differences in the rate of absorption of red light and infrared light by oxyhemoglobin and deoxyhemoglobin. This is achieved by placing a transvaginal sensor through the cervix adjacent to the fetal cheek or temple. Studies have demonstrated that in significant lactic acidosis, the SpO₂ levels drop to less than 30%, prompting immediate interventions [43]. FPO may be preferable to FBS as it is relatively non-invasive and requires a cervical dilation of only 2cm compared to 4cm for FBS. Furthermore, FPO allows for continuous monitoring, produces immediate test results and faces no issues of sampling failure. However, the accurate measurement of fetal SpO₂ might be affected by the variable redistribution of blood flow in response to fetal hypoxemia.

A systematic review with meta-analysis of 6 trials, including 7654 women, compared FPO with CTG versus CTG alone, concluded that there were no changes in the overall rate of cesarean sections but there was a significant decrease in cesarean section rate for non-reassuring fetal status [44]. Nonetheless, the review also concluded that a better tool for IPFM was required. When FPO was combined with FBS and EFM, a decrease in cesarean section rate was seen (67% versus 34%), with a reduction in the number of repeat FBS procedures (62% versus 34%) [45].

4.4. Fetal Electrocardiography

The fetal ECG is obtained from an electrode attached to the fetal scalp, connected to a CTG with STAN

monitor [46]. It is a graphical record of summated fetal cardiac electrical activity, which is sensitive to all factors affecting myocardial conduction, particularly oxygenation. The heart, as a central organ, is among the last of the fetal tissues to experience hypoxia due to the aforementioned compensatory mechanisms. In myocardial hypoxia, the energy-consuming process of myocardial cell membrane repolarization (T-wave on ECG), is inhibited by the resulting negative energy balance, causing catecholamine release which stimulates cardiac β -receptors [47]. This sympathetic activation produces myocardial glycogenolysis, producing lactic acid and potassium ion release. The local hyperkalemia increases T-wave height, and thus an elevated T/QRS ratio; this is the basis of the STAN software (Noventa Medical) which provides an automated analysis of CTG with ECG, based on a computerized ST-log function [48]. T/QRS elevations (Figure 4) are either 'episodic' (<10mins) or a 'baseline rise' (>10mins) with the latter indicating worsening fetal condition and asphyxia. Episodic T/QRS rises are usually related to fetal movements, not fetal hypoxia. Thus if the associated CTG is reassuring, they should be overlooked.

The ST-segment represents a short quiescent period between the QRS-complex (ventricular depolarization) and the T-wave (ventricular repolarization) when the myocardial cell-membrane returns to resting potential. This return to equilibrium is prevented by disturbances in myocardial pump function, often secondary to hypoxemia and produces elevations or depressions ('biphasic events') in the ST-segment. As mentioned earlier, the cardiac muscle responds to moderate hypoxia by T/QRS and ST-elevation. However, in the presence of sudden and severe hypoxia, the repolarization sequence is altered, reversing the flow of current and depressing the ST-segment (often with T-inversion) [49]. This reflects a myocardium which has not had time to mobilize its defense to hypoxemia and indicates an increased risk of cardiovascular failure. It is important to note that these changes are only significant in the presence of an abnormal CTG reading.

