

Evaluation of Perinatal Outcome by Antenatal CTG and Umbilical Artery Doppler in Pre-eclamptic Mothers

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ABSTRACT

This was a well-controlled hospital-based longitudinal prospective randomized study with sole focus on pre-eclampsia cases, where cardiotocography (CTG) and colored Doppler were the two special investigative tools applied to examine the perinatal outcome. The study concluded with a note that antenatal CTG is a useful objective test to know the intrauterine fetal status but it cannot forecast the fetal behavior during labor, neither does it provide a guide to optimize the timing of induction of labor (IOL) or termination by cesarean section. Color Doppler indices done after 34 weeks definitely give a qualitative assessment of fetoplacental perfusion but they cannot predict the said perfusion during labor - when there occurs a degree of compromise with the uterus contracting repetitively. Ultrasonography (USG) for fetal biometry and liquor volume is a good test to determine small for gestational age or intrauterine growth restriction (IUGR), as the case may be, taking cognizance of other factors e.g., pre-eclampsia, fetal congenital anomaly, etc. Every mother with pre-eclampsia needs to be evaluated clinically, biochemically and ultrasonologically. Understanding the limitation of antenatal CTG and color Doppler indices, these should be applied in a few selected cases e.g., increased fetal movement, IUGR, which is reassuring to both the patient and the doctor who can wait till a reasonable degree of fetal maturity occurs before one goes for IOL or a cesarean section. Patients with a suspicious CTG should undergo continuous CTG during labor; otherwise there is always a tendency to go for an early lower-segment cesarean section (LSCS). For a pre-eclamptic mother with a pathological CTG the decision is an elective LSCS; whereas, in cases with pathological CTG but normal Doppler indices, the judgment is too difficult. The answer then would depend on factors like whether the pre-eclampsia is controlled and whether the biochemical and hematological parameters are within normal limits. Of course, thanks to the presence of a special newborn care unit (SNCU) nearby.

Keywords: CTG, Doppler, pre-eclampsia

INTRODUCTION, REVIEW OF LITERATURE AND OBJECTIVES

Pre-eclampsia is a multisystem, highly variable disorder, unique to pregnancy and a leading cause of

maternal and perinatal mortality and morbidity. It is a syndrome defined by hypertension and proteinuria that also may be associated with a myriad of other signs and symptoms such as edema, visual disturbances, headache and epigastric pain. The increased incidence of perinatal morbidity and mortality seen in pregnancies complicated by pre-eclampsia is primarily due to the need for premature delivery and uteroplacental insufficiency resulting in a compromised blood flow to the fetus. The primary adoptive response of the fetus to placental insufficiency is a decrease in growth. Persistent placental insufficiency will result in decreased fetal movement to conserve energy, hemodynamic redistribution to favor the oxygenation of organs critical to the economy such as the brain, heart, suprarenal and attempt to improve the efficiency of the placental gas exchange by increasing the heart rate and the synthesis of red cells. Progressive decompensation like this will lead to a metabolic and respiratory acidosis,

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increased impedance to fetoplacental circulation, renal insufficiency with decreased amniotic fluid volume, myocardial compromise, absent or reversed atrial flow in ductus venosus, late deceleration in the fetal heart rate (FHR) tracing and fetal death. It would be ideal that this sequence of pathological changes elicited by placental insufficiency and fetal hypoxia could be identified in each of its different stages by a single test, which has not been achieved so far.

