J. Obstet. Gynaecol. Res. Vol. 30, No. 3: 169–180, June 2004

Invited Article

Sinusoidal heart rate pattern: Reappraisal of its definition and clinical significance

Houchang D. Modanlou[1] and Yuji Murata[2]

[1]*Division of Neonatology, Neonatal-Perinatal Medicine Fellowship Training Program and Department of Pediatrics, University of California Irvine, Irvine, California, USA, and* [2]*Department of Obstetrics and Gynecology, Osaka University, Osaka, Japan*

Abstract

Objectives: To address the clinical significance of sinusoidal heart rate (SHR) pattern and review its occurrence, define its characteristics, and explain its physiopathology.

Background: In 1972, Manseau *et al*. and Kubli *et al*. described an undulating wave form alternating with a flat or smooth baseline fetal heart rate (FHR) in severely affected, Rh-sensitized and dying fetuses. This FHR pattern was called 'sinusoidal' because of its sine waveform. Subsequently, Modanlou *et al*. described SHR pattern associated with fetal to maternal hemorrhage causing severe fetal anemia and hydrops fetalis. Both Manseau *et al*. and Kubli *et al*. stated that this particular FHR pattern, whatever its pathogenesis, was an extremely significant finding that implied severe fetal jeopardy and impending fetal death.

Undulating FHR pattern: Undulating FHR pattern may be due to the following: (1) true SHR pattern; (2) drugs; (3) pre-mortem FHR pattern; (4) pseudo-SHR pattern; and (5) equivocal FHR patterns.

Fetal conditions associated with SHR pattern: SHR pattern has been reported with the following fetal conditions: (1) severe fetal anemia of several etiologies; (2) effects of drugs, particularly narcotics; (3) fetal asphyxia/hypoxia; (4) fetal infection; (5) fetal cardiac anomalies; (6) fetal sleep cycles; and (7) sucking and rhythmic movements of fetal mouth.

Definition of true SHR pattern: Modanlou and Freeman proposed the following definition for the interpretation of true SHR pattern: (a) stable baseline FHR of 120–160 bpm; (b) amplitude of 5–15 bpm, rarely greater; (c) frequency of 2–5 cycles per minute; (d) fixed or flat short-term variability; (e) oscillation of the sinusoidal wave from above and below a baseline; and (f) no areas of normal FHR variability or reactivity.

Physiopathology: Since its early recognition, the physiopathology of SHR became a matter of debate. Murata *et al*. noted a rise of arginine vasopressin levels in the blood of posthemorrhagic/anemic fetal lamb. Further works by the same authors revealed that with chemical or surgical vagotomy, arginine vasopressin infusion produced SHR pattern, thus providing the role of autonomic nervous system dysfunction combined with the increase in arginine vasopressin as the etiology.

Conclusion: SHR is a rare occurrence. A true SHR is an ominous sign of fetal jeopardy needing immediate intervention. The correct diagnosis of true SHR pattern should also include fetal biophysical profile and the absence of drugs such as narcotics.

Key words: fetal anemia, pre-mortem heart rate pattern, pseudo-sinusoidal heart rate pattern, sinusoidal heart rate pattern.

Reprint request to: Houchang D. Modanlou, M.D., Department of Pediatrics, Irvine Medical Center, University of California, 101 The City Drive South, Building 2, Route 81, Orange, California 92868, USA. Email: modanlou@uci.edu

Introduction

Antenatal and intrapartum application of electronic fetal heart rate (FHR) monitoring for the evaluation of fetal condition are of common use in developed countries. The initial acceptance and the application of electronic FHR monitoring came about without rigorous scientific validities of its findings. During widespread use of electronic FHR monitoring in the US, it was found that its routine use during the intrapartum period was associated with significant decrease in perinatal mortality but it was also associated with a significant increase in operative deliveries.[1] Furthermore, it was found that the intrapartum electronic FHR monitoring was not superior to the frequent auscultations by an experienced obstetrical nurse although current shortage of experienced manpower makes frequent auscultation impractical.[2,3]

Recognized components of the FHR pattern are its baseline rate, variability and periodic changes associated with the uterine contractions. Baseline FHR within normal range, FHR reactivity in response to fetal movements or acoustic stimulation, and normal baseline variability signifies intact fetal central nervous system status. The presence of these findings is considered as evidence of fetal well-being. Conversely, the significance of alteration of baseline heart rate, reactivity and its variability are not very clear and have been subjects of considerable debate. A brief description of the physiology of FHR is required.

Despite automaticity intrinsic to myocardial contractility, FHR is under the direct influence of the autonomic nervous system. The autonomic nervous system and myocardium, and in turn, the heart rate are influenced by the actions of baroreceptors, chemoreceptors and hormonal factors. Renou *et al*.[4] recognized the direct influence of the parasympathetic and sympathetic nervous system on the heart rate and its variability. A continuous balance between the parasympathetic and sympathetic nervous system determines the slowing and accelerating FHR, respectively, as well as determining R-R interval differences (short-term variability) and the 2–5 cycles per minute variations of the FHR (long-term variability).

A rare but a peculiar FHR pattern is sinusoidal heart rate (SHR) pattern described to be associated with variety of fetal conditions. We have previously defined SHR pattern and its clinical significance.[5] Our definition of SHR pattern is one of the most widely accepted.[6] Based on our original definition we proposed that a true SHR pattern was an ominous sign of fetal jeopardy needing immediate fetal evaluation and intervention. We believe that a reappraisal of the subject of fetal SHR pattern is timely and is of clinical importance.

