J. Perinat. Med.
11 (1983) 97

# Short term variability of fetal heart rate during insulin-dependent diabetic pregnancies

P. Ämmälä, V. Kariniemi

Departments of Obstetrics and Gynecology, Helsinki University Central Hospital, Finland

## Introduction

The decrease of perinatal mortality in diabetic pregnancies is considered a significant achievement in modern obstetrics [2, 6, 14]. This favourable development is partially due to intensive monitoring of the fetus during pregnancy and labor. In spite of the improved fetal outcome, intrauterine fetal deaths still occur during diabetic pregnancies. Although the mechanisms of fetal death in diabetes are poorly understood, reported signs of asphyxia before and during labor [3, 6, 9] suggest that uteroplacental insufficiency may be one of the reasons. Nonstress testing (NST) and contraction stress testing (CST) have proved effective in fetal surveillance in many groups of high risk pregnancy [3, 5, 13]. In diabetic pregnancies, however, documented cases of fetal distress and intrauterine deaths have been reported to occur even within one day after negative NST [20] and CST [4]. Therefore, detection of fetuses at risk of fetal distress is still an important problem in managing diabetic pregnancies. Decreasing variability of FHR has been claimed to be prognostic for poor fetal outcome in other high risk pregnancies [8, 12, 15, 22, 18]. In the present study, the short term variability of antepartal FHR was quantitated in order to assess its clinical significance as a predictor of intrapartal fetal distress in insulin-dependent diabetic pregnancies.

## Curriculum vitae

PIRKKO ÄMMÄLÄ *was born in 1946 in Finland. She studied medicine in Helsinki University and graduated in 1973. She specialised in Obstetrics and Gynecology in 1980 and is working in the Departments of Obstetrics and Gynecology, Helsinki University Central Hospital. Field of interest: Perinatal medicine.*

## 2 Patients and methods

### 2.1 Normal pregnancies

The reference material consisted of 65 strictly normal pregnancies with good fetal outcome [12]. The first lower percentile of antepartal differential indices (DI) in this reference material was used as the normal limit of DI.

### 2.2 Diabetic pregnancies

The group studied consisted of 120 insulin-dependent diabetic mothers, who were treated at the Departments of Obstetrics and Gynecology of Helsinki University Central Hospital. Diabetes in pregnancy was classified according to WHITE

0300-5577/83/0011-0097$02.00

[19] as modified by PEDERSEN [17]. Patients who needed insulin only during pregnancy were classified as A/B (15 cases). Four mothers in class F had proliferative retinopathy and five had nephropathy. Twelve mothers had pre-eclampsia, six had a mild hypertensive disease, and three had cholestasis of pregnancy. All were singleton pregnancies.

### 2.3 Fetal distress

Antepartal NSTs were used as a primary clinical tool in fetal surveillance. All fetuses were monitored by cardiotocography (CTG) during labor or at least 24 hours before an elective cesarean section. Fetal distress was recorded when a perinatal death occurred or at least two of the following signs were present: Apgar score less than seven at one or five minutes, more than two late decelerations in FHR during labor or before cesarean section, total variability (visually evaluated) of FHR less than five beats per minute for at least five minutes under the same circumstances and acidosis in fetal scalp blood (pH $< 7.20$ and/or base excess $> 13.0$ mEq/l by SALING method). Classification of patients with modes of delivery and signs of fetal distress is presented in Tab. I.

### 2.4 Measurement of the short term variability of FHR

The DIs were measured by a previously described on-line method which utilizes abdominal fetal electrocardiography (aFECG) as a triggering signal [10]. The analysis of FHR variability was regarded as a failure when less than 30 per cent of fetal interval differences were accepted in the analysis. The FHR analyses were performed at one to four week intervals either during visits to the clinic or during the mothers' stay in the hospital. The time from testing DI to the delivery varied from less than one up to 139 days (mean 31, SD 26).

### 2.5 Assessment of the test

The value of antepartal DI as a predictor of intrapartal fetal condition was assessed from those pregnancies, where FHR analyses were performed during the last week before delivery (93 cases). The results of FHR analyses were divided into