In an attempt to stratify risk, a variety of antepartum screening tests are performed, which include few laboratory tests and sonographic assessments, besides history taking and clinical examination, including serial symphysiofundal height measurement. Antenatal cardiotocography (CTG) is a special test for evaluation of fetal status. Prof. Essar GS Dows and Prof. C Redman of United Kingdom were two pioneers in the eighties who devised the computer program to evaluate CTG. The basic objective of CTG is to assess co-ordination between fetal central nervous system (CNS) and the cardiovascular system based on the fact that a well-oxygenated healthy fetus with functionally intact CNS-cardiac axis will show accelerations (rise of FHR 15 beats/minutes for 15 seconds above baseline) with fetal movements - the so called reactive CTG. In addition, good FHR variability (≥ 5 bpm) suggests normal balance of sympathetic-parasympathetic activity, an indirect evidence of adequate oxygenation of fetal regulatory centers. Indeed, a normal FHR variability is the hallmark of fetal well-being. Accepted normal parameters for term fetus are:

- Baseline FHR 110-160 beats/minute
- Baseline variability should be > 5 beats/minute
- Presence of two or more accelerations of FHR exceeding 15 beats/minute, sustained for at least 15 seconds in a 20-minute period. This pattern is termed as 'Reactive.'
- Absence of deceleration.

However, a Cochrane meta-analysis of randomized controlled trials (RCTs) involving 1,558 high/intermediate risk pregnancies suggested that antepartum CTG alone has no significant impact on perinatal outcome. Though, initial studies have shown a strong correlation between abnormal CTG and poor perinatal outcome, when CTG is used alone, significant interobserver variations, poor specificity and high false-positive rates causing increased number of lower-segment cesarean section (LSCS) are other problems. The change in behavior of ultrasound waveform reflecting from a moving object - the Doppler effect - was

introduced in the assessment of umbilical artery flow at Dubling in 1977. Longitudinal Doppler studies of the umbilical artery show that the systolic/diastolic (S/D) ratio decreases as gestation progresses. This is an indirect evidence of decreasing placental resistance with advancing gestation. However, there is no definite agreement as to what constitutes an abnormal Doppler study. Most authors have accepted an S/D ratio >3.0 as the cut-off beyond 30 weeks gestation. Gradual increase in umbilical artery resistance leads to absent and subsequently reversed end-diastolic flow, which is associated with progressively worse perinatal outcome. The Doppler indices are calculated as ratios between peak systolic velocity (A), end-diastolic peak velocity (B) and mean velocity (mean). The indices most common in clinical practice, are pulsatility index (PI) = $(A-B)/\text{mean}$, and resistant index (RI) = $(A-B)/A$. With normal placental perfusion, the umbilical artery waveform has a pattern compatible with a low-resistance system, showing forward blood flow throughout the cardiac cycle. Inadequate placental perfusion causes progressive changes in the Doppler flow pattern of umbilical artery starting from absent or reversed end-diastolic flow, increase in resistance index, which correlate well with fetal acidosis. The first meta-analysis of umbilical artery Doppler in high-risk pregnancies published in 1995 demonstrated significant reduction in perinatal death.

Two large RCTs- one from South Africa and other from Canada, and one Cochrane review of routine Doppler studies of umbilical artery in high-risk pregnancies have shown conflicting reports of benefit regarding perinatal outcome. However, evidence from small RCTs does indicate less requirement of emergency cesarean section for fetal distress if Doppler velocity was used (NICE Guideline, 2010). The TRUFFLE study was designed to compare reduced short-term variations on CTG and Doppler velocimetry of ductus venosus to determine optimum timing of delivery of growth restricted fetus.

In this study, spanning 6 months, we tried to evaluate perinatal outcome in pre-eclampsia in terms of mode of delivery (vaginal/instrumental/LSCS), need for induction of labor (IOL), neonatal status according to specific parameters by means of antenatal CTG and umbilical artery Doppler in late third trimester at our institution, which is a tertiary maternity care center with an annual delivery rate of $>20,000$, delivering optimal care free of cost to a large population from three districts namely Bankura, Purulia and Paschim Medinipur in West Bengal. Our objective was to ascertain an optimum and cost-effective way

to treat pre-eclamptic mothers and to obviate special investigations like CTG and umbilical artery Doppler in each and every case and thereby save some cost as well as manpower.

