FETUS, PREMATURITY

Abstracts 388 – 537

388 Fetal growth: genetic control, variations and environmentally caused interferences

B. R. Elejalde[1], Maria Mercedes De Elejalde[2]
[1]Society for Maternal-Fetal Medicine, Glendale, Wisconsin,
[2]Medical Genetics Institute, S.C., Glendale, Wisconsin

OBJECTIVE: To find and to describe mathematically the genetic principles that control fetal growth and their exceptions.

STUDY DESIGN: Retrospective cohort study of anthropometric data from 38,881 ultrasounds and 52 million births in the USA and of the quantitative effect of independent variables (single gene mutations, chromosomal abnormalities, race, sex, gestational age, maternal weight, placental function, smoking, genetic disease, uterine perfusion, maternal diabetes, and hypertension), on the dependent variables: fetal growth, size and weight.

RESULTS: The following principles were derived and proven: 1. Genetically controlled growth: all the distributions of dependent variables are Gaussian and symmetric. 2. Individuality: a few fetuses had all the measurements at the same centile, most had great variability. 3. Variability of growth patterns: same mother's fetuses with the same or different father had different patterns, birth weights and mean centiles. 4. Constancy of development: Fetal growth is genetically controlled through the cellular cycle, matrix formation and programmed cellular death; the daily rate of growth is constant for each category (centile of growth). 5. Time related growth interference: the effect of race, fetal sex and smoking does not become statistically significant until around 32 weeks. The principles above suffer interferences type: 1. Supply: placental failure of different etiologies, 2. Hormonal: diabetes and other growth factors, 3. Vascular: hypertension, 4. Genetic: single and multiple gene mutations and abnormalities (including chromosomal) that markedly alter the genetically programmed (normal) growth pattern. The results of some of these interferences have recognizable patterns and some are modifiable by medical intervention.

CONCLUSION: The effects of the principles of fetal growth and of the interfering factors are the quantitative bases for clinical analysis of development, age, weight, disease, and for the study of the origin of adult disease in utero.

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389 Fetal tachyarrhythmias: the comparison between cases with or without intrauterine treatment: a retrospective data analysis in Japanese population

Keiko Ueda[1], Tomoaki Ikeda[2], Yasuki Maeno[3], Haruhiko Sagou[4]
[1]Nationalcardiovascular Center, Japan, Priantology, Suita, Osaka, Japan,
[2]Nationalcardiovascular Center, Japan, Perinatology, Suita, Osaka, Japan,
[3]Kurume University, Pediatrics, Fukuoka, Japan, [4]National Center for Child Health and Development, Japan, Perinatology, Tokyo, Japan

OBJECTIVE: Although the Fetal therapy(Ftx) for fetal tachycarrhythmias (FT) is now performed relatively often recently,the management of FT has not been standardized because of limited data on how Ftx affects the clinical course. The aim of this study was 1) to review the efficacy and safety of Ftx using the data on Japanese population and 2) to determine the impact of FTx on the FT natural history.

STUDY DESIGN: Data for 2004 to 2007 on fetuses with sustained FT were obtained from 750 Japanese perinatal care institutes.Cases were classified as supraventricular tachycardia (SVT), atrial flutter, ventrivcular tachycardia and others. Data on fetal diagnosis, the presence of fetal hydrops (FH), associated anomalies and Ftx (the types of antiarrhythmic agents, efficacy and side effects) were collected. Presence of neonatal tachycardia, gestational ages, delivery mode, neonatal management and outcome were also analysed. All cases were categorized into groups with or without Ftx and compared obstetrical and neonatal prognoses.

RESULTS: 82 cases (14 FH) were analyzed. SVT was the most common fetal diagnosis (n=44). Ftx was performed for 41 using various agents-(digoxin, flecainide and sotalol). The data showed high overall efficacy for FT and FT with FH (92.7% and 82.7%). 3 death cases were reported. As shown in thetable, treated cases showed significantly lower incidence of preterm birth , cesarean-section and neonatal tachycardia.

CONCLUSION: Ftx has successfully improved FT, even for the cases with HF. This nation-wide retrospective data analysis confirms that FTx has beneficial effects on the clinical course of FT. The main benefit of Ftx is a reduced incidence of premature birth, cesarean section and neonatal arrhythmias.

Fetal tachycardia with/without fetal therapy(*P<0.05).

