THIRD INTERNATIONAL CONFERENCE ON FETAL GROWTH

1 – 3 October 2014
Keble College, Oxford, UK

www.fetalgrowth.org

Programme and Abstracts

Contents	Page

Key to abstract numbers
Session number (1-11); order within session (1-x);
and type of presentation (K: keynote; S: short communication P: e-poster)

Times allocated for presentations

Keynote	20 minutes, 5 minutes for questions / discussion
Short oral	10 minutes, 2 minutes for questions / discussion
E - Poster	2 minutes, 1 minute for questions / discussion

Social Programme

Wednesday 1 October - **Welcome reception**
6.15 – 8pm with drinks and canapés,
at the Pitt Rivers Museum, South Parks Road, Oxford OX1 3PP

Thursday 2 October – **Gala Dinner**
7:30 for 8pm; Dress: smart-casual
Victorian Gothic Dining Hall, Keble College
NB - entrance by ticket only – please ask at registration desk

GENERAL INFORMATION

Admission to the conference is by badge only.
In the interest of security please make sure that your badge is clearly visible at all times.

Registration Desk, Exhibits, Coffee & Tea: Arco Building
Breakfast (Keble residents) **and Lunches:** Dining Hall

Wifi access at the conference: connect to '**Keble'**; password: **RedBrick2014**
Once on Keble registration website, password: **FG14;** room number (if day delegate): **0000**
Internet in bedrooms via Ethernet cable only (available from Porters lodge); Password: **FG14**

Keble College- OX1 3PG. **Car park:** Keble College Sports Ground, Woodstock Road, OX2 7EJ
For any queries or assistance, please contact **Porters Lodge: 01865 27 27 27**

Taxis: 001 Taxis: 01865 240 000; A1 Taxis: 01865 248 000

Welcome

Dear Delegate,

A warm welcome to the Third International Conference on Fetal Growth!

Once again we were pleased to see the response to this meeting, which confirms the increasing awareness of fetal growth, its central role in maternal and perinatal care, and the need for a dedicated conference focussing on this field.

In devising the programme, we were directed by the number and content of the many quality abstracts received, which fell neatly into the main themes of the sessions over three full days –the longest FG conference yet. The presentations include several 'breaking news' results of international projects. Indeed this is an active and productive time in fetal growth research, and this series of meetings is well poised to track developments.

As before, the oral presentations are balanced by protected time for plenary and open forum discussions, and we would like to encourage your active participation. Please make sure also to complete the feedback form in your conference pack, so that we can continue to improve and make the meeting as relevant as possible for researchers and clinicians from all specialities.

We hope you enjoy FG14!

Jason Gardosi
Professor of Maternal & Perinatal Health
Perinatal Institute, Birmingham, UK

Lesley McCowan
Professor of Obstetrics & Gynaecology
University of Auckland, New Zealand

Francesc Figueras
Professor of Obstetrics & Fetal Medicine
University of Barcelona, Barcelona, Spain

Exhibitors

www.mamaacademy.org.uk

MAMA Academy is a registered charity working alongside The Royal College of Midwives. All information on our mums side of the site has been written by our medical team of health professionals and the midwives side of our site has RCM accreditation. The aim of MAMA Academy is to equip all expectant mums and healthcare professionals with vital knowledge and education to give every baby the best chance of arriving safely and healthily. We want to help mums have healthy pregnancies and support midwives to aid consistency of maternity care right across the UK.

www.alere.com

Alere is the world's leading provider of rapid diagnostic tests. Our women's health products include Triage® PLGF, approved to aid diagnosis of preterm preeclampsia and to risk stratify women for preterm or urgent delivery, Actim® PROM for the detection of premature rupture of membranes, and Actim® Partus for the assessment of the risk of preterm labour. Please meet with representatives of Alere at the booth to learn more.

www.medaphor.com

MedaPhor is a global ultrasound training company, selling the award winning ScanTrainer ultrasound training simulator. The virtual reality simulator combines 'real-feel' haptic simulation with real patient scans and curriculum-based interactive learning, to provide fast and effective 24/7 ultrasound training in a non-clinical environment. ScanTrainer's unique ScanTutor learning software provides a personalized education environment that minimizes both the time required by an expert to teach and the need for a variety of patients to learn on. This makes the ScanTrainer system both resource efficient and highly cost effective. ScanTrainer comes with integrated core skills training modules and a wide range of advanced skills pathology modules and diagnostic case studies for the more experienced practitioner.

www.onatal.nl

Onatal is the first full web-based software for midwives in the Netherlands, developed by Micro Natal. Micro Natal serves over 65% of all midwifery practices and has always been a trendsetter in the development of software for midwives in the Netherlands. Based on this experience and track record, Onatal is developing wider applications of its information system functionality for the international market.

www.patientsknowbest.com

Patients Know Best is the world's first patient-controlled medical records system. It is a fully secure online tool which enables patients to better organise, manage and control their own health care provision – it also saves the time of physicians through allowing secure, online consultations. Founded by Dr. Mohammad Al-Ubaydli, a physician, programmer and expert in IT in healthcare, Patients Know Best has won social enterprise awards for its focus on patient care. Patients Know Best's first customers include Great Ormond Street Hospital, St Marks Hospital and Luton and Dunstable Hospitals NHS Trust. Patients Know Best integrates fully into the NHS secure network and is available for use by any patient with any clinician anywhere in the world. It is now used by over 40 hospitals in the UK, USA, Holland, Ireland, Kuwait, Australia and Hong Kong. Patients Know Best complies fully with UK NHS information governance requirements for dealing with medical data.

Wednesday 1 October

From 08:00	Coffee/Tea	Registration
Session no. & time	**Chairs / Speakers**	**Title of session / presentation**
09:15	Organising Committee	Welcome and Introduction
Session 1	Frank Bloomfield Lesley McCowan	**FETAL GROWTH RESTRICTION AND POSTNATAL DEVELOPMENT**
09:30	Isabelle Monier	1.1 S Probability of live birth after detection of fetal growth restriction between 22 and 27 weeks of gestation (EPIPAGE 2)
09:42	Terri Levine	1.2 S Early childhood neurodevelopment after intrauterine growth restriction: a systematic review
09:54	Edurne Mazarico	1.3 S Neurobehavior in intrauterine growth restricted infants with abnormal uterine artery Doppler
10:06	Karel Marsal	1.4 K Late onset IUGR and postnatal development up to 23 years of age
10:30	Plenary/Open Forum	
10:45	Coffee/Tea	
Session 2	Karel Marsal Jason Gardosi	**FETAL GROWTH RESTRICTION AND PERINATAL OUTCOME**
11:15	Ka Wai Pang	2.1 S Retrospective review of clinical characteristics of women with stillbirth in a large district general hospital: could we make a difference?
11:27	Edel Manning	2.2 S Fetal growth restriction and perinatal mortality in Ireland
11:39	Claire Dougan	2.4 S Prospective audit in a tertiary obstetric unit to determine detection rate of SGA babies and impact on intrapartum outcomes
11:51	Lorraine Ecclestone	2.3 S Standardised case reviews of perinatal deaths: the role of IUGR
12:03	Frank Bloomfield	2.5 K Neonatal hypoglycaemia: diagnosis, prevention, management and consequences
12:30	Plenary/Open Forum	
12:45 - 13:45	Lunch	
13:15	Sicco Scherjon Frank Bloomfield	**E- Poster Presentations** - see page 8
Session 3	Aris Papageorgiou Francesc Figueras	**MODELS AND STANDARDS OF FETAL GROWTH I**
13:45	Katherine Grantz	3.1 S Longitudinal changes in maternal weight gain and intrauterine fetal growth
13:57	Louise Simcox	3.2 S The role of 2D and 3D ultrasound parameters in the prediction of third trimester growth trajectories and final birthweight
14:09	Caroline Knight	3.3 S Fetal fat index (FFI): reference ranges for fetal thigh fat
14:21	John Kingdom	3.4 S Sonographic weight estimation of small for gestational age fetuses: is the optimal model related to fetal body proportion?
14:33	Gerry Visser	3.5 K Human fetal growth is constrained below optimal for perinatal survival
15:00	Plenary/Open Forum	
15:30	Coffee/Tea	
Session 4	Christoph Lees Francesc Figueras	**MODELS AND STANDARDS OF FETAL GROWTH II**
16:00	Aris Papageorghiou	4.1 K Intergrowth-21st: international standards for fetal growth and newborn size
16:25	Graham Parry	4.2 S Ethnic differences in fetal biometry in a healthy maternity population
16:37	Lucia Vaira	4.3 S Fetal growth assessment: a global perspective based on cloud computing
16:49	Linda Van Wyk	4.4 S Customised growth curves vs population based curves for the prediction of intra uterine growth restriction at term: A secondary analysis of the DIGITAT study
17:01	Jason Gardosi	4.5 K The role of customised assessment in defining optimal growth
17:25	Plenary/Open Forum	
18:00	Close	
18:15 - 20:00		**WELCOME RECEPTION**