MATERIAL AND METHODS

This was a prospective longitudinal study carried out in our department during 6 months. All pre-eclamptic mothers of >34 weeks of gestation with a single intrauterine fetus with cephalic presentation without any congenital anomaly were included in the study. Patients with prelabor rupture of membrane, antepartum hemorrhage (APH), bad obstetric history, elderly primi (>35 years), multifetal pregnancy, malpresentation, history of systemic illness e.g., antiphospholipid syndrome, chronic renal disease, heart diseases, psychiatric illness were excluded.

Known cases of pre-eclampsia were evaluated with history, examination and laboratory investigations including urine albumin, serum uric acid, platelet count, clotting time, renal and liver function tests. The cases were then randomized and allocated in the study group and control group. The study group had undergone an antenatal CTG for 40 minutes and umbilical artery Doppler study. Categorization of FHR traces was done following Royal College of Obstetricians and Gynaecologists (RCOG) criteria 2001 as normal, suspicious and pathological. Normal implied fetal well-being and as such a conservative approach; whereas, suspicious implied continued observation and additional test e.g., vibroacoustic stimulation (VAS) and pathological indicated an urgent delivery.

The study group had also undergone assessment of fetoplacental profile and a Doppler assessment of umbilical artery. $S/D \leq 3$ and $RI \leq 0.6$ were considered normal; raised indices, absent or reversed end-diastolic flows were taken as signs of fetal distress. The decision to deliver the baby at an optimum time through an appropriate route (vaginal/LSCS) was taken considering the gestational age and the results of CTG and umbilical artery Doppler indices.

The control group was followed up by daily clinical monitoring and routine USG for fetoplacental profile and liquor volume. They were delivered by appropriate route at an optimum gestational age according to these findings and consultant decision.

Study group, where a conservative approach was followed till maturity (37 weeks), were followed up

twice in a week by CTG and another Doppler study after 2 weeks. Control group, in similar situation, had another routine USG for FPP after 2 weeks. The neonatal outcomes of both groups were recorded in predesigned proforma and compared using Chi-square test and Student's *t*-test and statistical software Medcalc 12.3.0. Ethical clearance was obtained from College Ethical Committee and due consent was taken from patients and their husbands or a near relative.

OBSERVATION AND DISCUSSION

Two-third of our study population ($n = 35$) had a reactive CTG and one-third showed a nonreactive type (Table 1). Nearly, 92% patients of reactive CTG against 45% of those with nonreactive type had a normal delivery and 54% with nonreactive CTG had a cesarean delivery against only 4% of reactive type – the difference of picture is definitely significant ($p < 0.05$). Random application of CTG has increased the number of LSCS whenever CTG tracing gets abnormal has been supported by other authors in the past: Khursheed et al showed a 72% LSCS rate when CTG was of pathological pattern.

Overall, the incidence of vaginal delivery (normal and instrumental) among the study group was 80% (28 out of 35) and LSCS was 20%. In a tertiary care center, 20% LSCS rate among pre-eclampsia cases was quite acceptable against World Health Organization (WHO) standard of 15%. So, CTG in this study has favored decision towards cesarean section but it has not pushed the number to an unacceptably high rate, which needed an audit. The message here is that CTG in pre-eclampsia is a useful investigation that allows judicious decision making and does not cause unnecessary panic among obstetricians to take hasty decisions of LSCS which is obvious from the fact that 45% (5 out of 11) of nonreactive CTG cases were allowed a normal delivery. Though, a significantly higher incidence ($p = 0.003$) of low Apgar score was noted among nonreactive CTG, there was no perinatal death. Similar findings of increased neonatal hypoxia were noted by Chew et al in 2009. So, CTG can predict a low Apgar neonate but not enough to predict a perinatal death.