	Ftx (%)	non-Ftx (%)
n	41	41
hydrops	11 (26.8)	3 (7.3)
cesarean section	12 (29.3)*	29 (70.7)*
preterm	5 (12.2)*	17 (41.5)*
neonatal tachycardia	20 (48.8)*	32 (78)*
death	1 (2.4)	2 (4.9)

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390 Adverse neonatal effects of magnesium sulfate given to the mother

Mina Abbassi-Ghanavati[1], James A Alexander[1], Donald McIntire[1], Kenneth Leveno[1]
[1]University of Texas Southwestern Medical Center, Dallas, Texas

OBJECTIVE: Given the increasing indications for administration of magnesium sulfate to pregnant women, we sought to determine if such therapy was associated with adverse effects in the newborn infant.

STUDY DESIGN: This is a retrospective cohort analysis of women who received magnesium sulfate for prevention of eclampsia. Magnesium sulfate was given intravenously beginning with a 6 gram loading dose followed by 2-3 gram/hour based on serum magnesium levels. Newborn hypotonia was diagnosed if at birth the infant exhibited less than normal tone/activity unresponsive to naloxone and persistent at admission to the nursery. Maternal serum magnesium levels were measured within four hours of delivery. Women undergoing general anesthesia were excluded.

RESULTS: Between January 2000 and February 2009, 6827 women with preeclampsia were treated with magnesium sulfate as described and 388 (5.7%) infants were diagnosed to have hypotonia. There was a direct relationship between maternal magnesium levels and hypotonia and this persisted after correction for gestational age and umbilical artery pH (Figure 1). A similar adjusted analysis was also performed for intubation in the delivery room and magnesium concentration in maternal blood was significantly associated with intubation.

Figure 1. Probability of neonatal hypotonia in relation to maternal magnesium levels.

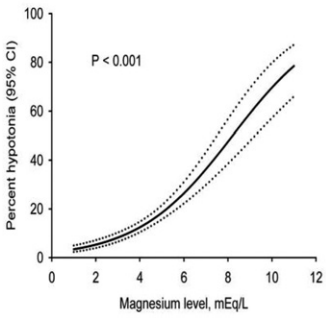
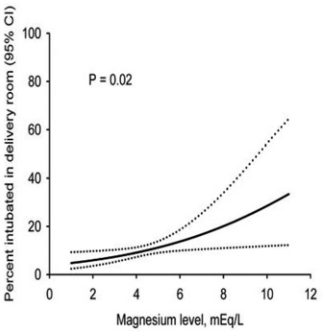


Figure 2. Probability of intubation of the infant in the delivery room in relation to maternal magnesium levels.



CONCLUSION: The concentration of magnesium in maternal blood is directly related to hypotonia in the newborn infant as well as the need for intubation of the infant at birth.

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391 The development of clinically significant hemolytic disease of the fetus and newborn due to anti-C combined with one or more additional red blood cell antibody

Kara Markham[1], Karen Rossi[2], David Krugh[2], Richard Oshaughnessy[2]
[1]Ohio State University, hilliard, Ontario, [2]Ohio State University, Columbus, Ohio

OBJECTIVE: The hemolytic effect of anti-c is felt to closely mirror that of anti-RhD, resulting in the potential development of hemolytic disease of the fetus and newborn (HDFN) in affected pregnancies. As anti-RhD has recently been shown to confer an increased risk of HDFN when combined with other red blood cell antibodies, the purpose of this study was to evaluate for a similar effect with antibody combinations involving anti-c.

STUDY DESIGN: The Ohio State University Medical Center Maternal Alloimmunization Program maintains an IRB-approved, computerized database of all pregnancies complicated by red blood cell alloimmunization. For the purpose of this study, significant HDFN was defined as a requirement for intrauterine transfusion (IUT), birth or cord hemoglobin of <10 g/dL, or the need for neonatal exchange transfusion.

RESULTS: In total, 51 patients were identified as having a combination of anti-c and at least one additional red blood cell antibody. Such pregnancies were approximately four times more likely to develop significant complications of HDFN ($p<0.001$) and twice as likely to require invasive management with IUT ($p=.0445$) when compared to patients with anti-c alone. The most frequently encountered antibody combination was anti-c + anti-E. When each antibody combination was considered separately, only the combination of anti-c + anti-Jka + anti-S showed a statistically significant increased risk of HDFN compared to anti-c alone.

CONCLUSION: The presence of multiple red blood cell antibodies appears to confer an increased risk of clinically significant HDFN in the presence of antibodies to the c antigen. This should be considered when managing pregnancies affected by such antibody combinations.