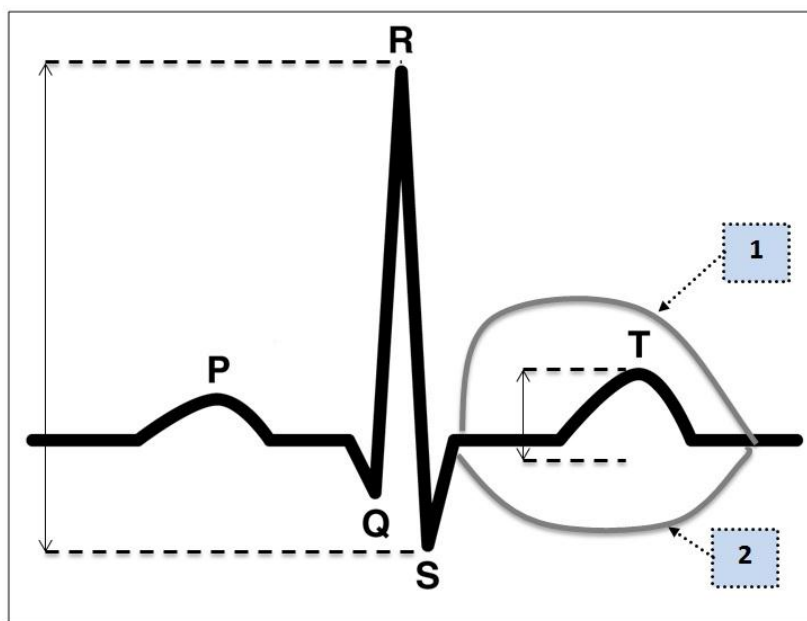


Figure-3. Fetal ECG showing T/QRS ratio

Source:Widmark, et al. [49]

In the recent past, numerous RCTs have emerged, comparing STAN-assisted and conventional modes of fetal surveillance, some of which have shown STAN to be associated with a lower incidence of instrumental delivery, neonatal encephalopathy and decreased need for FBS. These findings have been corroborated by Cochrane review in 2011 which concluded that there was 'modest support for the use of fetal ST waveform analysis [50]. A study of 4,495 cases showed a 75% reduction in metabolic acidosis, and 44% decrease in operative deliveries after interim analysis and retraining [51]. STAN allows for a form of non-invasive, continuous monitoring while providing an assessment of central oxygenation (namely heart and brain) whereas FBS and FPO only assess peripheral

oxygenation. A study comparing CTG with fetal ECG, found an OR of 0.65 (95%CI 0.53–0.78) for operative delivery due to fetal distress, and 0.39 (0.21–0.72) for metabolic acidosis at birth, in favor of CTG+STAN [52].

ST-analysis has its limitations in fetuses with structural/congenital cardiac defects and in preterm fetuses (<36weeks) as the endo-epicardial interphase is poorly developed leading to errors.

4.5. Recent Advances in IPFM

Near-infrared (NIR) spectroscopy involves radiating tissues with NIR light (wavelength 700–1100nm) and measuring the different NIR spectra which are reflected back [53]. Variations exist due to in-vivo chromophores (hemoglobin and cytochrome-aa3) whose absorption characteristic vary by oxygenation status. This technique has been shown to accurately measure changes in neonatal cerebral blood volume, Watkin, et al. [54] but a Cochrane systematic review concluded that it fails to bear clinical value [55]. However 'Intensity-Modulated' NIR spectroscopy (IMNIRS) may permit measurement of cerebral saturation between contractions, potentially detecting relevant changes in fetal oxygen status. The clinical implications of this method remain to be further investigated.

Magnetocardiography involves a strong magnetic coil generated by a SQUID (superconducting quantum interference device) and its proponents believe that it is a significant advancement in demonstrating QRS complexes and full PQRST waveforms, improving on the advances made by the fetal ECG [56].

Continuous intrapartum, intrauterine measurement of the amniotic fluid's meconium concentration has shown some early promise [57]. The non-invasive measurement of fetal temperature is also being studied [58]. Monitoring of maternal/fetal pyrexia and associated fetal acidosis is another area of ongoing research in intrapartum monitoring [59].

The INFANT trial is a multicentric, RCT assessing the efficacy of the INFANT software (INtelligent Fetal AssessmentNT) designed by K2 medical systems. It currently has 47,152 mothers enrolled, and is investigating primary outcomes including mortality and morbidity (neonatal encephalopathy and NICU admissions within 48 hours of birth, for ≥ 48 hours); and secondary outcomes (duration of labour and maternal admission, and health service utilisation.) 7000 randomly selected women will be followed up 2 years after randomisation.

The study aims to determine whether software decision support can improve CTG interpretation and better labor outcomes, and whether such a system is cost-effective, in terms of the cost per poor perinatal outcome avoided. No results have been released as of yet.