Thursday 2 October

08:00	Coffee/Tea	Registration
Session no. & time	**Chairs / Speakers**	**Title of session / presentation**
Session 5	Neil Sebire, John Kingdom	**THE PLACENTA AND IUGR**
08:30	Neil Sebire	5.1 K Placental pathology of early and late IUGR: findings, variants, methodologies
08:55	Noelyn Anne Hung	5.2 S Immunohistochemical detection of hpv L1 capsid protein in villous sycytiotrophoblast knots is associated with premature labour and FGR
09:07	Anne Sørensen	5.3 S Placental function in FGR – a correlation between placental bold MRI, placental histopathology and fetal outcome
09:19	John Kingdom	5.4 S Birth weight customization improves the association between SGA and placental pathology in nulliparous women
09:31	Lucy Higgins	5.5 S Identifying the placental phenotype of adverse pregnancy outcome: potential novel biomarkers of the at-risk pregnancy
09:43	Fengxiu Ouyang	5.6 S Pre-pregnancy BMI, gestational weight gain and gestational diabetes in relation to childhood obesity in offspring: the mediation effect of placental weight
09:55	Samantha Benton	5.7 S Low maternal PIGF is associated with histological evidence of placental dysfunction in pregnancies with suspected intrauterine growth restriction
10:12	Plenary/Open Forum	
10:30	Coffee/Tea	
Session 6	Lucy Chappell, Lesley McCowan	**SCREENING AND SURVEILLANCE I**
11:00	Anguita Burgos	6.1 S How useful is uterine artery Doppler flow velocimetry in the prediction of IUGR
11:12	Laura Howe	6.2 S Are two scans better than one? Predicting SGA from scan data at 20 and 24 weeks gestation
11:24	Folasade Akhanoba	6.3 S Prevalence of small for gestational age and preterm delivery in low PAPP-A pregnancies
11:36	Francesc Figueras	6.4 S The role of angiogenic factors for first trimester screening of fetal growth restriction
11:48	Lesley McCowan	6.5 S Second trimester prediction of SGA- findings from the SCOPE study.
12:00	Andrew Sharp	6.6 S PIGF bedside testing in standard clinical care: 6 months experience from a large teaching hospital
12:12	Lucy Chappell	6.7 K Third trimester biomarkers for prediction of small for gestational age infants: the PELICAN studies
12:30	Plenary/Open Forum	
12:45 - 13:45	Lunch	
13:15	Karel Marsal, Neil Sebire	**E- Poster Presentations** - see page 8
Session 7	Francesc Figueras, Jason Gardosi	**SCREENING AND SURVEILLANCE II**
13:45	Anguita Burgos	7.1 S Value of the 32-34 week ultrasound in the diagnosis of growth restricted fetuses born at term
13:57	Suseela Vavilala	7.2 S Effectiveness of policy of routine ultrasound scans in 3rd trimester in the detection of SGA in India
14:09	Francesc Figueras	7.3 S Routine 3rd trimester ultrasound at 32 vs 36 weeks in the detection of FGR: randomized trial
14:21	Michelle Southam	7.4 S Effectiveness of different scan policies in detection of SGA birthweight in high risk pregnancies
14:33	Stefania Triunfo	7.5 S Routine versus contingent third trimester screening for late fetal growth restriction
14:45	Asma Khalil	7.6 S Changes in fetal Doppler indices as a marker of failure to reach growth potential at term
15:00	Plenary/Open Forum	
15:30	Coffee/Tea	
Session 8	Carol Paeglis, Sally Giddings	**IMPLEMENTING ANTENATAL GROWTH ASSESSMENT PROGRAMMES**
16:00	Jason Gardosi	8.1 S Impact of improved antenatal recognition of IUGR on stillbirth rates in England
16:10	Sally Giddings	8.2 S The Growth Assessment Protocol and its national roll-out in the UK
16:25	Carol Paeglis	8.3 S The role of supervision and competency assessment in improving fetal growth surveillance
16:35	Alison Brodrick	8.4 S Implementing GROW in a tertiary referral unit
16:45	Kristel Zeeman	8.5 S Successes and pitfalls of implementing GROW in the Netherlands
16:55	Lesley McCowan	8.6 S The New Zealand Experience
17:00	Plenary/Open Forum	
		STRESS, RELAXATION AND FETAL GROWTH
17:30	Emma Austin	8.7 S The impact of depression, anxiety and stress on fetal growth
17:45	Birgit Arabin	8.8 K Early music programs: an option to support neurodevelopment in healthy and growth retarded babies from pre- to postnatal life?
18:00	Close	
19:30 for 20:00		**GALA DINNER**

Friday 3 October

08:00	Coffee/Tea	Registration
Session no. & time	**Chairs / Speakers**	**Title of session / presentation**
Session 9	Gerry Visser Lesley McCowan	**MANAGEMENT OF EARLY AND LATE IUGR**
08:30	Karel Marsal	9.1 K Management and follow-up of early onset IUGR fetuses
08:50	Ann David	9.2 S Ethics and social acceptability of gene therapy for severe early onset FGR (EVERREST)
09:00	Christoph Lees	9.3 K Results of the Truffle Trial
09:20	Francesc Figueras	9.4 K Management of late onset IUGR
09:40	Sicco Scherjon	9.5 K Further insights from the DIGITAT trial & follow-up
10:00	Plenary/Open Forum	
10:30	Coffee/Tea	
Session 10	Lucy Chappell Francesc Figueras	**PROTOCOLS, AUDIT AND RESEARCH**
11:00	Lesley McCowan	10.1 K Overview of national protocols for assessment and management of IUGR
11:25	Fergal Malone	10.2 K Perinatal Ireland: protocol development and implementation
11:45	Jason Gardosi	10.3 S Cost benefit analysis of RCOG guidelines for investigation and management of the SGA fetus
12:00	Faculty Plenary,	- Protocols and practicalities for fetal growth surveillance and management
	Roundtable &	- Priorities in audit and research for reducing adverse outcome
	Open Forum	- Summary of good practice points
12:45 - 13:45	Lunch	
13:15	Birgit Arabin, Christoph Lees	**E- Poster Presentations** - see page 8
Session 11	Dharminthra Pasupathy Jason Gardosi	**MACROSOMIA**
13:45	Dharminthra Pasupathy	11.1 K Macrosomia - definition, management and outcome
14:05	David Bailey	11.2 S Obstetric outcomes at term in pregnancies with large for gestational age babies
14:17	Mandy Williams	11.3 S Obesity, fetal growth and pregnancy outcome
14:29	Matias Vieria	11.4 S Risk factors for neonatal morbidity in LGA infants
14:41	Tracy Tomlinson	11.5 S Clinical prediction of fetal overgrowth in pregnancies complicated by diabetes
14:53	A Nawathe	11.6 S Insulin growth factors and their binding protein expression in pregnancies affected by diabetes and obesity
15:05	Plenary/Open Forum	
Session 12		**BEST ABSTRACTS**
15:30		Oral presentation of best posters
15:45		Prizes for best oral communication and poster
16:00	**Close; Coffee/Tea**	

E-Poster presentations

Date and Time	Presenter	No. and title of abstract
Wednesday 1 October **13:15-13:45**	Carolyn Drews-Botsch Graham K Parry Anna Caetono Renuka Sekar Kate Morse Andrew Sharp Ramos Ruiz García Solbas	1.1 P Measurement of early childhood obesity in children born SGA vs AGA 1.2 P The Contribution of soft issue to birthweight 1.3 P Assessment of Intracranial structure volumes in foetuses with growth restriction by means of three-dimensional ultrasound using the extended imaging virtual organ computer-aided analysis method. 1.4 P An Audit following implementation of customised growth charts in a tertiary unit 1.5 P Audit: the essential link to evaluation of customised growth charts in clinical practice. 1.6 P Antenatal detection of small for gestational age before and after introduction of customised growth charts: experience of a large teaching hospital. 1.7 P Diagnosis of fetal growth restriction on twin pregnancies, using different fetal growth standardised formulas 1.8 P Incidence of fetal growth restriction in preterm and term pregnancies
Thursday 2 October **13:15-13:45**	Bill Clow Natalie Hung Noelyn Hung Tamas Marton Ana Zamarian Sinding M Annabel Dieh Carolina Freire	2.1 P Amnion disruption sequence: a new perspective on the pathological mechanism. 2.2 P The immunohistochemical detection of HPV L1 Capsid protein in the placenta and maternal cervical smear history. 2.3 P Histopathology of treated chronic histiocytic intervillositis. 2.4 P Normal values of brain- thymus weight ratio in non-IUGR perinatal deaths. 2.5 P Evaluation of angiogenic factors combined with Doppler parameters in healthy controls and fetal growth restriction 2.6 P Placental T2* in normal pregnancy and in two cases of fetal growth restriction. 2.7 P The impact of screening for the Small-for-dates fetus using low maternal pregnancy associated plasma Protein-A2. 2.8 P Relationship between nucleated red blood cell counts and obstetric and neonatal outcomes in SGA fetuses with normal umbilical artery Doppler.
Friday 3 October **13:15-13:45**	Rebecca Spencer Stefan Savchev Bottino Guerrero Ramos Ruiz A Nawathe Martínez Alonso Burgos Anguita Bottino Guerrero	3.1 P Developing a therapy for severe early onset fetal growth restriction: the challenges of designing a multinational phase I/IIA clinical trial protocol. 3.2 P An integrated model with classification criteria to differentiate late onset fetal growth restriction vs. small for gestational age 3.3 P Does second trimester uterine artery Doppler screening modify perinatal outcomes? 3.4 P Emergency caesarean delivery performed because of a non-reassuring fetal heart rate, on a term pregnancy with a not diagnosed growth restricted fetus 3.5 P Differential placental expression of insulin like growth factors and their binding proteins in pregnancies affected by growth disorders. 3.6 P Intrauterine growth restriction or small-for-gestational-age fetus diagnosis in twin pregnancy depending on whether it is the first or second twin. 3.7 P Route of delivery in growth restricted fetuses born at term. 3.8 P Obstetric complications and adverse perinatal outcomes correlated with uterine artery Doppler assessment during the second trimester of pregnancy.