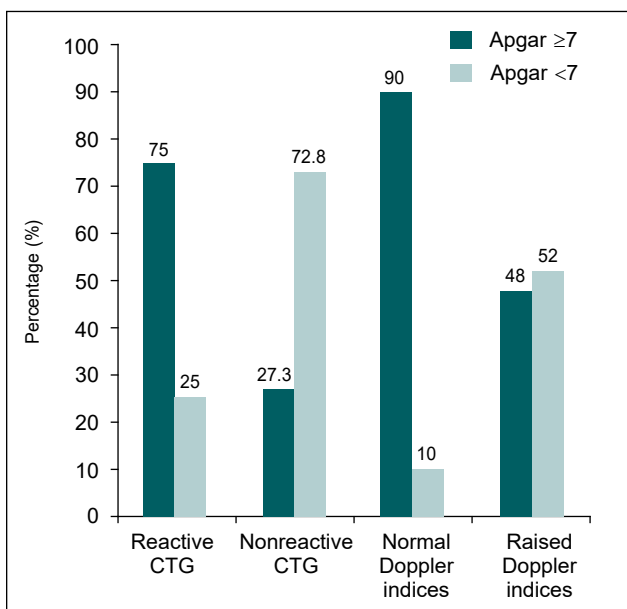
More than two-third (25 out of 35) of the study group had high umbilical artery Doppler indices (Table 2) but incidence of LSCS was not significantly higher ($p = 0.24$). However, among the neonates, the low Apgar score was significantly associated with raised Doppler indices, 52% against 10% ($p = 0.01$):

Table 1. No. of Patient Showing Reactive or Nonreactive CTG in the Study Population

CTG	Mode of delivery			Apgar score at 1 min	
	Normal	LSCS	Forceps	≥7	<7
Reactive (n = 24)	22 (91.6%)	1 (4.2%)	1	18 (75%)	6 (25%)
Nonreactive (n = 11)	5 (45.5%)	6 (54.5%)	-	3 (27.3%)	8 (72.8%)
Total (n = 35)	27 (77.14%)	7 (20%)	1	21 (60%)	14 (40%)
	P = 0.002			P = 0.003	

Table 2. Umbilical Artery Doppler Indices of the Study Population

Umbilical artery Doppler indices	Mode of delivery			Apgar score at 1 min	
	Normal	LSCS	Forceps	≥7	<7
Normal (n = 10)	8 (80%)	1 (10%)	1	9 (90%)	1 (10%)
Raised (n = 25)	19 (76%)	6 (24%)	-	12 (48%)	13 (52%)
Total (n = 35)	27 (77.14%)	7 (20%)	1	21 (60%)	14 (40%)
	P = 0.2004			P = 0.01	

**Figure 1.** Association of low Apgar score with raised Doppler indices.

(Fig. 1). This finding validates the fact that umbilical artery Doppler shows the extent of fetoplacental perfusion during fetal diastole and is a recognized tool to show intrauterine fetal status. Sharma et al got almost similar findings in their study in 2010.

The mean gestational age at birth of the study group and control group were not statistically different ($p = 0.792$). The labor events; the incidence of IOL versus spontaneous onset labor, incidence of vaginal delivery versus LSCS; Apgar score at 1 minute and 5 minutes; mean neonatal birth weight, number of hypoxic

neonates requiring Bag Mask (BM) resuscitation and special newborn care unit (SNCU) admission when compared vis-a-vis with the control group had shown quite similar results with p value ranging from 0.125 to 0.816 (Table 3). A range of well-defined studies including one evidence-based meta-analysis from 1992 to 2001 could find no significant difference in neonatal outcome and LSCS rate with Doppler velocimetry. In 2010, Alfirevic et al in a Cochrane review on "Fetal and umbilical Doppler ultrasound in high-risk pregnancies" could not identify a difference in the requirement of intubation and assisted ventilation among neonates between Doppler velocimetry group and control group without Doppler velocimetry. Figure 2 shows CTG findings of the study population.

CONCLUSION

Therefore, universal application of antenatal CTG and umbilical artery Doppler does not do anything better than a routine USG among mature fetuses to forecast perinatal outcome. It is the labor monitoring and 24 hours cesarean section facility that matters when emergency arises in the form of prolonged labor, meconium staining and fetal bradycardia. Over the years, scientists have explored this area to determine the postnatal events with antenatal CTG and Doppler, which has remained a grey area even today because beyond 34-36 weeks of gestation, it is uncommon to find absent or reversed EDF in the umbilical arteries caused by uteroplacental insufficiency. Abnormal umbilical artery Doppler after 35 weeks should prompt consideration of other causes, especially aneuploidy (Trisomies 18, 21).