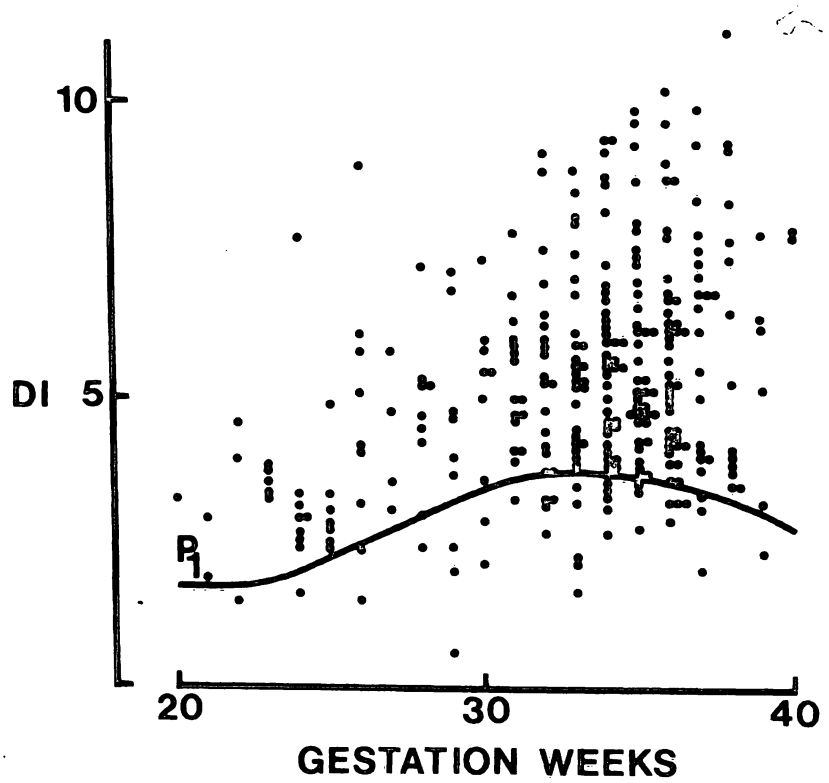


Fig. 1. Distribution of the 308 DIs measured from 5 minute samples of abdominal fetal electrocardiograms of 110 diabetic pregnancies. The first lower percentile limit of DI in normal pregnancies with good fetal outcome has been drawn for reference. Thirty fetuses had 37 pathological DIs.

Tab. I. Distribution of pregnancies, modes of delivery and signs of fetal distress in different classes of diabetes mellitus. (Abbreviations: CS = cesarean section, VE = vacuum extraction, S = spontaneous vaginal delivery, FBA = fetal blood analysis).

| WHITE'S class | Number of pregn. | Mode of delivery | | | Signs of fetal distress | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | CS | VE | S | Perin. deaths | APGAR score < 7 | Late decel. | Fixed baseline | Acid. in FBA | Fetal distress |
| A/B, B | 41 | 16 | 2 | 23 | 1 | 2 | 12 | 15 | 1/12 | 11 |
| C | 36 | 28 | 1 | 7 | – | 4 | 5 | 8 | 1/6 | 7 |
| D, F | 43 | 39 | – | 4 | 1 | 5 | 15 | 13 | –/2 | 13 |
| Total | 120 | 83 | 3 | 43 | 2 | 11 | 32 | 38 | 2/20 | 31 |
| % | 100 | 69 | 3 | 28 | 2 | 9 | 27 | 32 | 10 | 26 |

five categories: Failures of the analysis, correct positives (fetuses with one or more pathological DIs and fetal distress), correct negatives (fetuses with normal DIs and without fetal distress), false positives (fetuses with one or more pathological DIs without subsequent fetal distress) and false negatives (fetuses with normal DIs with subsequent fetal distress). Four statistical descriptors were used to assess the clinical value of the test (DI): Sensitivity was defined by the percentage of fetuses with a correct positive result in the group with fetal distress. Predictive value was the correct positives as a percentage of all positive results. Specificity was the percentage of fetuses with correct negative results in the group without fetal distress. Relative risk was the ratio of the percentage of positives that were true positives to the percentage of negatives that were false negatives [1]. Statistical significance of difference between the two percentages in the calculation of relative risk was assessed by the chi squared test with YATES' correction.

## 3 Results

No intrauterine deaths occurred. Two newborn infants died (one with multiple malformations and the other with asphyxia and prematurity). The perinatal mortality was thus 1.7%. Five infants were born with major congenital malformations (4%). One mother (White class D complicated by severe pre-eclampsia) suffered from a cerebral hemorrhage after cesarean section and never regained consciousness.

FHR analysis never succeeded during ten pregnancies and was successful at least once in 110 pregnancies, with a total of 308 measured DIs. The scattergram of antepartal DIs in diabetic pregnancies is presented in Fig. 1. Fetal distress developed in 28 out of 110 pregnancies with successful FHR analysis. Modes of delivery and the signs of fetal distress in different classes are shown in Tab. I. Thirty fetuses had 37 pathological DIs out of 308 measured.