Historical background

In 1972, Manseau *et al*.[7] reported 11 cases of oscillatory or sine wave FHR pattern, with the oscillation frequency of 2–4 cycles per minute and amplitude of 5–15 beats, named as SHR pattern. Among these 11 cases, 9 patients with SHR pattern were affected with Rh isoimmunization. There were seven fetal deaths, six of them with severe Rh isoimmunization. In the same year, Kubli and associates[8] noted SHR pattern, with oscillation frequency of 2–5 cycles per minutes, in 12 patients resulting in nine deaths *in utero*. Both groups described FHR pattern with a regular rhythmicity of variation resembling sine wave. Manseau *et al*.[7] described also that the SHR patterns were alternating with a flat or absence of short-term variability of the baseline heart rate. Both groups implied that SHR pattern is an ominous sign of fetal jeopardy. In 1974, Baskett and Koh[9] reported a case of SHR pattern associated with severe fetal hypoxia and neonatal death. They concluded that the central nervous system control of the fetal heart was completely deranged by hypoxia, producing the SHR pattern. In 1976, Rochard *et al*.[10] reporting on their experience of antenatal nonstress testing in high-risk pregnancies, noted a sinusoidal FHR pattern at the same oscillation frequency described by Kubli *et al*.[8] in 20 patients with severe Rh isoimmunization. Ten (50%) died either *in utero* or in the neonatal period, an additional eight (40%) required prolonged hospitalization. Eighteen of the 20 patients had moderate to severe hydrops fetalis. They suggested that SHR pattern most likely represents a virtual absence of central nervous system control over the heart rate. In 1976, Cetrulo and Schifrin,[11] reported ominous FHR patterns proceeding intrauterine fetal demise in four cases. In that series, among various abnormal FHR patterns prior to death, there was a case of SHR pattern.

In 1977, Modanlou *et al*.[12] described SHR pattern in a fetus at 34 weeks gestation with massive feto-maternal hemorrhage resulting in severe fetal anemia and hydrops fetalis. The newborn had a hemoglobin/hematocrit of 3.1 g/9.7%, respectively. In 1978, Muller-Heubach *et al*.[13] reported the appearance of SHR pattern following intrauterine fetal transfusion. In the same year, Hatjis *et al*.[14] reported a case of sinusoidal FHR pattern in a patient with severe Rh isoimmunization

that resolved following intrauterine blood transfusion, with no recurrence of SHR pattern. In 1978, Gal and Jacobson[15] also reported SHR patterns in two cases: one preterm fetus at 30 weeks gestation that died *in utero;* and another case of post-term pregnancy complicated with meconium aspiration, moderate acidosis at birth and neonatal polycythemia. They suggested that SHR pattern is an alarming sign of fetal distress and supported the belief that the SHR pattern represents the absence of central nervous system control over the heart. They further stated that sinusoidal FHR would represent the end stage of severe fetal distress as this pattern appears to be ominous, which warrants immediate intervention. Conversely, Gray *et al*.[16] reported their experiences with SHR pattern appearing soon after the administration of alphaprodine (Nisentil) for the relief of labor pain in 42.5% of 40 patients they studied. These authors noted that SHR pattern appeared approximately 19 min following alphaprodine administration and persisted for approximately 60 min. All infants were delivered with normal 5-minute Apgar scores without any perinatal deaths. In 27 cases of sinusoidal FHR pattern during labor, Ayromlooi *et al*.[17] examined its relation to fetal status and neonatal outcome. Compared to a control group, those with SHR pattern had significantly lower fetal scalp pH and significantly lower Apgar scores at birth. They stated that over 96% of the fetuses had cord-related deceleration patterns, and nearly 63% had obvious cord complications. The latter publication did not contain any representative FHR tracing. They postulated that sinusoidal FHR pattern is an umbilical cord-related phenomenon, resulting from alternating hypovolemia and hypervolemia.

Katz *et al*.[18] reported their experience with two cases of SHR pattern during labor with continuous fetal scalp pH monitoring. They noted only mild to moderate fetal acidosis during the appearance of SHR pattern with some resolution to less acidosis at the disappearance of SHR pattern. They stated that their observations supported the interpretation of the SHR pattern as a compensatory autonomic response to fetal hypoxia, rather than due to loss of autonomic control of the fetal heart rate. They further suggested that the SHR is a sign of fetal stress, but not of a sufficient impact to mandate immediate delivery. The same group further described 16 cases of SHR pattern.[19] The cases were analyzed with respect to perinatal outcome, fetal scalp and umbilical arterial pH, and characteristics of FHR pattern. No perinatal death was reported in that series. The authors suggested that the effects of tissue hypoxia on the medullary centers in the fetal brain which regulate heart rate might account for this unusual FHR pattern. They further elaborated that FHR is regulated by a feedback-controlled system in which sensitivity is increased by hypoxia. They suggested that autonomic nervous system control is not deranged, but discharging alternately, struggling to maintain homeostasis in a strong compensatory effect under condition of hypoxia.