Oral presentations (K=keynote; S=short communication)

1.1 S PROBABILITY OF LIVE BIRTH AFTER DETECTION OF FETAL GROWTH RESTRICTION BETWEEN 22 AND 27 WEEKS OF GESTATION: A POPULATION STUDY IN FRANCE

Isabelle Monier and Jennifer Zeitlin
for the EPIPAGE 2 Study Group

Objective: To investigate the probability of very preterm live birth after early antenatal detection of fetal growth restriction (FGR).
Method: Data come from the EPIPAGE 2 study, a population-based prospective study of very preterm births in France in 2011. We included all singleton fetuses without severe congenital anomalies born between 22 and 31 weeks of gestation age (GA). We identified those detected with FGR between 22 and 27 weeks of GA, based on ultrasound measurements. We studied three outcomes: termination of pregnancy (TOP), stillbirth and live birth. Percentages and means were weighted to account for a 2 month longer recruitment period for births 22 to 26 weeks GA (8 versus 6 months).
Results: Out of 3329 singletons born between 22 and 31 weeks of GA, 11.4% were detected antenatally with FGR between 22 and 27 weeks of GA. In 8% of these cases, a TOP was carried out, 21% were fetal deaths and 71% were live born. The probability of live birth was 51%, 49%, 53% and 67% when detection occurred at 22, 23, 24 and 25 weeks of GA respectively versus 94% and 92% at 26 and 27 weeks. 94% of live births were by prelabor caesarean. Survival after live birth was 83% if detection occurred between 22 and 25 weeks of GA (mean GA at birth=26.9 (0.2)) and 80% between 26 and 27 weeks (mean GA at birth=27.9 (0.1)). However, survival was 43% versus 75% respectively if terminations and fetal deaths were considered.
Conclusion: There is a threshold-effect associated with the probability of live birth and survival after early detection of FGR at 26 weeks GA in France.

1.2 S EARLY CHILDHOOD NEURODEVELOPMENT AFTER INTRAUTERINE GROWTH RESTRICTION: A SYSTEMATIC REVIEW

Terri Levine; Ruth Grunau; Fionnuala McAuliffe; RagaMallika Pinnamaneni; Adrienne Foran; Fiona Alderdice
Queen's University Belfast, School of Nursing and Midwifery; Perinatal Ireland

Objective: Children who experienced intrauterine growth restriction may be at increased risk for adverse developmental outcomes in early childhood. Our objective was to carry out a systematic review of early childhood neurodevelopmental outcomes up to three years following intrauterine growth restriction.
Method: PubMed, Embase, PsycINFO, Maternity and Infant Care, and CINAHL databases were searched using the search terms intrauterine; fetal; growth restriction; child development; neurodevelopment; early childhood; cognitive; motor; speech; language. Studies were determined to be ineligible if participants did not meet specified criteria for growth restriction, follow-up was not within the range of 0-3 years, methodology was inadequately described, non-IUGR comparison groups were not included, or full English text of the article was not available. A specifically designed data extraction form was used. The methodological quality of included studies was assessed using well-documented quality-appraisal guidelines.
Results: Of 731 studies reviewed, 16 were included. Poorer neurodevelopmental outcomes following intrauterine growth restriction were described in 11. Ten found motor, 8 cognitive, and 7 language delay. Other delays included social development, attention, and adaptive behaviour. Eight used fetal or birth weight or abdominal circumference to define IUGR; 8 required abnormal Doppler parameters.
Conclusions: The 16 studies reviewed here indicate that IUGR often results in neurodevelopmental delay. However, IUGR itself is inconsistently defined across studies and often conflated with SGA. Due in part to inconsistent differentiation between IUGR, SGA, and extremely low birth weight infants, findings differ significantly across studies. Further follow-up studies would be helpful to expand existing knowledge of the effects of IUGR on neurodevelopment in early childhood, but also important is an increased standardisation of definitions, study designs, and outcome measures. Moreover, there is a great need for additional neuroimaging data and the development of interventions designed to improve neurodevelopmental outcomes in children who have experienced intrauterine growth restriction.

1.3 S NEUROBEHAVIOR IN INTRAUTERINE GROWTH RESTRICTED INFANTS WITH ABNORMAL UTERINE ARTERIES DOPPLER

Edurne Mazarico, Stefan Savchev, MD Gómez Roig, Eduard Gratacós, Francesc Figueras
Barcelona Center for Maternal-Fetal and Neonatal Medicine, Barcelona, SPAIN

Objective: To evaluate the neurobehavioral outcomes of intrauterine growth restricted (IUGR) newborns with abnormal uterine arteries Doppler.
Methods: A cohort of consecutive intrauterine growth restricted newborns with abnormal uterine arteries Doppler ultrasound finding was created and compared with a group of infants with size appropiate for gestational age, who were sampled from our general neonatal population. Neonatal behavior was evaluated at corrected age of 40 +/- 1 weeks with Neonatal Behavioral Assessment Scale (NBAS), which assesses both cortical and subcortical functions by evaluationg 35 items. Items are grouped into 6 clusters: habituation, motor, social-interactive, organization of state, regulation of state and autonomic nervous system. The social-interactive cluster was subscored for visual and auditory stimuli. In addition, an aggregation of individual items (alertness, quality of the alert responsiveness, and cost of attention) wasused to evaluate the capacity of infant attention.
Results: A total of 110 newborns (55 IUGR and 55 appropiate for gestational age) were included. Among all the neurobehavioral areas studied, IUGR were poorer in motor, social-interactive (visual and auditory), organization of state, autonomic nervous system and attention, with significance for social-interactive (visual and auditory), organization of state and attention. The average mean differences in scores between the study groups were 0,83 (95% confidence interval: 0,39-1,26) for social-interactive, 0,93 (95% confidence interval: 0,45-1,41) for visual social-interactive, 0,68 (95% confidence interval: 0,29-1,07) for auditory social-interactive, 0,38 (95% confidence interval: 0,078-0,68) for organization of state and 0,68 (95% confidence interval: 0,17-1,12) for attention.
Conclusion: IUGR newborns with abnormal uterine arteries Doppler had poorer neurobehavioral competencies, which suggests delayed neurologic maturation.

1.4 K LATE ONSET IUGR AND POSTNATAL DEVELOPMENT UP TO 23 YEARS OF AGE

Maršál K, Brodszki J, Tideman E, Ley D
Department of Clinical Sciences Lund, Lund University, Lund, Sweden

Objective: To investigate the postnatal cardiovascular, cognitive and neurological development of growth restricted fetuses.
Method: The background population of 138 fetuses diagnosed as SGA after 32 gestational weeks was examined at 7 years, and a subcohort of 21 SGA fetuses with ARED-flow in descending aorta (IUGR-cases) at 18 and 23 years; the results were compared to controls. The children/adolescents were submitted to clinical neurological and ophthalmological examinations, psychological tests, digital analysis of the ocular fundus photographs, and to a number of non-invasive examination methods based on ultrasound, laser Doppler or magnetic resonance imaging.
Results: In comparison with controls, at 7 years of age, the IUGR infants had normal blood pressure, normal aortic stiffness, but increased pulse pressure (1). They showed minor neurological dysfunction and impaired intellectual performance (2,3). At 18 years, the IUGR individuals had normal blood pressure, increased heart rate at rest, decreased number of retinal vessel branching points, smaller diameter of large vessels (abdominal aorta, popliteal artery), and higher flow mediated dilatation of brachial artery (4,5). The performance and total IQ were lower, the nerve optic area was reduced and the rate of abnormal perimeter was increased (6-8). At 23 years, echocardiography showed a smaller diameter of ascending aorta with otherwise normal findings. The aortic augmentation index was higher, but there were no changes in the diameter, intima-media thickness or distensibility of carotid artery (9). MRI of the brain showed an increased rate of white matter abnormalities.
Conclusions: The late-onset IUGR (SGA with severe intrauterine blood flow changes) is in the postnatal life associated with impaired vessel growth and vascular dysfunction, as well as with suboptimal cognitive development and minor neurological deficiencies.

References: 1. Ley et al., Acta Paediatr 1997;86:299. 2. Ley et al., UOG 1996;8:160. 3. Ley et al., UOG 1996;8:166. 4. Brodszki et al. Circulation 2005;111:2623. 5. Hellström et al. Pediatrics 2004;113:e77. 6. Tideman et al. UOG 2009;29:614. 7. Ley et al. Ped Res 2004;56:139. 8. Martin et al. J Ped Ophthalmol Strab 2004;41:212. 9. Bjarnegård et al. UOG 2013;41:177.

2.1 S RETROSPECTIVE REVIEW OF CLINICAL CHARACTERISTICS OF WOMEN WITH STILLBIRTH IN A LARGE DISTRICT GENERAL HOSPITAL: COULD WE MAKE A DIFFERENCE?

Ka Wai Pang, Victoria Steel, Jane Ramsay
Ayrshire Maternity Unit, Crosshouse Hospital, Kilmarnock

Objective: National statistics fail to address small for gestational age (SGA) in the classification of causes of stillbirth. In many cases SGA is not detected prior to loss. In 2012, stillbirth rates in our unit were higher than national averages. In an attempt to demonstrate opportunities for improvement in the face of financial challenges, a review of two years of data was performed to establish if predictable or preventable features could be identified.
Method: All stillbirths identified in 2011 and 2012 were subjected to rigorous review applying RCOG guideline 31 'Investigation and Management of SGA Fetus'. The prevalence of risk factors and compliance with appropriate care bundle was documented. Birth weight centile was recorded and recalculated using individual customised data.
Results: Using the risk assessment (RA) tool, 66.7% of stillbirths were identified as being at high-risk for SGA and 58.3% of them actually had SGA (<10th centile). Amongst this group, 66.7% had extra surveillance scans, 16.7% had no scans and 16.6% had intra-uterine death (IUD) <26 weeks. Nearly half of the group receiving ultrasound surveillance did not have the sufficient frequency of scans and of this group a third had failure to diagnose SGA associated with stillbirth. One third of those with SGA related stillbirth had no surveillance scan and 71.4% of this group had severe SGA and fetal death in the 3rd trimester. Despite this no suspicion of SGA had been raised from clinical assessment. Diagnosis of SGA increased from 44.4% to 55.6% when using customised birth weight centile calculator and severe SGA increased from 13.9% to 36.1%.
Conclusions: SGA is common amongst stillbirths and has a higher diagnostic rate when using customised birth weight centiles. By using a RA tool and complying with care bundles including not only serial ultrasound surveillance but also robust clinical assessment, greater than one third of stillbirths from the high-risk group could potentially have been saved.