Two antepartal DIs, one ten days and the other two days before cesarean section of a 29 weeks old fetus predicted correctly its neonatal death at 13 hours' age. Three antepartal DIs at two weeks' intervals and the latest two weeks before cesarean section of another fetus at its 36th week failed to predict its death at two hours' age. The baby had multiple anomalies.

Assessment of the last week's DI as a predictor of fetal distress in labor is presented in Tab. II.

Tab. II. Antepartal differential index (DI) as a predictor of fetal distress in diabetic pregnancies (* = $p < 0.001$)

| Number of fetuses | Failures of analyses | Differential index | Fetal distress yes | Fetal distress no | Sensitivity % | Predictive value % | Specificity % | Relative risk |
|---|---|---|---|---|---|---|---|---|
| 93 | 3 | pathologic | 12 | 6 | 67 | 71 | 92 | 8.5* |
| | | normal | 5 | 67 | | | | |

Antepartal DI detected 12 of the 17 fetuses with fetal distress (sensitivity 67%). Twelve of the 18 fetuses with at least one pathological DI developed fetal distress (predictive value 71%). Sixty-seven of the 73 fetuses without fetal distress had normal DIs (specificity 92%). The risk of fetal distress after a pathological DI was 8.5 times that after a normal DI (relative risk), which is highly significant.

## 4 Discussion

**The present study suggests that antepartal DI is a rather reliable predictor of fetal outcome during diabetic pregnancies.**

Fetal distress developed in 26% of the cases, which is in agreement with previous reports [7]. The most frequent signs of fetal distress were fixed baseline of FHR (32%) and late decelerations (27%), which indicate the role of uteroplacental insufficiency in developing fetal distress of diabetic pregnancies. Fixed baseline of FHR probably indicates a decreased function of autonomous nervous system. Thus this study also supports some previous reports on high frequencies of abnormal FHR patterns during diabetic pregnancies and labors [2, 9, 14, 20]. A new and somewhat astonishing finding of the present study was, that signs of fetal distress were equally frequent in different WHITE'S classes of diabetes.

We have stated previously that false positives are not a problem of antepartal DI in other risk groups. **The present study shows that in diabetic pregnancies the number of false positives is comparable with those in other risk groups** [12, 22]. We have observed that low DIs during diabetic pregnancies are associated with maternal hyperglycemia [11]. Whether episodes of low DIs during diabetic pregnancies are associated with lowered intervillous placental blood flow, as we presume, remains to be investigated. We have observed previously that the failure rate of aFECG is the main problem of antepartal analysis of FHR variability [12, 22]. In the present study the failure rate is of the same magnitude as in the previously studied risk groups. We do not regard the failure rate as a major problem since visual evaluation of cardiograms is continuously improving as FHR analyses are performed by the obstetric staff. The person analyzing can provide an immediate answer as to whether the analyzed strip is normal or abnormal.


### Summary

The clinical significance of quantified short term variability of antepartal fetal heart rate (FHR) in prediction of fetal distress in labor was assessed in 120 insulin-dependent diabetic pregnancies. FHR was recorded by abdominal fetal electrocardiography (aFECG), from which the differential indices (DI) describing the short term variability of FHR were analyzed by a microprocessor-based on-line method. The analysis was successful in 308 of 350 trials (87%). In ten pregnancies, no acceptable a FECG was obtained. Fetal distress developed in 28 of the 110 pregnancies with successful FHR analysis. There were no intrauterine deaths in this series, but two newborn infants died (perinatal mortality 1.7%). Ninety-three pregnancies with FHR analyses within one week of delivery were included in the assessment of the test. **DI predicted 12 of the 17 cases of fetal distress (sensitivity 67%).** Twelve of the 18 cases with a pathological DI developed fetal distress (**predictive value 71%**). DIs were normal in 67 of the 73 pregnancies without fetal distress (**specificity 92%**). Risk of fetal distress after a pathological DI was 8.5 times that after normal DIs (relative risk), which is highly significant.