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392 Clinically significant hemolytic disease of the fetus and newborn due to anti-K combined with one or more additional red blood cell antibody

Kara Markham[1], Rossi Karen[2], Oshaughnessy Richard[3]
[1]Ohio State University, hilliard, Ohio, [2]The Ohio State University, Obstetrics and Gynecology Fetal Therapy Program, Columbus, Ohio, [3]The Ohio State University, Obstetrics and Gynecology, Columbus, Ohio

OBJECTIVE: Alloimmunization to the Kell family of red blood cell antigens is an important cause of morbidity and mortality in obstetrics. The process leading to fetal anemia in such cases is novel in that both hemolysis of existing red blood cells and suppression of ongoing erythropoiesis are proposed to contribute to the development of hemolytic disease of the fetus and newborn (HDFN). The purpose of this study is to outline our experience with pregnancy outcomes in women who have anti-K antibodies in combination with other red blood cell antibodies.

STUDY DESIGN: The Ohio State University Medical Center Maternal Alloimmunization Program maintains an IRB-approved, computerized database of all pregnancies complicated by red blood cell alloimmunization. For the purpose of this study, significant HDFN was defined as a requirement for intrauterine transfusion, birth or cord hemoglobin of <10 g/dL, or the need for neonatal exchange transfusion.

RESULTS: Fifty-eight patients were identified as having a combination of anti-K and at least one additional red blood cell antibody. Pregnancies complicated by alloimmunization to the Kell antigen as well as an additional red blood cell antigen were nearly three times more likely to develop significant HDFN than those affected by anti-K alone ($p=.0451$). While the most frequently encountered antibody combination was anti-K and anti-Fya, the only specific antibody combination associated with a clinically significant increase in the occurrence of HDFN was anti-K + anti-D ($p=.0019$).

CONCLUSION: The presence of multiple red blood cell antibodies appears to increase the occurrence of clinically significant HDFN in the presence of anti-K. Clinicians should have a heightened awareness of the potential for severe disease in such pregnancies and should monitor these patients closely in an effort to improve obstetrical and neonatal outcomes.

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393 Prevalence and progression of recipient twin cardiomyopathy in early stage twin-twin transfusion syndrome (TTTS)

Mounira Habli[1], Erik Michelfelder[1], David Wall[1], William Polzin[1], Foong.Yen Lim[2], David Lewis[3], Timothy Crombleholme[1]
[1]Cincinnati Children's Hospital, Cincinnati, Ohio, [2]Cincinnati Children's Hospital Medical Center, Fetal Care Center, Cincinnati, Ohio, [3]University of Cincinnati, Cincinnati, Ohio

OBJECTIVE: Management of TTTS in early stages (I, II) is controversial. We describe the prevalence, severity, and incidence of progression of recipient twin (RT) cardiomyopathy (CM) in early Quintero Stage I and II TTTS.

STUDY DESIGN: Among 451 TTTS evaluated between 2004-2009, 124 (27%) cases of stages I and II were reviewed. The cases were "upstaged" to Cincinnati IIIA, IIIB, or IIIC if mild, moderate, or severe recipient cardiomyopathy (RTCM) was detected on echocardiography (ECHO), respectively. Progression of RTCM was defined by worsening of cardiomyopathy in subsequent ECHO or failure to respond to amnioreduction (AR). Outcome data included progression of RTCM, treatment, and survival at birth. Data were compared by Chi-square, Fisher's exact, or T- test as appropriate.

RESULTS: There were 77/124 (62%) stage I and 47/124 (38%) stage II cases. 65% (81/124) were upstaged to Cincinnati IIIA (26/81), IIIB (23/81) and IIIC (32/81). Treatment included observation in 11 (9%), AR in 26 (20%), AR followed by laser procedure (SFLP) in 43 (35%), SFLP in 43 (35%), and cord coagulation (RFA) in 1. 43/80 (54%) cases treated by observation or AR initially progressed at a mean of 1.4 ± 1.5 weeks. The incidence of progression increased significantly if RTCM was more advanced initially: 9/27 (33%) Stage I, 8/15 (53%) Stage II, 8/16 (50%) IIIA, 10/10 (100%) IIIB, and 8/12 (67%) IIIC ($p < 0.01$). Overall fetal survival was 82% (174/212) in 106 cases with outcome data.

CONCLUSION: Echocardiography demonstrates a high incidence of RTCM in early stage TTTS. Progression is more likely for RT with more advanced CM.

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