2.2 S FETAL GROWTH RESTRICTION (FGR) AND PERINATAL MORTALITY IN IRELAND

Edel Manning, Paul Corcoran, Richard A Greene on behalf of the Perinatal Mortality Group
National Perinatal Epidemiology Centre, Department of Obstetrics & Gynaecology, University College Cork, Ireland

Objective: We established a national clinical audit on perinatal deaths to better identify causes of death, associated risk factors and the evidence of intrauterine growth restriction (IUGR) among perinatal deaths in Ireland.
Method: Following a pilot study, the national audit was initiated and all 20 Irish maternity units have provided anonymised data on perinatal deaths since 2011. Customised birthweight centiles were calculated for all perinatal deaths in 2011 and 2012 using the Gestational Related Optimal Weight (GROW) software.
Results: A total of 976 perinatal deaths were reported for 2011 (n=491) and 2012 (n=485). Stillbirths (SB), early neonatal (ENND) and late neonatal deaths accounted for 622 (63.7%), 279 (28.6%) and 75 (7.7%) of the 976 deaths, respectively. The common causes of death in SB were congenital anomaly (25.9%) and placental conditions (20.1%) with IUGR attributed to 3.7% of cases. ENNDs were generally due to congenital anomaly (49.8%) or respiratory disorder (31.9%) - primarily severe pulmonary immaturity. Low birthweight was common, especially for SBs. Just over 40% of SBs (41.4%) were below the 3rd customised birthweight centile and over half (53.4%) were below the 10th customised birthweight centile compared to 27.8% and 39.9% of the cases of ENND, respectively. Birthweight centiles were significantly lower in perinatal deaths attributed to major congenital anomaly (Table 1). Considering the 256 perinatal deaths unrelated to major congenital anomaly, it was reported that a diagnosis of IUGR was made for one third of the cases below the 10th customised birthweight centile (n=86, 33.6%).
Conclusions: Fetal growth restriction is highly prevalent in cases of perinatal deaths in Ireland and for the majority a diagnosis of IUGR was not made antenatally. The use of customised centile growth charts should be considered. This would impact on antenatal detection of IUGR and a reduction in perinatal deaths.

Table 1: Distribution of customised birthweight centiles of perinatal deaths due and not due to major congenital anomaly, 2011-2012

Centile	Stillbirth (N=607)		Early neonatal death (N=273)	
	Cause of death: major congenital anomaly		Cause of death: major congenital anomaly	
	Yes (n=158)	No (n=449)	Yes (n=137)	No (n=136)
Zero	82(51.9%)	106(23.6%)	45(32.8%)	12(8.8%)
< 3rd	98(62.0%)	157(35.0%)	59(43.1%)	18(13.2%)
< 10th	107(67.7%)	220(49.0%)	75(54.7%)	36(26.5%)
10-49th	27(17.1%)	148(33.0%)	35(25.5%)	64(47.1%)
50-89th	13(8.2%)	62(13.8%)	16(11.7%)	30(22.1%)
90th+	11(7.0%)	19(4.2%)	11(8.0%)	6(4.4%)

Note: Centiles could not be calculated for 15 stillbirths and six early neonatal deaths

2.3 S STANDARDISED CASE REVIEWS OF PERINATAL DEATH: THE ROLE OF IUGR

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Background Confidential enquiries of adverse perinatal outcomes have identified an urgent need to improve unit based case reviews to establish the causes of perinatal deaths.
Method SCOR (standardised clinical outcome review) is a software programme developed to improve the identification of substandard care factors and learning points at unit level. The application is completed by the risk manager on behalf of a multi-disciplinary review team. It facilitates assessment of management in each stage of perinatal care, identifies a taxonomy of issues and prompts auditable action plans.
Results The majority of perinatal deaths had foregoing fetal growth restriction (FGR). The application was able to establish the root cause through a series of prompts. Examples included 1. inappropriate assessment and recognition of FGR risk at the beginning of pregnancy; 2. fundal height measurements not done or not plotted accurately; 3. lack of referral for scan when indicated; 4. in high risk pregnancy, no or insufficient scans; 5. failure to implement appropriate investigations e.g. Doppler; 6. plotting on wrong chart; 7. protocol violation / inappropriate action in management; 8. intrapartum surveillance inappropriate for fetus' risk status; 9. failure to expedite delivery; 10. delay in neonatal resuscitation due to lack of awareness.
Conclusion A structured approach results in better identification of substandard care factors and has contributed to the understanding of upstream causes and implementation of action plans to enhance learning and prevention

2.4 S PROSPECTIVE AUDIT OF ANTENATAL PATIENTS IN A TERIATRY OBSTETRIC UNIT TO DETERMINE DETECTION RATE OF SMALL FOR GESTATIONAL AGE BABIES AND THE IMPACT THIS HAS ON INTRAPARTUM OUTCOMES

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Using ReCoDe, 43% of UK stillbirths are attributed to intrauterine growth restriction (IUGR).[1] Gardosi et al. found with *customised* growth charts, a Small for Gestational Age (SGA) fetus, defined as <10th centile, is associated with poor neonatal outcomes and is synonymous with IUGR.[2] RCOG guidelines stratify antenatal care regarding SGA.[3]
Objectives: Using RCOG Guideline 31, our objectives were:

- Ascertain whether patients have accurate management for SGA risks at booking appointment.
- Determine percentage of SGA babies born and if SGA was diagnosed antenatally.
- Identify intrapartum outcomes in the SGA group versus matched controls.

Methods: A 50 day, prospective data collection in a tertiary hospital. 840 charts included, 815 located.

- Reviewed charts for evidence that fetal surveillance was undertaken where SGA risk factors existed.
- Ascertained whether SGA birth weights were detected antenatally using customised charts.
- Reviewed evidence of pathological CTGs, expidited delivery and neonatal unit admission in 155 SGA cases and 155 controls matched for risk of SGA.

Results:

- In SGA group, slight increase in pathological CTG's (42vs27) and delivery due to presumed fetal distress. (35vs27)
- 31% of SGA babies with pathological CTG's were admitted to the neonatal unit compared to 11% of control cases.

Conclusions: Correct SGA risk management increases detection of SGA. Even in correctly managed women, detection rate was only 54% and remains a challenge. Education and reconfiguration of booking service is advised. Although SGA babies showed worse immediate outcomes, long-term outcomes couldn't be determined by this study. Further work establishing whether this guideline will reduce the number of undiagnosed SGA infants with poor neonatal outcomes is required.

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2.5 K NEONATAL HYPOGLYCAEMIA: DIAGNOSIS, PREVENTION, MANAGEMENT AND CONSEQUENCES

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Hypoglycaemia is a common and well-recognised neonatal complication of fetal growth restriction. The consequences of severe hypoglycaemia are well recognised, but there are few robust data to help guide practice around which babies should be monitored for hypoglycaemia, how these babies should be defined, what the consequences of mild and moderate hypoglycaemia are for long-term outcomes and, therefore, what the best management or preventative approaches are.

This presentation will discuss these issues and, while data may not be available to provide definitive answers at this time, on-going studies should provide valuable data within the next 12 months or so and should also identify the next questions that need to be answered to address this very important topic.

3.1 S LONGITUDINAL CHANGES IN MATERNAL WEIGHT GAIN AND INTRAUTERINE FETAL GROWTH

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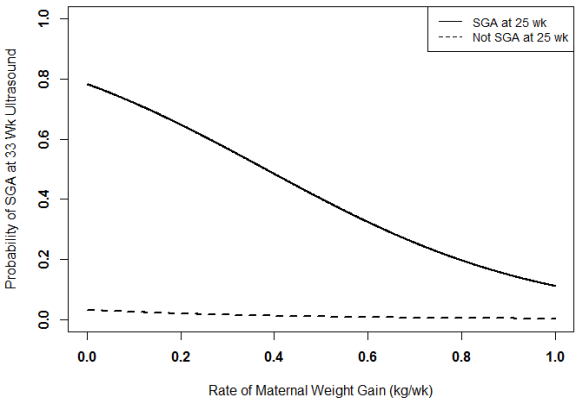
Objective: Total pregnancy weight gain is associated with infant birthweight; however, few have examined associations between longitudinal changes in maternal weight and changes in fetal anthropometrics.
Method: In a prospective cohort of 1,763 Scandinavian singleton pregnancies with longitudinal maternal weight (median=12) and ultrasound measurements (17, 25, 33, and 37 weeks), we first estimated trajectories across gestation of maternal weight and fetal biometrics [abdominal circumference (AC, mm), biparietal diameter (BPD, mm), femur length (FL, mm), and calculated estimated fetal weight (EFW, grams)] using linear mixed (random effects) models. We estimated the association between maternal weight changes (per 5kg) and corresponding fetal growth from 0-17, 17-28, and 28-37 weeks adjusting for prepregnancy body mass index, height, age, parity, chronic diseases, and smoking. We estimated the probability of fetal small-for-gestational-age (SGA) at the 33 week ultrasound across the spectrum of maternal weight gain rate by SGA status at 25 weeks.
Results: For every 5 kg increase in maternal weight, FL increased 0.35mm (95%CI 0.24-0.46), 0.33mm (95%CI 0.22-0.44), and 0.10mm (95%CI 0.02-0.18) for 0-17, 17-28 and 28-37 weeks, respectively; BPD increased early (0.79mm; 95%CI 0.48-1.10 and mid-pregnancy (0.46mm; 95%CI 0.29-0.62) only; and associations with fetal AC (4.11mm; 95%CI 3.24-4.99) and EFW (94.6g; 95%CI 73.7-115.6) peaked mid-pregnancy. If a normal weight woman with SGA at 25 weeks gained according to the 2009 Institute of Medicine's recommended rate of 0.42 kg/week her probability of SGA at the 33 week visit was 46.7% versus 60.4% with weight gain of 0.26 kg/week (10th percentile of sample). (Figure)
Conclusion: Maternal weight gain early in pregnancy was most associated with growth in FL and BPD while changes later in pregnancy had a stronger association with AC and EFW. Among women with fetal SGA detected in the second trimester, higher weight gain was associated with decreased probability of persistent SGA.