**Keywords:** Antepartal, diabetes mellitus, electrocardiography, fetal heart, heart rate variability.


### Zusammenfassung

**Kurzfristige Änderungen der fetalen Herzfrequenz bei Schwangerschaften mit insulinpflichtigem Diabetes**

Wir ermittelten die klinische Bedeutung von quantitativ erfaßten kurzfristigen Änderungen der fetalen Herzfrequenz (FHR) für die Prognose eines fetalen Distress-Syndroms unter der Geburt in 120 Schwangerschaften mit insulinpflichtigem Diabetes. Die FHR wurde mittels der abdominal abgeleiteten fetalen Elektrocardiographie (aFECG) aufgezeichnet und daraus die Differentialindices (DI), die die kurzfristigen Änderungen der FHR beschreiben, über ein Mikroprozessor-System mit der On-Line-Methode bestimmt. In 308 von 350 Aufzeichnungen

kamen wir zu verwertbaren Daten. Bei 10 Schwangeren konnte kein brauchbares aFECG abgeleitet werden. Ein fetales Distress-Syndrom entwickelte sich in 28 der insgesamt 110 Fälle mit erfolgreicher FHR-Analyse. In dieser Untersuchungsgruppe gab es keinen Fall von intrauterinem Fruchttod, aber 2 Neugeborene starben (perinatale Sterblichkeit: 1,7%). Bei der Bewertung unserer Methode wurden 93 Schwangerschaften, in denen innerhalb einer Woche vor der Entbindung FHR-Analysen erstellt worden waren, berücksichtigt. **Der DI sagte in 12 von 17 Fällen, in denen ein fetales Distress-Syndrom auftrat, dieses richtig voraus (Empfindlichkeit: 67%).** Ein pathologischer DI wurde in 18 Fällen erhoben; davon entwickelten dann 12 ein fetales Distress-Syndrom (**Prädiktabilität 71%**). Die DI's waren bei 67 der 73 Schwangerschaften ohne fetales Distress-Syndrom als normal eingestuft worden (**Spezifität: 92%**). Wenn ein pathologischer DI vorlag, war das Risiko eines fetalen Distress-Syndroms 8,5 mal höher als nach normalen DI's; dieser Unterschied ist hochsignifikant.

**Schlüsselwörter:** Diabetes mellitus in der Schwangerschaft, Elektrocardiographie, fetale Herzfrequenz, fetale Herzfrequenzänderungen.

**Résumé**

**Instabilité à court terme du rythme cardiaque foetal au cours de la grossesse des diabétiques insulino-dépendantes** La signification clinique de l'instabilité à court terme quantifiée du rythme cardiaque foetal (RCF) pendant la grossesse pour la prédiction de la souffrance foetale en cours de travail a été étudiée chez 120 grossesses de diabétiques insulino-dépendantes. Le RCF a été enregistré par électrocardiographie foetale par voie abdominale (ECGFa), à partir duquel l'indice différentiel (ID) qui représente l'instabilité à court terme du RCF a été analysé au moyen d'un micro-ordinateur fondé sur une méthode linéaire. L'analyse a été couronnée de succès dans 308 enregistrements sur 350 tentatives (87%). ON n'a pas pu obtenir d'ECGFa satisfaisant pour 10 grossesses. Une souffrance foetale est apparue chez 28 des 110 grossesses ayant eu une analyse du RCF couronnée de succès. Il n'y a pas eu de morts foetales in utero dans cette série, mais 2 nouveaux-nés sont décédés (soit une mortalité périnatale de 1,7%). 93 grossesses ayant eu une analyse du RCF au cours de la semaine précédant l'accouchement ont été incluses dans l'évaluation du test. **L'ID a permis la prédiction de 12 des 17 souffrances foetales (sensibilité de 67%).** 12 des 18 cas avec un ID pathologique ont présenté une souffrance foetale (**valeur prédictive: 71%**). L'ID a été normal dans 67 des 73 grossesses sans souffrance foetale (**spécificité: 92%**). Le risque de souffrance foetale après un ID pathologique est 8,5 fois plus élevé qu'après un ID normal (risque relatif) ce qui est hautement significatif.

**Mots-clés:** Antepartum, coeur foetal, diabète sucré, électrocardiographie, instabilité du rythme cardiaque.

**Bibliography**

[1] ARMITAGE, P.: Statistical methods in medical research. Blackwell Scientific Publications, Oxford 1974

[2] AYROMLOOI, J., L. I. MANN, R. R. WEISS, N. A. TEJANI, M. PAYDAR: Modern management of the diabetic pregnancy. Obstet. and Gynec. 49 (1977) 137

[3] BARRETT, J. M., S. L. SALYER, F. H. BOEHM: The nonstress test: An evaluation of 1000 patients. Amer.J.Obstet.Gynec. 141 (1981) 153

[4] FLOOD, B., J. LEE: Fetal death during a negative contraction stress test. Obstet. and Gynec. 52 (1978) 41S

[5] FREEMAN, R. K.: The use of the oxytocin challenge test for antepartum clinical evaluation of uteroplacental respiration function. Amer. J. Obstet. Gynec. 121 (1975) 481