Table 3. Perinatal Outcome in the Study and Control Group

Parameters	Study group	Control group	P value
Gestational age at birth (weeks)			
Mean; SD	38.6, 1.77	38.92, 1.88	<i>t</i> -test
34-37	2	6	p = 0.792
>37	33	29	
Labor events			
IOL	9	11	Chi-sq. <i>t</i> -test
SOL	26	24	p = 0.298
Mode of delivery			
ND	27	24	Chi-sq. <i>t</i> -test
LSCS	7	8	p = 0.537
Forceps	1	3	
Apgar score			
Mean; SD	6.51, 1.90	6.69, 1.683	Chi-sq. <i>t</i> -test
≥7 at 1 min	21	19	p = 0.147
<7 at 1 min	14	16	
Apgar score			
Mean, SD	7.46, 0.99	7.86, 1.29	Chi-sq. <i>t</i> -test
≥7 at 5 min	33	32	p = 0.125
<7 at 5 min	2	3	
Birth weight (g)			
Mean, SD	2691, 392	2670, 356	Chi-sq. <i>t</i> -test
1,500-2,500	6	11	p = 0.816
>2,500	29	24	
Need for resuscitation			
Yes with Bag Mask (BM)	14	16	Chi-sq. <i>t</i> -test
No	21	19	p = 0.404
SNCU admission			
Yes	7	9	Chi-sq. <i>t</i> -test
No	28	26	p = 0.285

IOL = Induction of labor; SOL = Spontaneous of labor; ND = Normal delivery; LSCS = Lower-segment cesarean section; SD = Standard deviation; SNCU = Special newborn care unit.

In absence of aneuploidy, assessment of intrauterine growth restriction (IUGR) in late pregnancy is challenging because umbilical artery Doppler has a limited value in this setting. The timing of delivery is contentious because a favorable perinatal outcome is expected even with early delivery once diagnosis of IUGR has been made by fetal ultrasound biometry, amniotic fluid index, umbilical and middle cerebral artery Doppler indices. Elective induction of labor with continuous FHR monitoring may result in successful vaginal delivery although fetal distress and meconium staining in labor are common complications.

The current study, though conducted on a small sample, can be considered as a pamphlet that speaks

the need of careful clinical monitoring along with a routine USG after 34 weeks, thanks to the presence of SNCU attached to the maternity ward. Control of blood pressure by labetalol or nifedipine (both the drugs are freely available at our ward); sending blood samples for Hb%, hematocrit, platelet count, serum urate, liver enzymes and 24 hours urine for protein; with or without the presence of IUGR on USG provide valuable clue to choose between immediate delivery by LSCS, IOL followed by fetal monitoring and trial of labor for at least six hours and/or prophylactic MgSO₄ injection followed by emergency LSCS.