In 1980, several case reports of SHR pattern during labor were reported[20–27] with mixed interpretation of its significance. The fetal SHR pattern associated with severe fetal anemia and/or intrapartum asphyxia were noted to be ominous and clinically significant, needing immediate evaluation and intervention. Cases associated with amnionitis and narcotic administration during labor to relieve pain, were reported to be related to the effects of drug on the FHR and had a good outcome. From our study group, Elliott *et al*.[27] reported SHR pattern in a case of severely Rh sensitized fetus. Sinusoidal FHR pattern was also evident in the newborn infant during the first 3 h of life despite the infant having high arterial oxygen tension. The SHR pattern in the neonate disappeared during the course of an exchange transfusion. It was postulated that since the SHR pattern disappeared during the exchange transfusion, tissue hypoxia of the central nervous system was the etiologic reason for the SHR pattern. During 1981–1982, there were several case reports as well as some systematic reviews of FHR patterns noted to be SHR pattern.[28–40,41] Similarly, cases related to fetal anemia, as the consequence of Rh isoimmunization or vasa previa, were interpreted as an ominous FHR pattern needing immediate evaluation and intervention. Conversely, fetal SHR patterns noted during the administration of narcotics during labor, for the relief of pain, were interpreted merely as the effects of drugs on FHR with no pathological significance and good clinical outcome. Meanwhile, in 1981, controversy developed among some perinatologists regarding the appropriate interpretation of fetal SHR patterns.[42,43] The controversy necessitated a critical review of the available literature on the subject of fetal SHR pattern. That effort resulted in a proposal for the definition of true SHR pattern which appeared to signify an ominous FHR pattern associated with high perinatal morbidity and mortality.[5] Although other authors, based on their clinical experience, attempted to modify our original definition,[45–48] our proposed definition appears to have been accepted widely by the obstetrical community.[6,48] From 1983 to 2003, the authors noted

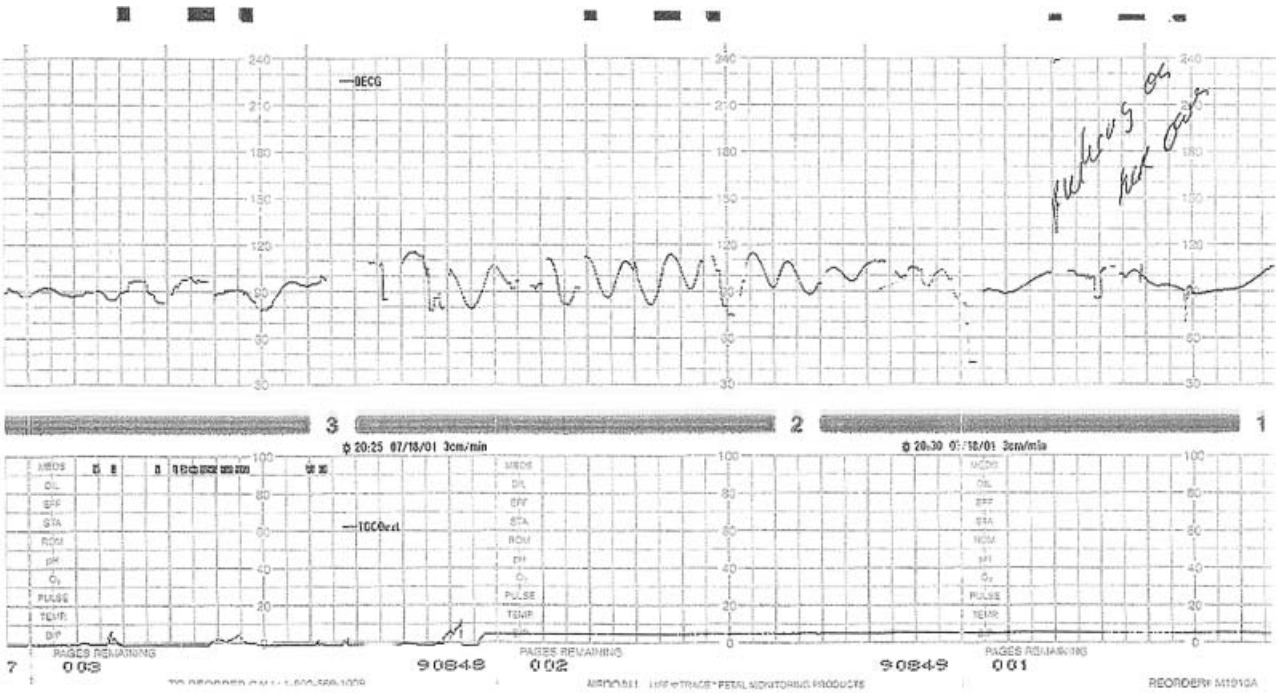


Figure 1 Fetal heart rate (FHR) tracing recorded in a fetus at 32 weeks gestation. The pregnancy was complicated with vasa previa and sudden massive maternal vaginal bleeding. The FHR tracing was obtained approximately 24 h postvaginal bleeding. Cesarean section was performed with the appearance of sinusoidal heart rate pattern. Soon after birth, the infant's hemoglobin and hematocrit were 3.0 g and 9.1%, respectively.

more than 70 additional literature citations on the subject of SHR pattern; some of which will be reviewed.

Undulating or sine wave FHR pattern

Undulating or sine wave FHR pattern can be classified as follows:

1 True SHR pattern.
2 Pre-mortem FHR pattern.
3 Drug induced.
4 FHR during sleep cycle and behavioral states.
5 Equivocal/pseudosinusoidal FHR pattern.
6 FHR pattern other than SHR pattern or misdiagnosed.