Figure. Probability of Small-for-Gestational-Age (SGA) at 33 wk Ultrasound



3.2 S THE ROLE OF 2D AND 3D ULTRASOUND PARAMETERS IN THE PREDICTION OF THIRD TRIMESTER GROWTH TRAJECTORIES AND FINAL BIRTHWEIGHT

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Objectives: New Ultrasound Parameters in Pregnancy (NUPs) is a prospective longitudinal study of fetal growth using 2D and 3D ultrasound measurements and individualised growth assessment (IGA) to predict final birthweight. The primary aim of the project is to enable earlier detection of late-onset fetal growth restriction (FGR), which if undetected remains one of the primary causes of unexplained stillbirth.
Methods: 73 low risk women were recruited at St. Mary's Hospital, Manchester following informed consent (LREC:10/H1013/9). Measurements of 2D and 3D fetal size parameters, as well as fetal Doppler measurements were obtained at scan intervals of 6-8 weeks from 14 weeks gestation until 36 weeks gestation. Automated volume measurements were obtained using 4Dview software (GE Healthcare). Individualised growth assessment (IGA) using the IGAP software (http://iGAP.research.bcm.edu) was used to predict third trimester growth trajectories and birthweight. Additionally, multiple linear regression analysis was used to identify predictors of birthweight at different scan intervals.
Results: Rossavik growth models using an Estimated Fetal Weight (EFW) formula that includes biparietal diameter (BPD), Abdominal Circumference (AC) and fractional thigh volume (TVol) predicted third trimester growth with a systematic error of -0.48 ± 7.7%. Relatively early pathological deviations were seen for TVol in 2 fetuses with FGR, both of which had normal abdominal circumference measurements at the time of the scan. Multiple linear regression analysis of birthweight demonstrated TVol to be a significant predictor when measured at 28 and 36 weeks (see table). 2D ultrasound parameters become less predictive of birthweight in the late 3rd Trimester.
Conclusion: Ultrasound measurements that include fetal soft tissue estimation such as TVol appear to be more sensitive predictors of final birth weight. IGA and TVol should be prospectively evaluated in a high risk obstetric population to assess if earlier detection of late onset FGR can be achieved.

Measure	Coefficient	t-ratio	p
Ultrasound 26-28 weeks (n=73)			
Total Thigh Volume (cm³)	0.414	2.8	0.008
Fractional Thigh Volume (cm³)	0.540	3.5	0.001
Head Volume (cm³)	0.565	1.8	0.129
Thigh Circumference (cm)	0.227	1.4	0.161
BPD (mm)	0.520	3.5	0.001
Head Circumference (mm)	0.370	2.2	0.029
Abdominal Circumference (mm)	0.534	3.7	<0.001
Femur Length (mm)	0.598	3.8	<0.001
EFW (Hadlock) (grams)	0.729	4.7	<0.001
Ultrasound 34-36 weeks (n=15)			
Total Thigh Volume (cm³)	0.709	2.1	0.062
Fractional Thigh Volume (cm³)	0.734	3.9	0.002
Head Volume (cm³)	0.232	0.6	0.585
	0.496	2.0	0.064
BPD (mm)	0.337	1.3	0.216
Head Circumference (mm)	0.468	1.8	0.099
Abdominal Circumference (mm)	0.749	3.9	0.002
Femur Length (mm)	0.303	1.1	0.313
EFW (Hadlock) (grams)	0.776	4.1	0.001
EFW (BPDACTvol) (grams)	0.860	5.8	<0.001
EFW (IGA Predicted – BPDACTvol) (grams)	1.262	2.7	0.021

Results adjusted for Age at Ultrasound Assessment
Table – Multiple Linear Regression Analysis of Different Ultrasound Parameters to predict final birthweight

3.3 S FETAL FAT INDEX (FFI): REFERENCE RANGES FOR FETAL THIGH FAT

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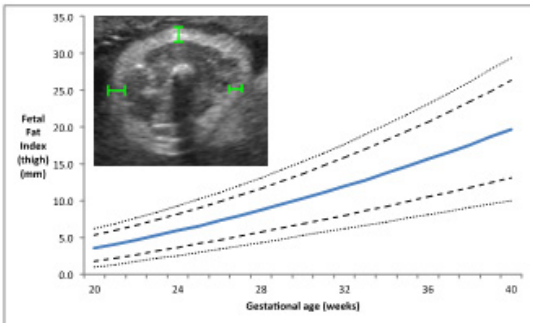
Objective: The Fetal Fat Index (FFI) is a quick, simple, multiple-sample method of fat thickness. Previous work with fetal arm measurements showed that FFI was more representative than single-sampling and correlated well with fat area and volume. Our aims with this study were to use the technique in fetal thigh images and volumes, and produce reference ranges for future research.
Method: Axial mid-femoral volumes from 20-40 weeks' gestation were acquired in optimally healthy pregnant women from Oxford, UK (INTERGROWTH-21st study). A specifically-designed MATLAB tool (based on Lee et al's 50% fractional limb volume) enabled fat volume assessment. Lean volume (muscle and bone) was subtracted from limb volume to give fat volume. The central, perpendicular 2D slice was extracted and fat depth measured at 9, 12 and 3 o'clock positions (6 o'clock position was obscured by femoral acoustic shadow). The measurements were added to give the thigh FFI value. Fat volume and FFI were compared using Pearson's correlation coefficient. FFI 3rd, 10th, 50th, 90th and 97th centiles were calculated using polynomial regression.



Results: 458 scans were measured from 214 women. There was a positive correlation between fetal thigh fat volume and FFI (r=0.86), suggesting FFI's potential as a quicker, 2D-based surrogate for fat volume. The mean difference in fat depth was 1.4mm (range 0.1-10.1mm). FFI reference ranges were 50th centile 3.5mm at 20 weeks to 19.7mm at 40 weeks.
Conclusions: FFI is a quick, simple method of fetal thigh fat assessment in the second and third trimesters and correlates well with 3D fetal thigh fat volume measurements. Reference ranges have been calculated from a healthy population to aid future research with this technique.

3.4 S SONOGRAPHIC WEIGHT ESTIMATION OF SMALL FOR GESTATIONAL AGE FETUSES: IS THE OPTIMAL MODEL RELATED TO FETAL BODY PROPORTION?

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Background: Most sonographic models for fetal weight estimation (EFW) do not perform as well in SGA fetuses, possibly due to to differences in the relative proportions and composition of the various fetal body parts between SGA and normally grown fetuses.
Objective: To perform a systematic comparison the accuracy of different sonographic models for fetal weight estimation among several subgroups of SGA fetuses.
Methods: We compared the accuracy of 33 different models using a cohort of 305 SGA fetuses who sonographic EFW within 7 days of delivery. Models were ranked based on the multiple measures of predictive accuracy within the overall SGA group as well as within specific subgroups of SGA fetuses based on fetal body proportion (small AC, short FL, small HC, symmetrically small fetuses), Doppler studies, and gestational age. Cluster analysis was used to identify homogenous subgroups of models based on the systematic and random errors.
Results: 1) There was a wide variation in the accuracy of the different models (systematic error -11.6% - 15.7%, random error 7.7% - 15.7%). 2) In the overall SGA group, the most accurate model was the SGA-specific model by Scott et al (AC- FL- HC), followed by models of Hadlock (AC-FL-BPD-HC, AC-FL-BPD, AC-FL-HC), Woo (AC-BPD) and Warsof (AC-BPD). 3) The optimal model for weight estimation varied with fetal body proportions, presence of Doppler abnormalities, and early vs. late SGA. 4) Overall, the model of Hadlock (AC-FL-BPD-HC) had the best performance across all subgroups of SGA fetuses, followed by the models of Hadlock (AC-FL-HC, AC-FL-BPD and AC-FL), and the SGA-specific models of Scott (AC- FL-HC) and Sabbagha (AC-FL-HC and GA).
Conclusion: The optimal sonographic model for EDW among SGA fetuses may need to be tailored to the characteristics of the specific SGA fetus including its body proportions, Doppler abnormalities and early vs. late SGA.

3.5 K HUMAN FETAL GROWTH IS CONSTRAINED BELOW OPTIMAL FOR PERINATAL SURVIVAL

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Background: Use of fetal growth charts assumes that optimal size at birth is at the 50th centile. The interaction between maternal constraint and risks associated with size at birth may indicate that this assumption is not valid for perinatal mortality.
Methods: Data of over 1 million births between 28 and 43 weeks gestation from singleton pregnancies without congenital abnormalities in the period from 2002 to 2008 were collected from the Netherlands Perinatal Registry. Distribution of perinatal mortality according to birth weight centile and gestational age was studied.
Results: There were 5075 (0.43%) perinatal deaths. Highest mortality occurred in infants with a birth weight below the 2.3rd centile (25.4/1.000 births) and the lowest mortality with birth weights between the 80th and 84th centile (2.4/1.000 births) of routinely used growth charts. Antenatal deaths were lowest with birth weights between the 90th and 95th centile. Data were almost identical when analysis was restricted to infants born ≥ 37 weeks.
Conclusion: From an immediate survival perspective, optimal fetal growth requires a birth weight between the 80th – 84th centiles for the population. Median birth weight in the population is by definition substantially lower, implying that the majority of fetuses exhibit some form of maternal constraint of growth. This finding is consistent with adaptations evolved in humans in conjunction with large head size and bipedalism, to reduce risk of obstructed delivery. These data also fit remarkably well with those on long-term adult cardiovascular and metabolic health risks, which is lowest in case of a birth weight around the 90th centile.