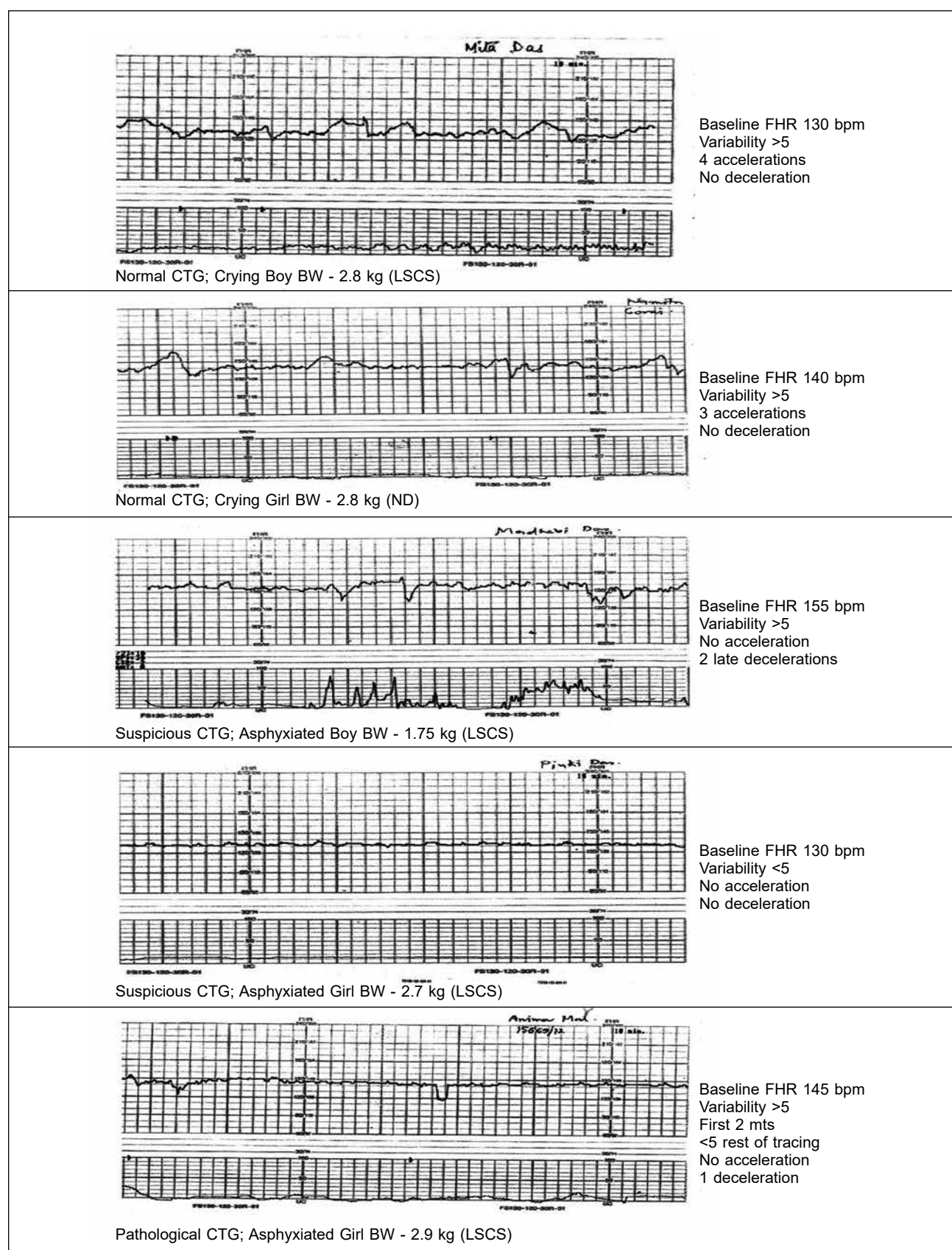


Figure 2. CTG findings of the study population.

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EMA Recommends Fenspiride Suspension Because of Heart Risks

EMA's safety committee (PRAC) has recommended an EU-wide suspension of fenspiride medicines, used in children and adults to relieve cough caused by lung diseases. The suspension is a precautionary measure to protect patients while the PRAC reviews the risk of QT prolongation and torsades de pointes (abnormalities of the heart's electrical activity that may lead to heart rhythm disturbances).

The USPSTF recommends that primary care providers screen women who have family members with breast, ovarian, tubal or peritoneal cancer or have an ethnicity or ancestry associated with BRCA1 or BRCA2 gene mutations with one of several screening tools designed to identify a family history that may be associated with an increased risk for potentially harmful mutations in breast cancer susceptibility genes (BRCA1 or BRCA2). Women with positive screening results should receive genetic counseling and, if indicated after counseling, genetic testing.

Allergic Rhinitis often precedes Asthma¹



Effective treatment
of Allergic Rhinitis may
reduce Asthma progression¹

For effective treatment
in Allergic Rhinitis and Allergic Rhinitis with Asthma



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1. Respir Res. 2005 Dec 28;6:153