True SHR pattern, as we defined previously[5] is an ominous FHR pattern needing immediate fetal evaluation and intervention based on individual case presentation and fetal viability outside of the uterus. This pattern is commonly seen to be associated with the following conditions: (a) severe fetal anemia as the result of Rh isoimmunization;[7,8,10,27] (b) massive feto-maternal hemorrhage;[12,49–57] (c) twin-to-twin transfusion syndrome;[58] (d) vasa previa with bleeding;[59–61] (e) traumatic fetal bleeding and severe anemia;[62,63] (f) fetal intracranial hemorrhage;[64,65] and (g) severe fetal asphyxia in humans as well as in the experimental fetal lambs.[9,66] Sinusoidal FHR pattern was noted before and after intrauterine fetal blood transfusion for severe fetal anemia due to Rh isoimmunization.[13, 14,67] True fetal SHR pattern has been also reported in cases of severe neonatal hypoxia,[68] congenital hydrocephalus,[69] gastroschisis,[70] and during maternal cardiopulmonary bypass.[71]

Figure 1 is representative sinusoidal FHR pattern. This FHR tracing was recorded in a fetus at 32 weeks gestation with vasa previa and massive maternal vaginal bleeding necessitating emergency cesarean section. Capillary hemoglobin and hematocrit, soon after birth, were 3.0 g and 9.1%, respectively.

Pre-mortem fetal heart rate patterns

At present, intrapartum fetal death is a rare occurrence but catastrophic fetal compromise still occurs with severe placenta abruption, umbilical cord prolapse, and uterine rupture. The latter is more common with

unrecognized or unknown previous classical cesarean section and sporadically with the use of vaginal prostaglandin during vaginal delivery after low segment cesarean section. In these cases, FHR patterns are normal prior to the catastrophic episodes. In rare cases of severe intrapartum fetal asphyxia/hypoxia/acidosis, SHR pattern may appear prior to fetal death or the newborn may be born severely depressed with metabolic acidosis, and significant neonatal morbidity. Another FHR pattern similar to SHR pattern with undulatory shape but, generally with higher amplitude, is premortem FHR pattern. Like SHR pattern premortem FHR pattern is always preceded by other abnormalities of the FHR pattern such as loss of variability and or persistent late decelerations. Pre-mortem FHR pattern was observed and reported by Hon and Lee[72] prior to general introduction of the electronic FHR monitoring during labor. It was also reported during the early years of its application for routine clinical use.[11,73] This ominous FHR pattern, associated with severe hypoxia and acidosis, is not uniform in its appearance and is followed by a gradual decrease in baseline FHR and complete absence of heart rate variability or fixed FHR pattern. As it was noted by Freeman and associates[74] the baseline FHR is unstable and is characterized by a blunted slow wandering heart rate pattern. Not uncommonly, fetal cardiac arrhythmia is noted prior to fetal cardiac arrest.[74] Not infrequently premortem FHR pattern may appear during the second stage of labor associated with severe cord compression.[75] Fetuses with this ominous FHR pattern may suffer fetal or neonatal death. The surviving neonates tend to have significant morbidity and long-term neurological sequelae. Figure 2 is an example of FHR pattern prior to delivery in a fetus at term gestation. The FHR rate pattern appears sinusoidal in appearance for a few minutes. The neonate had Apgar scores of zero at one, zero at 5, 1 at 10 and 2 at 20 min of life. He had multiorgan manifestations of severe intrapartum asphyxia/hypoxia and persistent metabolic acidosis with flat EEG on two occasions. He was taken off the ventilator by the third day of life. Figure 3a,b is another example of an ominous premortem FHR pattern obtained approximately within 1 h of delivery. Uterine contractions were not recorded on Fig. 3b as the caretakers were employing vacuum to expedite delivery. The child's Apgar scores were 1 at one, 2 at 5 and 4 at 10 min of life. The infant developed generalized seizures within 1 h of life. The infant survived with cerebral palsy and developmental delay.