4.1 K INTERGROWTH-21ST: INTERNATIONAL STANDARDS FOR FETAL GROWTH AND NEWBORN SIZE

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Background: In 2006, WHO produced international growth standards for infants and children up to age 5 years on the basis of recommendations from a WHO expert committee. Using the same methods and conceptual approach, the Fetal Growth Longitudinal Study (FGLS), part of the INTERGROWTH-21st Project, aimed to develop international growth and size standards for fetuses.

Methods: The multicentre, population-based FGLS assessed fetal growth in geographically defined urban populations in eight countries, in which most of the health and nutritional needs of mothers were met and adequate antenatal care was provided. We used ultrasound to take fetal anthropometric measurements prospectively from 14 weeks and 0 days of gestation until birth in a cohort of women with adequate health and nutritional status who were at low risk of intrauterine growth restriction. All women had a reliable estimate of gestational age confirmed by ultrasound measurement of fetal crown–rump length in the first trimester. The five primary ultrasound measures of fetal growth—head circumference, biparietal diameter, occipitofrontal diameter, abdominal circumference,and femur length—were obtained every 5 weeks (within 1 week either side) from 14 to 42 weeks of gestation. The best fitting curves for the five measures were selected using second-degree fractional polynomials and further modelled in a multilevel framework to account for the longitudinal design of the study.

Findings: We screened 13 108 women commencing antenatal care at less than 14 weeks and 0 days of gestation, of whom 4607 (35%) were eligible. 4321 (94%) eligible women had pregnancies without major complications and delivered live singletons without congenital malformations (the analysis population). We documented very low maternal and perinatal mortality and morbidity, confirming that the participants were at low risk of adverse outcomes. For each of the five fetal growth measures, the mean differences between the observed and smoothed centiles for the 3rd, 50th, and 97th centiles, respectively, were small: 2·25 mm (SD 3·0), 0·02 mm (3·0), and –2·69 mm (3·2) for head circumference; 0·83 mm (0·9), –0·05 mm (0·8), and –0·84 mm (1·0) for biparietal diameter; 0·63 mm (1·2), 0·04 mm (1·1), and –1·05 mm (1·3) for occipitofrontal diameter; 2·99 mm (3·1), 0·25 mm (3·2), and –4·22 mm (3·7) for abdominal circumference; and 0·62 mm (0·8), 0·03 mm (0·8), and –0·65 mm (0·8) for femur length. We calculated the 3rd, 5th 10th, 50th, 90th, 95th and 97th centile curves according to gestational age for these ultrasound measures, representing the international standards for fetal growth.

Interpretation: We recommend these international fetal growth standards for the clinical interpretation of routinely taken ultrasound measurements and for comparisons across populations.

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4.2 S ETHNIC DIFFERENCES IN FETAL BIOMETRY IN A HEALTHY MATERNITY POPULATION

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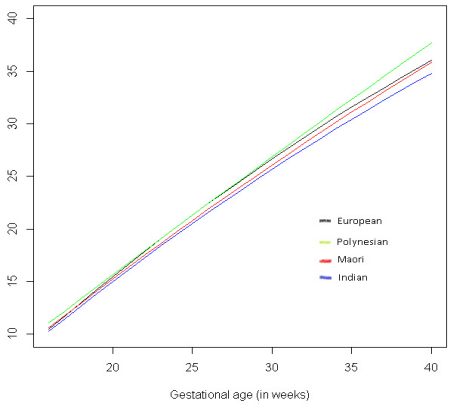
Ultrasound biometry charts in common use have been developed using data predominantly from European pregnant women. In New Zealand there are significant differences in birthweight between babies born to mothers from different ethnic backgrounds. The aim was to evaluate serial biometry in fetuses from different maternal ethnic groups, using standard and novel ultrasound measurements, in normal pregnancies. We hypothesised that fetal growth would be characterised by different patterns of skeletal and soft tissue biometry in different ethnic groups.

Methods: This longitudinal observational ultrasound study recruited healthy pregnant women with BMI in the normal range by ethnic specific criteria from 4 ethnic groups: European (NZE), Māori, Pacific Island or Indian. Each participant was scanned at 4 weekly intervals from 16 to18 weeks until delivery. Ultrasound measurements were: biparietal diameter (BPD), head circumference (HC), humeral diaphyseal length (HDL), abdominal circumference (AC) and femur length (FL). 3D ultrasound measurements were: thigh circumference (ThighC), partial thigh volume (ThighV), arm circumference (ArmC) and partial arm volume (ArmV). Statistical analysis included multilevel linear mixed effects modelling, which accounts for correlation of longitudinal measurements.



Results: 121 participants were recruited. Maternal characteristics were similar, between ethnic groups except for weight.. There were significant differences in skeletal growth parameters – BPD, HC and HDL (table1). Fetal soft tissue measurements showed different growth velocity by ethnicity from the early third trimester. After adjustment for height and weight ethnicity had an independent effect on BPD, HC, HDL, AC, ArmV,ThighC and ThighV.

Soft tissue biometry	
Abdominal circumference	p = 0.000118
Arm circumference	p = 0.0589
Thigh circumference	p = 0.0589
Skeletal biometry	
Head circumference	p = 0.0384
Humeral length	p = 0.0025
Femoral length	p = 0.1328

Conclusions: In a cohort of healthy pregnant women with normal ethnic BMI we have demonstrated significant differences in ultrasound soft tissue biometry measurements which begin in the early third trimester. Consideration should be given to developing ethnic specific ultrasound charts for the New Zealand population.

4.3S FETAL GROWTH ASSESSMENT: A GLOBAL PERSPECTIVE BASED ON CLOUD COMPUTING

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Objective: Twenty years since their definition [1], customised fetal growth charts represent a mature and well-established alternative to "literature-based" growth curves. The increasing acceptance of this best practice suggests for a new and ambitious perspective: the creation of a single virtual database able to embrace the world production of fetal growth data. The clinical comprehension of this large amount of data is extremely challenging because of the underlying idea to finally grab a total comprehension of the phenomenon.

Methods: To collect and analyse all possible and available data about fetal growth poses two main methodological issues: the analysis approach and the technologies that should be used to collect, store and process data.

The first theme is related to the fact that analysing the whole collection of growth data is deeply different from analysing small subsets of local data [2]. A global database asks for new clinical approaches, new ideas and new models to distil the knowledge, which is embedded in data. To face the technology challenge, cloud computing, big data analytics and ubiquitous computing approaches are the natural candidates.

Results: A prototype has been designed and developed in order to validate the effectiveness of the proposed approach, including a new method, based on multidimensional analysis, in order to develop customised and flexible intrauterine growth curves. A first test on the field, performed on local scale, is discussed to prove the feasibility of the overall idea [3].

Conclusions: Starting from a massive amount of ultrasound-based biometric fetal measures, authors propose a system to collect, process and share fetal growth data on global scale and to give customised growth curves to support personalised diagnosis. We feel that the availability of such a global online service can foster a deeper and grounded knowledge of fetal-growth related phenomena.

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[3] Bochicchio M.A., Vaira L., Longo A., Malvasi A., Tinelli A."Multidimensional Analysis of Fetal Growth Curves". BigData In: Bioinformatics & Health Care Informatics (BBH 2013)

4.4 S CUSTOMISED GROWTH CURVES VS POPULATION BASED CURVES FOR THE PREDICTION OF INTRA UTERINE GROWTH RESTRICTION AT TERM: A SECONDARY ANALYSIS OR THE DIGITAT STUDY

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Objective: To assess the effect of the use of customised growth curves versus the standard population based curves in the prediction of intra-uterine growth restriction at term and adverse outcome.
Method: In the DIGITAT trial (Disproportionate Intra Uterine Growth Restriction Trial at Term) (n=1116), pregnant women between 36+0 and 41+0 weeks' gestation who had a singleton foetus in cephalic presentation with suspected intrauterine growth restriction based on population based curves were included. The birth weight and estimated fetal weight were plotted in both curves (population and customised) and the number of children below the 10th and 2.3rd centile were compared. We also compared adverse neonatal outcome and adverse outcome at two years of age between these curves.
Results: Customised growth curves detect significantly more foetus with a birth weight below the 10th and below the 2.3rd centile. 75% of children had a birth weight below the 10th centile according to population based curves compared to 86% of children when using customised curves (p<0.001). 24% had a birth weight <p2.3 according to the population based curves vs 55% when using customised curves (p=0.001). There were no difference in adverse neonatal outcome directly after birth or adverse outcome at 2 years of age between the children that had a birth weight below the 10th centile according to the population based curves vs customised growth curves.
Conclusion: When using the customised growth curves a larger percentage of children are identified as IUGR. However, neonatal outcome and outcome at two years of age does not differ between children identified as IUGR according to the customised curves or population based curves.

4.5 K THE ROLE OF CUSTOMISED ASSESSMENT IN DEFINING OPTIMAL GROWTH

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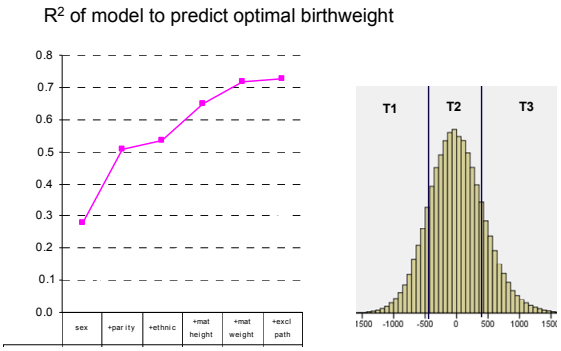
The concept of the individually customised growth potential has enhanced our understanding of the importance of intrauterine growth restriction and its effects on pregnancy outcome. Measurement using a gestation related optimal weight (GROW) standard improves the distinction between constitutional and pathological smallness.