[6] GABBE, S. G., J. H. MESTMAN, R. K. FREEMAN, U. T. GOEBELSMANN, R. I. LOWENSOHN, D. NOCHIMSON, C. CETRULO, E. J. QUILLIGAN: Management and outcome of pregnancy in diabetes mellitus, classes B to R. Amer. J. Obstet. Gynec. 129 (1977) 723

[7] GAROFF, L.: Prediction of fetal outcome by urinary estriol, maternal serum placental lactogen, and alpha-fetoprotein in diabetes and hepatosis of pregnancy. Obstet. and Gynec. 48 (1976) 659

[8] HON, E. H., S. T. LEE: Electronic evaluation of the fetal heart rate VIII. Patterns preceding fetal death, further observations. Amer. J. Obstet. Gynec. 87 (1963) 814

[9] JORGE, C. S., R. ARTAL, R. H. PAUL, U. GOEBELSMANN, J. GRATACOS, S.-Y. YEH, S. H. GOLDE, J. H. MESTMAN: Antepartum fetal surveillance in diabetic pregnant patients. Amer. J. Obstet. Gynec. 141 (1981) 641

[10] KARINIEMI, V., T. KATILA, H. LAINE, P. ÄMMÄLÄ: On-line quantification of fetal heart rate variability. J. Perinat. Med. 8 (1980) 213

[11] KARINIEMI, V., M. FORSS, R. SIEGBERG, P. ÄMMÄLÄ: Reduced short term variability of fetal heart rate in association with maternal hyperglycemia during insulin-dependent diabetic pregnancies. (submitted)

[12] KARINIEMI, V., P. ÄMMÄLÄ: Short-term variability of fetal heart rate during pregnancies with normal and insufficient placental function. Amer. J. Obstet. Gynec. 139 (1981) 33
[13] KEEGAN JR., K. A., R. H. PAUL: Antepartum fetal heart rate testing IV. The nonstress test as a primary approach. Amer. J. Obstet. Gynec. 136 (1980) 75
[14] KITZMILLER, J. L., J. P. CLOHERTY, M. D. YOUNGER, A. TABATABAII, S. B. ROTSCHILD, I. SOSENKO, M. F. EPSTEIN, S. SINGH, R. K. NEFF: Diabetic pregnancy and perinatal morbidity. Amer. J. Obstet. Gynec. 131 (1978) 560
[15] LAUERSEN, N. H., K. H. WILSON, A. BILEK, V. SAN JEEVA RAO, M. KURKULOS: A new modality in nonstress testing: Evaluation of beat-to-beat fetal heart rate variability. Amer. J. Obstet. Gynec. 141 (1981) 521
[16] NYLUND, L., N.-O. LUNELL, R. LEWANDER, B. PERSSON, B. SARBY, S. THORNSTRÖM: Uteroplacental blood flow in diabetic pregnancy: Measurements with indium 113m and a computer-linked gamma camera. Amer. J. Obstet. Gynec. 144 (1982) 298
[17] PEDERSEN, J.: The pregnant diabetic and her newborn. Munksgaard, Copenhagen 1977
[18] WEINGOLD, A. B., M. L. YONEKURA, J. O'KIEFFE: Nonstress testing. Amer. J. Obstet. Gynec. 138 (1980) 195
[19] WHITE, P.: Pregnancy and diabetes. In: A. MARBLE, P. WHITE, R. F. BRADLEY, L. P. KRALL (eds.): Joslins Diabetes mellitus. Lea and Febiger, Philadelphia 1971
[20] WHITTLE, M. J., D. ANDERSON, R. I. LOWENSOHN, J. H. MESTMAN, R. H. PAUL, U. GOEBELSMANN: Estriol in pregnancy VI: Experience with unconjugated plasma estriol assays and antepartum fetal heart rate testing in diabetic pregnancies. Amer. J. Obstet. Gynec. 135 (1979) 764
[21] YEH, S.-Y., A. FORSYTHE, E. H. HON: Quantification of fetal heart rate beat-to beat interval differences. Obstet. and Gynec. 41 (1973) 355
[22] ÄMMÄLÄ, P., V. KARINIEMI: Short-term variability of fetal heart rate in cholestasis of pregnancy. Amer. J. Obstet. Gynec. 141 (1981) 217

Received August 19, 1982. Revised November 16, 1982. Accepted December 27, 1982.

Veikko Kariniemi, M. D.
1st Department of Obstetrics and Gynecology
Helsinki University Central Hospital,
Haartmanink. 2, 00290 Helsinki 29
Finland