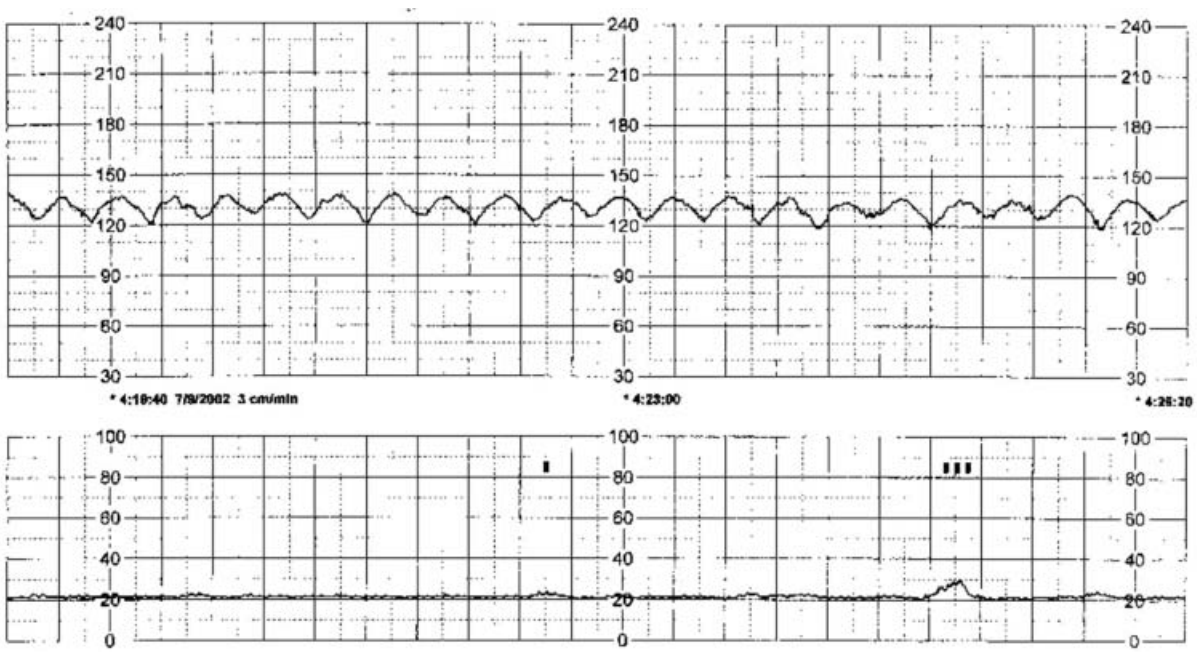
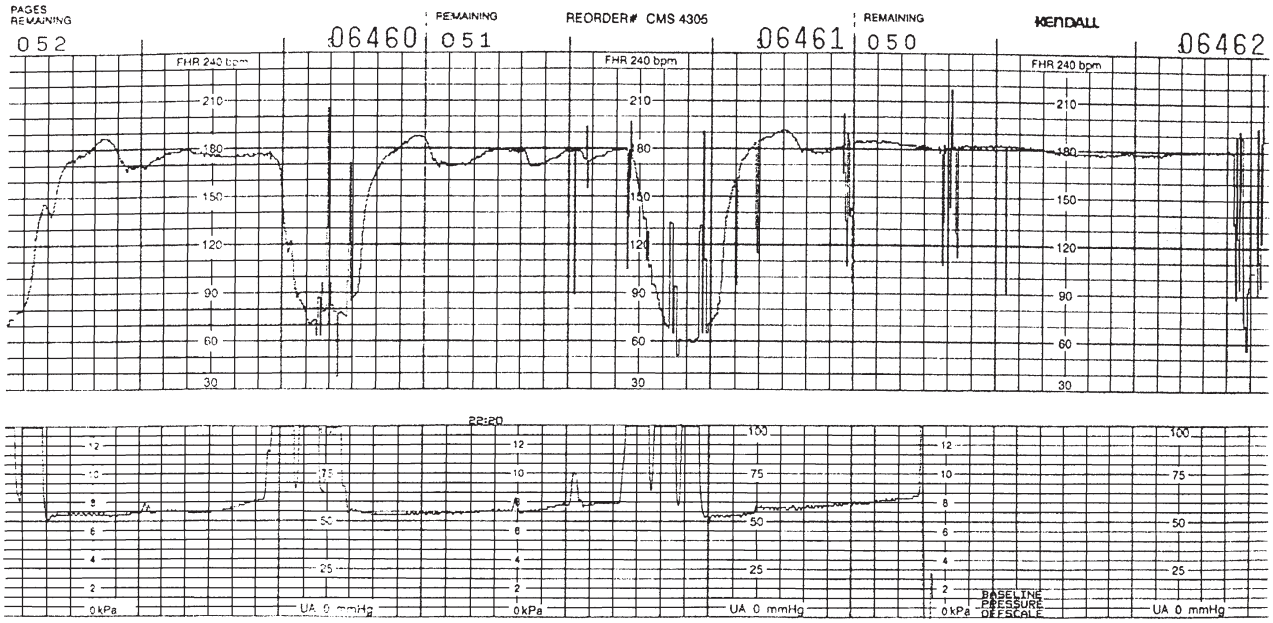


Figure 2 Fetal heart rate tracing recorded within 1 h prior to delivery at term gestation. Note period of sinusoidal-like heart rate. Infant's Apgar scores were zero at one, zero at 5, one at 10, and two at 15 min of life. The infant had flat EEG twice and was taken off ventilator support by the third day of life.

(a)



(b)