Comparisons with conventional birthweight and fetal weight standards have shown that the prediction of optimal birthweight varies according to the number of variables adjusted for, from R^2 of 0.28 with adjustment for sex only, to 0.72 when also maternal height, weight, parity and ethnic origin are included. Customised SGA within subgroups of maternal size correlates closely to perinatal mortality, in contrast to when SGA is defined by a population based standard. This also applies to ethnic minority groups. When measured by a population average EFW standard such as Hadlock, third trimester fetal weights in South Asian mothers in the UK include an excess of 56% of cases which are categorised as 'SGA' but have the same risk of perinatal mortality as that of the non SGA population. Significant variation in birthweight between ethnic groups exist after excluding pathological factors and social deprivation. Recent work has defined coefficients for customising birthweight standards in 18 countries, as well as for babies from mixed relationships in a British multi-ethnic population.

5.1 K PLACENTAL PATHOLOGY OF EARLY AND LATE IUGR: FINDINGS, VARIANTS AND METHODOLOGIES

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Several patterns of placental pathology associated with fetal intrauterine growth restriction (FGR) and small for gestational age (SGA), with and without abnormal Doppler ultrasound assessment and maternal serum markers, have now been described. These include changes typically associated with uteroplacental vascular disease with secondary villous effects, such as decidual atherosis and placental infarction, and a range of other histological lesions such as villitis, distal villous immaturity, massive perivillous fibrin deposition and others. In general, severe early onset IUGR is associated with more 'typical' uteroplacental findings, whereas later onset IUGR is associated with less marked placental histological abnormalities and greater frequency of other lesions.

Although current data allow determination of associations between placental histological lesional patterns and outcomes such as IUGR, interpretation of the significance of lesions sometimes remains difficult in an individual case, and methodological problems hamper our understanding. With the introduction of more detailed clinical phenotyping in conjunction with development of novel 'discovery-based' methods of investigation it is hoped that pathophysiological pathways can become more clearly defined

5.2S IMMUNOHISTOCHEMICAL DETECTION OF HPV L1 CAPSID PROTEIN IN VILLOUS SYCYTIOTROPHOBLAST KNOTS IS ASSOCIATED WITH PREMATURE LABOUR AND FGR

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Department of Pathology, University of Otago Dunedin School of Medicine, New Zealand.

Objective: To examine the histopathological features of placentae positive for the immunohistochemical detection of HPV L1 capsid protein.
Methods: A cross sectional study of 120 singleton placentae collected for the Otago Placenta Study from 2009 to 2014, comprised 36 pre-term cases, 38 idiopathic fetal growth restriction cases (FGR, ≤5th personalised growth centile (PGC), as determined by the Gestation Network Calculator for NZ), 33 normal term pregnancies >10th PGC, and 12 stillbirths for which no cause was found. Known maternal and/or fetal medical conditions were excluded. A transmural placental section was subject to HPV L1 IHC (clone K1H8,Dako, Glostrup, Denmark) which is expressed among low risk and high risk HPV types. Descriptive and univariate association analysis for relative risk were determined.
Results: Sixty four percent (77/120) of cases were positive for HPV in the placenta using L1 HPV IHC. Two histopathological patterns of positivity were identified, namely, type 1 (comprising 81%) decidua positive, and type 2 (comprising 19%) villous syncytiotrophoblast knots positive. Type 1 and HPV negative cases had similar FGR rates at 25%, however, in the type 2 cases 84% had FGR. The relative risk of FGR in the type 2 HPV L1 positive cases compared to HPV L1 negative cases was 3.31 (95% CI 1.88, 5.80, p<0.001), Premature labour occurred in 21% of negative cases, 30% of type 1 cases and 62% of type 2 cases. The relative risk of premature labour compared to the negative cases was 2.94 (95% CI-1.42, 6.07, p=0.004).
Conclusion: These results suggest HPV infection (as detected by positive HPV L1 capsid protein IHC in villous trophoblast knots) of the placenta is associated with pregnancy complications. Multivariate analyses adjusting for confounding variables are progressing in a larger cohort.

5.3 S PLACENTAL FUNCTION IN FGR – A CORRELATION BETWEEN PLACENTAL BOLD MRI, PLACENTAL HISTOPATHOLOGY AND FETAL OUTCOME.

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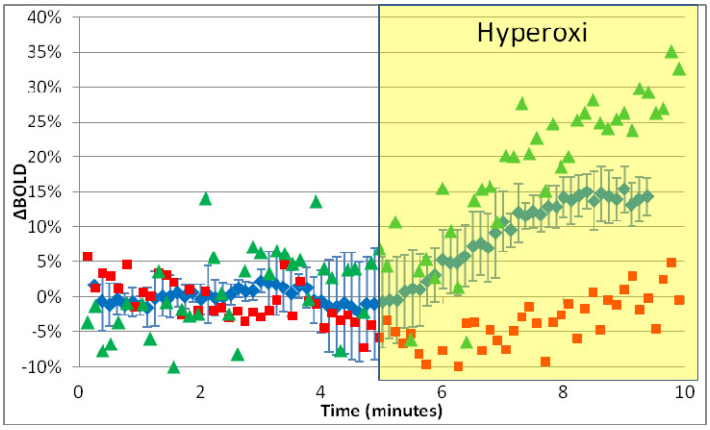
Objective: The hyperoxic placental BOLD response reflects the placental oxygen transport in normal pregnancy. In two cases of fetal growth restriction (FGR) the placental BOLD response was estimated and correlated with fetal outcome and post partum histopathological placental findings.
In both cases fetal wellbeing was estimated by Doppler flow examination of umbilical and fetal blood flow.
Case 1: Week 30 + 3. Fetal weight 956g (-43%). Brainsparing,normal ductus venosus bloodflow.
Case 2: Week 24 + 5. Fetal weight 361g (-51%). Brainsparing and abnormal ductus venosus bloodflow. Oligohydramnious and reduced fetal movements. Normal controls (n=8)
Method: Dynamic T2* weighted placental BOLD MRI (TE=50, TR=8000, Flip: 90°) was performed. Maternal hyperoxia was induced by using a facial mask, and the hyperoxic placental BOLD response was estimated. Placental histopathological examination was performed postpartum.
Results (Figure 1): Case 1 (Green), Case 2 (Red), Normal controls (Blue).
Case 1: Placental BOLD response above normal Case 2: No increase in placental BOLD signal



Outcome: Case 1: Acute cesarean section because of non-reassuring fetal heart rate pattern. The neonate had an uneventful admission to neonatal unit, and development at one year is normal.
Case 2: No intervention was performed because of the very poor prognosis and the fetus died in uterus in week 25. The histopathological examination demonstrated hyperaccelerated maturation in both cases. In Case 2 extensive placental infarcts and intervillous fibrin deposition was found.
Conclusion: Case 1 demonstrated a strong placental BOLD response suggesting a good placental oxygen transport following this case had a good outcome. In contrast, Case 2 demonstrated no hyperoxic increase in placental BOLD signal suggesting a very poor placental oxygen transport, and this case had an adverse outcome. The BOLD findings were supported by the histopatological examination of placenta postpartum. In FGR pregnancy, placental BOLD MRI has the potential to become a non-invasive test of placental function, and thereby a predictor of fetal outcome.

5.4 S BIRTH WEIGHT CUSTOMIZATION IMPROVES THE ASSOCIATION BETWEEN SGA AND PLACENTAL PATHOLOGY IN NULLIPAROUS WOMEN

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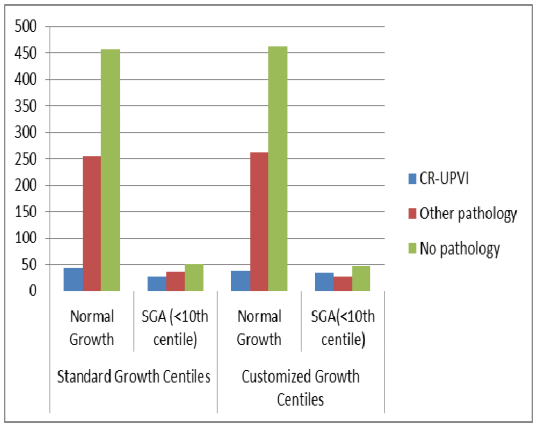
Objective: To determine the utility of customized growth centiles to improve the relationship between small for gestational age (SGA) and the types of placental pathology (small, infarcted) considered causal in IUGR.



Methods: A prospective cohort study was conducted in 1100 healthy nulliparous women, of which 866 had placental pathology at delivery. SGA infants (<10th centile for gestational age) were identified based on standard Canadian growth charts customized only by fetal sex. Extended customization using the Gardosi method, taking into account maternal features (ethnicity, weight and height), and fetal factors (gestational age at delivery and sex) was performed. Placental pathology examinations were performed blinded to clinical outcomes by a perinatal pathologist. Placental pathology was grouped into one of three categories: 1) chorion regression and/or uteroplacental vascular insufficiency (CR-UPVI), 2) other pathology (including chronic maternal inflammation, severe chorioamnionitis, hemorrhagic pathology, fetal vascular disease, chorangiosis, distal villous immaturity, or massive perivillous fibrinoid deposition) and 3) no pathology (includes mild chorioamnionitis).

Results: Of 866 women, 13% were SGA at delivery by standard growth charts, compared to 12% by customized growth charts. 59% of placentas were normal, 8% had CR-UPVI and 33% had other pathology. Figure 1 shows the distribution of placental pathology by standard and customized growth. The proportion of SGA infants with CR-UPVI pathology at delivery (PPV) increased from 35% to 42% by customization. The rates of other pathology did not differ between SGA (31%) and normal pregnancies (34%).

Conclusions: Customization of birth weight centiles strengthens the relationship between apparently causal pathology and SGA in healthy nulliparous women. Though this cohort demonstrated a surprisingly high rate of other pathologies, when combined into one category they showed no relationship with impaired fetal growth.