4.6. IPFM in Low Resource Settings

Scanty options exist for IPFM in low-resource settings as EFM and other mentioned techniques are expensive and predisposes to high rates of cesarean section. To address the issue of cost effectiveness, an RCT by Mahomed K et al found that intermittent auscultation using an handheld windup (clockwork) 'Doptone' device resulted in similar rates of operative delivery as a continuous CTG (28% versus 24%) [60]. Women also reportedly preferred the use of 'Doptone' rather than a Pinard stethoscope or CTG [61]. However, more research, innovation and entrepreneurship are needed [62].

Table-2. Evolution of Intrapartum Fetal Monitoring

Technique of IPFM	Initiated	Advantages	Disadvantages	Recommended use
FHR Monitoring				
A) Intermittent Auscultation	Early 1900's	<ul style="list-style-type: none"> • Less costly • Allows freedom of movement • Allows water immersion 	<ul style="list-style-type: none"> • Use restricted in Obese mothers • Requires greater staffing 	Recommended for women who have a low risk of fetal distress at onset of labour
B) Continuous CTG	1960's	<ul style="list-style-type: none"> • Objective measurements of FHR pattern parameters • Continuous recording useful for clinical audit/medico-legal issues • Reduction in neonatal seizures • Has high negative predictive value (correctly identifies uncompromised fetus) 	<ul style="list-style-type: none"> • Limits maternal mobility • Restricts massage, different positions and/or water immersion • ↑risk of caesarean/operative delivery • Has a low positive predictive (may incorrectly identify a fetus as compromised) 	Recommended for women identified as high risk, before or during labour (Stress tests: Not recommended)
C) Admission CTG	1960's			Not recommended
D) Internal CTG		<ul style="list-style-type: none"> • Shown to be more accurate than external CTG 	<ul style="list-style-type: none"> • Requires rupture of membranes for use 	Recommended when appropriate
Fetal scalp blood sampling	1962	<ul style="list-style-type: none"> • Significantly increases the sensitivity of EFM • Prognostic: predicts the degree/absence of brain damage 	<ul style="list-style-type: none"> • Invasive procedure (↑Infection risk) • Equipment: availability & cost • Requires Expertise & special equipment • Risk of sampling failure • Discomfort & anxiety to mother • Required cervical dilatation : >4cm 	Recommended as an adjunct to EFM to increase sensitivity, and thus reduce the risk of operative delivery.
Fetal pulse oximetry	1990's	<ul style="list-style-type: none"> • Non-invasive. Immediate results • Allows continuous monitoring • No sampling failure • Required cervical dilatation: 2cm 	<ul style="list-style-type: none"> • Measurement of fetal SpO₂ compromised by redistribution of blood flow in fetal hypoxia • Requires cephalic presentation 	Not recommended (Cochrane review showed no decrease in rate of C-sections)
Fetal Electrocardiography	1990's	<ul style="list-style-type: none"> • Non invasive • Electrode placed relatively easily 	<ul style="list-style-type: none"> • ↓ Accuracy in with congenital fetal cardiac anomalies & preterm fetuses. • Requires rupture of membranes 	Recommended as an adjunct to EFM to reduce the risk of operative delivery.

Source: [21, 22, 33, 45, 46, 50]

5. CONCLUSION

Despite many advances made in the field of intrapartum fetal monitoring, rates of cesarean sections remain spuriously high. Furthermore, hypoxic-ischemic encephalopathy continues to affect neonates globally. There is dire need of a sufficiently specific test for fetal distress to lower the rate of cesarean sections, and recent advances are not yet available to the low-resource populations in dire need of them. Effective IPFM must rely on the sequential utilization of two or more monitoring methods to reduce the incidence of HIE.

With a growing global population, and the steadily increasing prevalence of medical disorders in pregnancy (particularly gestational diabetes and pregnancy-induced hypertension) which have been associated with a greater risk of intrapartum fetal distress, the need for better monitoring techniques will become more urgent. There yet remains much work to be done: recent developments should reassure clinicians that better tools may soon become available, as research continues to advance.

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