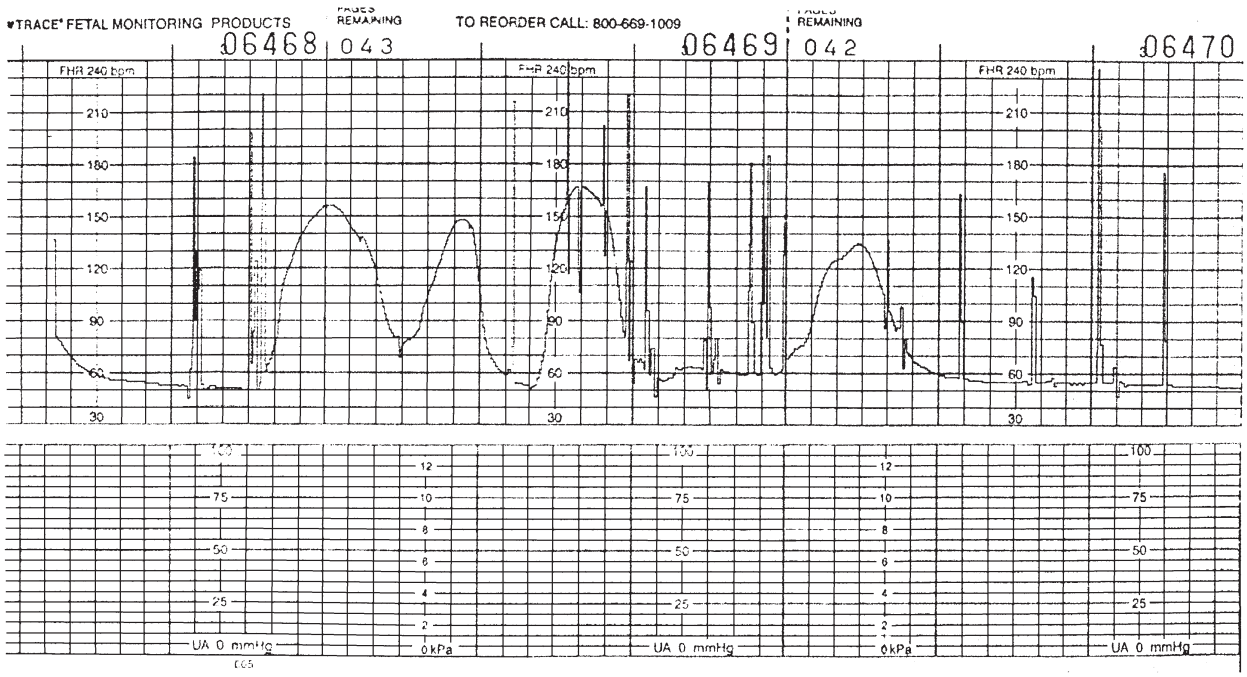


Figure 3 (a) Fetal heart rate tracing during the second stage of labor in a term gestation pregnancy. Note baseline heart rate of 180 bpm associated with deep variable decelerations during uterine contractions. (b) Continuation of heart rate tracing of 3a prior to delivery. Note undulatory heart rate with baseline rate of 60 bpm. The infant was delivered with vacuum application. His Apgar scores were one at 1, two at 5, and four at 10 min of life. The infant developed seizures within 1 h of life. He survived with neurologic sequelae.

Drug-induced SHR patterns

In a systematic review of FHR tracings during labor in 40 patients who received alphaprodine for the relief of labor pain, Gray *et al*.[16] noted SHR pattern in 17 (42.5%) patients. The SHR pattern appeared approximately 19 min following alphaprodine administration and persisted for approximately 60 min. Similarly, Veren *et al*.[40] compared 34 patients who received intrapartum alphaprodine to 27 patients without alphaprodine. They noted SHR pattern in 11 (32%) of the study subjects compared to only one (3.7%) of the control group. Both groups noted that the majority of infants had normal Apgar scores at birth because alphaprodine, at non-toxic dosages, had no deleterious effect on the fetus. Subsequently, SHR pattern was observed following the administration of meperidine,[39,76] butorphanol,[77,78] and nalbuphine hydrochloride.[79,80] In one case, sinusoidal-like FHR pattern appeared following fetal intravascular administration of pancuronium bromide,[81] and in another case, intermittent SHR pattern appeared during the course of maternal chemotherapy for acute myelogenous leukemia.[82] From the review of cited manuscripts it is clear that SHR patterns were of limited duration, are not preceded by abnormal FHR pattern and can be related to the administration of the drug. When considering the appearance of SHR pattern during the intrapartum period, the clinician should rule out the effects of narcotics administered for the relief of labor pain.

Fetal and neonatal SHR patterns, and behavioral state

In two cases, intermittent SHR patterns have been observed by real-time ultrasonography.[83] The patterns observed in these two fetuses were similar to that found in the neonate during sucking. Subsequent observations confirmed the appearance of SHR pattern with rhythmic movements of the fetal mouth and sucking.[84–87] Similar observations of SHR pattern was also noted with fetal breathing movements thought to be related to fetal respiratory arrhythmia.[87,88] Ninomiya *et al*.[89] experimentally induced SHR pattern in fetal lambs with the infusion of arginine vasopressin. In their experiment, an intermittent SHR pattern was observed in relation to fetal sleep cycles. Sinusoidal FHR pattern appears more frequently during non-rapid eye movements (NREM) than rapid eye movement (REM) sleep. Similarly, we have observed SHR pattern in neonates during NREM sleep.

Pseudo-SHR pattern

In our review of the literature we failed to appreciate a clear definition of pseudo-sinusoidal FHR pattern. In our original proposal for the definition of true SHR pattern[5] we provided an example of pseudo-sinusoidal FHR tracing. We suggested such FHR pattern as an undulatory heart rate pattern of short duration preceded and followed with normal FHR pattern.

Ito *et al*.[90] reviewed FHR patterns associated with abruption placenta, and proposed a specific definition of pseudo-sinusoidal FHR pattern as follows: (1) oscillation frequency synchronized with the frequency of uterine contractions; (2) an amplitude of 19 bpm or more, which is positively correlated with the area of placental separation; (3) uniform frequency and amplitude; and (4) a frequency of 1.3 cycles/minute or less, which is clearly different from the true SHR pattern. Reviewing their FHR patterns exhibited in Fig. 1, they appear to be rather repetitive late decelerations associated with frequent uterine contractions than sinusoidal patterns. Frequency of the pattern is 0.5–1.5 cycles per minute, corresponding well with uterine contractions, and it is also reasonable to observe a positive correlation between the depth of late deceleration and the degree of hypoxia of the fetus represented by the area of placental separation.

Murphy *et al*.[91] prospectively reviewed FHR tracing in 1520 women in labor. No SHR patterns were observed, but pseudo-sinusoidal FHR patterns were found in 230 of the 1520 (15%) of tracings reviewed. They correlated pseudo-sinusoidal FHR patterns with low amplitude in association with the use of narcotics and epidural analgesia while those with intermediate amplitude were more related to fetal sucking and transient episodes of fetal hypoxia such as that caused by periodic umbilical cord compression. They concluded that pseudo-sinusoidal FHR patterns in labor is usually associated with a normal fetal outcome but also suggested a careful fetal assessment in the presence of such FHR patterns. Similar to Murphy *et al*.,[91] Neesham *et al*.[92] reported a case of pseudo-sinusoidal FHR rate pattern with fetal anemia and they also suggested a classification of minor, intermediate and major pseudo-sinusoidal FHR rate pattern. Groutz *et al*.[93] described intermittent episodes of SHR rate pattern as pseudo-sinusoidal when there were periods of normal FHR rate pattern in a case of fetal cardiac anomaly. All of the investigators recommended careful fetal evaluation to rule out specific fetal problem associated with the detection of pseudo-sinusoidal FHR rate pattern.

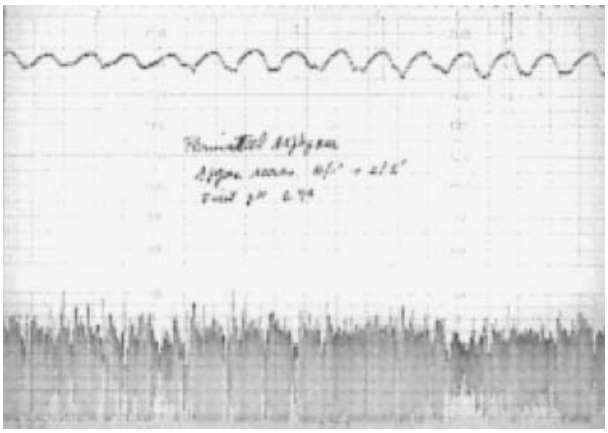


Figure 4 Representative neonatal sinusoidal heart rate tracing during the first day of life, in a post-term infant who suffered severe intrapartum asphyxia/hypoxia. By the second day of life the infant had a flat or fixed heart rate of 180 bpm. His baseline heart rate gradually decreased and developed cardiac arrhythmia prior to death.

Neonatal SHR pattern

In 1979, Reid *et al*.[68] described SHR patterns in eight neonates with prematurity, respiratory distress syndrome, central nervous system bleeding and perinatal asphyxia. Six infants died, two survived with major central nervous system sequelae. As previously noted, Elliott *et al*.[27] observed SHR pattern in a case of severe Rh sensitized fetus prior to an emergency delivery. The SHR pattern persisted during the first 3 h of life and disappeared during an exchange transfusion. Subsequently, we, as well as many other authors, have observed SHR pattern in ill neonates who suffered severe intrapartum asphyxia and hypoxia with persistent acidosis leading to death or significant morbidity. Figure 4, is a neonatal heart rate tracing in a term infant who suffered severe intrapartum asphyxia/hypoxia. The infant's first arterial pH was 6.9. SHR pattern (upper panel) was recorded during the first day of life. The infant was on a ventilator. Lower panel shows uniform ventilator rate. The infant expired by the second day of life.

Definition of true SHR pattern

From the original description by Manseau *et al*.[7] and Kubli *et al*.[8] in 1972–1980, several reports appeared in the literature suggesting that SHR pattern was not necessarily an ominous FHR pattern requiring immediate intervention. This led to disagreement and editorial correspondence[42,43] among some authors regarding the interpretation and clinical significance of SHR pattern. Therefore, we embarked on a review of the literature and published FHR tracings and proposed definition of true SHR pattern as follows: (a) stable baseline heart rate of 120–160 bpm with regular oscillations; (b) amplitude of 5–15 bpm, rarely greater; (c) frequency of 2–5 cycles per minute, as long-term variability; (d) fixed or flat short-term variability; (e) oscillation of the sinusoidal wave form above and below a baseline; and (f) no areas of normal FHR variability or reactivity.[5] Based on the above definition, 23 publications with 41 FHR tracings were reviewed. Twenty-seven tracings were found to be true SHR pattern, 11 non-sinusoidal and three were equivocal FHR patterns. Of the 27 true SHR patterns, 24 cases were associated with fetal or neonatal death and/or severe fetal and neonatal morbidity (13 cases of severe Rh isoimmunization, three cases with hydrops fetalis and severe anemia, and eight with perinatal asphyxia and central nervous system damage). Two cases were associated with alphaprodine administration during labor with good outcome. One case was a fetus with gastroschisis at 35 weeks gestation. Other investigators[44–47,91,92] have also proposed a definition of SHR pattern. Murphy *et al*.[91] classified SHR patterns into mild (amplitude 5–15 bpm), intermediate (16–24 bpm), and major (25 or more bpm) to quantify fetal risk.

Experimental studies of SHR pattern

In a landmark study of the chronically instrumented fetal lamb Murata *et al*.[94] observed SHR pattern. The study was performed on a set of twins with intact vagal nerve. One twin received phlebotomy of 10 mL per day through a vein catheter everyday and a minimal blood sample was taken from the other twin as a control. The phlebotomized fetus exhibited a SHR pattern at 15 days of experiment. Hematocrit was approximately 20%, with slight metabolic acidosis. AVP was above 15 μIU/mL. No noticeable changes were observed in the parameters from the control fetus throughout the experiment, with hematocrit of 32–35% and AVP <1μIU/mL. The frequency of SHR was consistently between two and four cycles per minute. On further observation by these authors, they were able to produce SHR pattern in fetal lamb with surgical or chemical (atropine) vagotomy and simultaneous infusion of arginine vasopressin. Experiments in fetal lambs undergoing extracorporeal membrane oxygenation Ikeda *et al*.[95] noted that SHR patterns were associated with fluctuation of fetal arterial pressure at the

same frequency. Two types of FHR and arterial blood pressure relationship were recognized: reciprocal type; and synchronized type. The synchronized type was associated with a lower pH and base excess than was the reciprocal type. They concluded that a synchronized type SHR pattern may indicate more advanced fetal compromise with more deteriorated fetal baroreflex.

Physiopathology of SHR pattern

From the foregoing review it appears that SHR pattern can occur during physiologic state such as during periodic sucking and breathing movements.[83–89] SHR pattern occurring during behavioral state could be defined as physiologic SHR pattern. This type of SHR pattern is intermittent and it is preceded and followed by periods of normal baseline heart rate pattern. Similarly, SHR pattern occurring with the administration of drugs such as alphaprodine is due to the effects of the drugs on the central nervous system and the heart rate. SHR pattern associated with the administration of drugs is temporary and should disappear with the clearance of the drugs by fetal/placental and maternal system. Conversely, pathologic SHR pattern is more commonly seen with severe fetal anemia of different etiologies and in some fetuses with severe intrapartum asphyxia, hypoxia and acidosis. Manseau and associates[7] stated that they had no precise opinion about the physiopathology of this unusual FHR pattern except that it occurred mostly in severely Rh sensitized fetuses. Basket and Koh[9] suggested that the nervous control of the fetal heart was completely deranged by hypoxia, producing SHR pattern. Rochard *et al*.[10] suggested that SHR pattern most likely represent a virtual absence of central nervous system control over the heart. Young *et al*.[19] suggested that fetal hypoxia is the common denominator in SHR pattern but the autonomic nervous control is not deranged, but discharging alternately, struggling to maintain homeostasis in a strong compensatory effect under conditions of hypoxia. Elliott *et al*.[27] suggested that a possible common pathway is tissue hypoxia of the fetal heart and central nervous system. Modanlou and Freeman[5] suggested that SHR pattern is associated with hypoxia of cardiac center of the brainstem. In severely acidotic fetal lambs, Ikeda *et al*.[95] showed that SHR pattern was associated with synchronized type fluctuation of arterial blood pressure and decreased blood flow to medulla oblongata. In similar experiment in fetal lambs by Murata *et al*.[94] blood level of arginine vasopressin was elevated with severe fetal anemia and SHR pattern. Interestingly, SHR pattern could not be reproduced by infusion of arginine vasopressin alone. However, with high dosage of atropine (chemical vagotomy) or with surgical vagotomy, SHR patterns were produced with high dosages of arginine vasopressin infusion. Freeman and associates[74] described true SHR pattern as FHR with an absence of short-term variability and with uniform long-term variability. In our systematic study of the heart rate patterns in ill newborn infants, we observed that short-term variability was reduced early in the course of neonatal hypoxemia, with loss of long-term variability occurring with more severe hypoxemia leading to flat or fixed baseline heart rate.[96] If recovery occurred, long-term variability was first to appear with the appearance of short-term variability later during the course of recovery. Using power spectral analysis of R-R interval variability before and during the SHR pattern in fetal lambs, Suzuki *et al*.[97] showed that SHR pattern may represent very low-frequency component inherent in FHR variability that appears when low- and high-frequency components are reduced as a result of strongly suppressed autonomic nervous system. We also observed SHR patterns in preterm infants with periodic breathings and during neonatal generalized seizure activities. Periodic breathings are known to be associated with central nervous system hypoxia. Central nervous system hypoxia also occurs with generalized seizure activities. These observations lead us to believe that true SHR pattern is associated with hypoxemia and tissue hypoxia of the central nervous system and autonomic nervous system dysfunction.

Conclusion

True SHR pattern is a rare occurrence in the fetus and neonate. In the fetus, true SHR pattern occurs with severe anemia and asphyxia/hypoxia/acidosis. In ill neonate, SHR pattern occurs with at least a moderate degree of hypoxemia/acidosis and central nervous system tissue hypoxia. The latter is supported by an experimental study showing that with severe acidosis and the presence of SHR pattern, perfusion to medulla oblongata is decreased. The diagnosis of true SHR pattern should exclude the use of narcotics and sedatives. Additionally, the presence of normal heart rate pattern soon before and after the appearance of SHR pattern excludes the diagnosis of true SHR pattern. We believe that the original definition of SHR pattern by Modanlou and Freeman[5] is a useful tool for clinical application. We suggest that when in doubt regarding the diagnosis of true SHR pattern, the clinician should

employ fetal biophysical profile or fetal actocardiogram, as suggested by Ito *et al*.[98] and Maeda *et al*.[99] before intervention on behalf of the fetus.

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