Funding: AFP Innovation Grant, UHN/MSH University of Toronto

5.5 S IDENTIFYING THE PLACENTAL PHENOTYPE OF ADVERSE PREGNANCY OUTCOME: POTENTIAL NOVEL BIOMARKERS OF THE AT-RISK PREGNANCY

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Objective: Identification of the at-risk fetus is a key challenge in maternity care. Present biomarkers do not detect adverse pregnancy outcome (APO) with high efficiency. We hypothesised that a distinct placental phenotype is identifiable in pregnancies with adverse pregnancy outcome (APO) compared with normal outcome (NPO) and aimed to identify novel placental biomarkers of APO.

Method: Placentas were obtained from pregnancies complicated by reduced fetal movements (RFM) after 28 weeks gestation. APO was defined as stillbirth, individualised birth weight centile <10, umbilical artery pH <7.10/base excess <-10.0 or neonatal intensive care admission. Placentas were examined for biometry, villous vascularity (CD31 immunostaining), chorionic plate arterial function (thromboxane sensitivity, U46619 EC_{50}; nitric oxide sensitivity, SNP EC_{50}; vessel compliance, Tau; peak active tension (PAT) generation) and endocrine function (measurement of human chorionic gonadotrophin (hCG), human placental lactogen (hPL), progesterone, placental growth factor (PlGF) and sFlt in tissue lysate and explant conditioned media (ECM) by ELISA). Comparison was performed by Mann-Whitney U test with statistical significance $p < 0.05$.

Results: 82 placentas were studied (19 (23.2%) from APO pregnancies). Compared with NPO pregnancies, APO pregnancy placentas were smaller (Length: 19.7 v. 21.9cm, p =0.0005. Width: 15.9 v. 18.9cm, p <0.0001. Volume: 364 v. 502cm^3, p <0.0001), less vascular (1042 v. 1315 vessels/mm^2, p =0.002). Some aspects of vascular and endocrine function were altered in APO (SNP EC_{50}: 30.4 v. 12.0nM, p =0.02. Lysate hCG: 19.9 v. 60.2mIU/mg, p =0.0, ECM sFlt 27794 v. 1707pg, p =0.02). Other placental measures including depth, U46619 EC_{50}, Tau, PAT and other lysate/ECM hormone concentrations were not significantly different between groups (p>0.05).

Conclusions: A placental phenotype of APO can be identified *ex vivo* in RFM pregnancies. If these placental biomarkers can be measured accurately *in vivo*, they may aid prediction of APO in this and other high-risk populations.

5.6 S PREPREGNANCY BMI, GESTATIONAL WEIGHT GAIN AND GESTATIONAL DIABETES IN RELATION TO CHILDHOOD OBESITY IN OFFSPRING: THE MEDIATION EFFECT OF PLACENTAL WEIGHT

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Objective: High prepregnancy body mass index (BMI), excessive gestational weight gain (GWG), and gestational diabetes (GDM) are associated with the risk of childhood obesity. The extent to which these effects may be mediated through the placenta is unknown. This study aimed to examine the extent to which placental weight mediates the effects of prepregnancy BMI, GWG, and GDM on childhood obesity.
Method: We used data from the Collaborative Perinatal Project (CPP) for 33893 mothers and their singleton infants delivered in 1959-1965, totaling 154,590 postnatal weight and recumbent length or height measures for offspring at around 4, 8, and 12 months, and 3, 4, and 7 years of age. We performed sequential generalized estimating equation (GEE)-linear models excluding and including placental weight to evaluate its mediation effect.
Results: 5196 (15.3%) and 2153 (6.4%) of mothers were overweight and obese, respectively; 5875 (17.3%) had excessive GWG, and 350 (1%) had diagnosed GDM. From infancy through 7 years of age, 11103 (7.2%) children were obese. After adjustment for maternal age, education, race, smoking during pregnancy, parity, preterm status, and child's age and sex, childhood BMI was 0.06 (95% CI, 0.06- 0.07) kg/m^2 higher for each kg/m^2 increment in maternal prepregnancy BMI. Inclusion of placental weight in model attenuated the association by 17%, to 0.05. Similarly, adding placental weight in models attenuated the associations with childhood BMI (kg/m^2) for GWG (100 gram/week) (β=0.12, 95% CI: 0.11- 0.13) by 25%, and for GDM (β=0.23, 95% CI: 0.05- 0.40) by 52%. Highest versus lowest quintile of placental weight was associated with 1.46-fold (95%CI 1.33-1.60) higher odds of childhood obesity with adjustment for confounders and infant weight status.
Conclusions: Placental weight partly mediates the effects of prepregnancy BMI, excessive GWG and GDM on childhood BMI. High placental weight is a predictor of infancy/childhood obesity.

5.7 S LOW MATERNAL PLGF IS ASSOCIATED WITH HISTOLOGICAL EVIDENCE OF PLACENTAL DYSFUNCTION IN PREGNANCIES WITH SUSPECTED INTRAUTERINE GROWTH RESTRICTION

Samantha J Benton[1], Lesley McCowan[2], Julien Yockell-Leveire[3], Laura Magee[1], Yuxiang Hu[1], David Grynspan[3], (the late) Andrée Gruslin[3], Peter von Dadelszen[1]
University of British Columbia, Canada[1,] University of Auckland, New Zealand[2,] University of Ottawa, Canada[3]

Objective: We sought to investigate if low maternal placental growth factor (PlGF) antenatally identified histological lesions of placental dysfunction in pregnancies with suspected intrauterine growth restriction (IUGR).
Method: Blood samples were collected from a cohort of women with singleton pregnancies at the time of an EFW or AC <10th percentile for gestational age (GA) on ultrasound between 20-40 weeks. PlGF was quantified on the Triage® PlGF assay (Alere). Women were grouped based on PlGF concentration at sampling (<5th or ≥5th percentile for GA based on cut-offs derived from uncomplicated pregnancies). The outcome of interest was a placental pathology grading of ≥2 for lesions of maternal malperfusion, villous maldevelopment, non-infectious villitis, perivillous fibrin deposition, interplacental hematoma and placental weight. Each lesion was graded from 0-3 (absent-severe) by an experienced pathologist, blinded to pregnancy outcome and PlGF levels, based on Redline's scheme (Redline 2004). A 2x2 contingency table was used to calculate the relative risk for the placental outcome by PlGF <5th or ≥5th percentile at sampling. Sensitivity and specificity were calculated with 95% CIs.
Results: Of the 73 women recruited, 29 (40%) women had a PlGF <5th percentile for GA at the time of sampling. Of these, 20 (69%) had the placental outcome. 44 (60%) women had PlGF ≥5th percentile at sampling and one of these women (2%) had had the placental outcome (Relative risk= 30.3, 95% CI: 4.3, 214.0, *P*<0.0001). A PlGF <5th percentile (positive test) identified the placental outcome with 95% [76, 100] sensitivity and 83% [70, 92] specificity (Table 1: Performance of a positive PlGF test to identify the placental outcome.)

Sensitivity [95% CI]	Specificity [95% CI]	PPV [95% CI]	NPV [95% CI]	+LR [95% CI]	-LR [95% CI]
95 [76, 100]	83 [70, 92]	69 [49, 85]	98 [88, 100]	5.5 [3.0, 10.0]	0.06 [0.009, 0.4]

Conclusion: PlGF may provide an additional method to antenatally identify placental dysfunction in pregnancies with suspected IUGR.

6.1 S HOW USEFUL IS UTERINE ARTERY DOPPLER FLOW VELOCIMETRY IN THE PREDICTION OF INTRAUTERINE GROWTH RESTRICTION

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Objective: The aim of the study was to evaluate if growth restricted fetuses born at term had elevated uterine artery mean pulsatility index measured at 20 week ultrasound examination.
Methods: deliveries at term (> 37 weeks) attended in our hospital during the last fifteen months were reviewed and those newborns with a birth weight less than 2500 gr were selected. The outcome measures studied were: uterine artery mean pulsatility index (PI) measured at 20 weeks, sonographic fetal weight estimated at 32-34 weeks ultrasound, birth weight and its percentile according to Figueras formula (EJOGRM 2008).
Results: 34'7% of growth restricted fetuses born at term had elevated uterine artery mean pulsatility index measured at 20 weeks (PI > 95th percentile). Only 27% of growth restricted fetuses diagnosed on 32-34 weeks ultrasound examination had pathological uterine artery test. Furthermore, 23'5% of fetuses with an estimated fetal weight on 32-34 ultrasound below 10th percentile had elevated uterine artery mean PI >95th percentile.
Conclusions: Mst growth restricted fetuses born at term have a low rate of pathological uterine artery mean pulsatility index measured at 20 weeks of gestation. Therefore, an ultrasound examination on 35 weeks of gestation is recommended to an appropriate diagnosis of late-onset intrauterine growth restricted fetuses.

6.2 S ARE TWO SCANS BETTER THAN ONE? PREDICTING SMALL FOR GESTATIONAL AGE INFANTS FROM SCAN DATA AT 20 AND 24 WEEKS GESTATION

Peter R Stone, Laura D Howe, Rennae S Taylor, Alistair Stewart, Eliza Chan, Katie Groom, Gus A Dekker, Lesley ME McCowan, On behalf of the SCOPE Consortium.
Department of Obstetrics and Gynaecology, University of Auckland, New Zealand. MRC Integrative Epidemiology Unit, University of Bristol, UK. School of Population Health, University of Auckland, New Zealand. The Women's and Children's Division, Lyell McEwin Hospital, University of Adelaide, Australia

Objective: Approximately 40% of stillbirths are small for gestational age (SGA), and only a minority of these infants are identified as SGA before birth. We assessed whether scans at 20- and 24-weeks' gestation enable better prediction of SGA infants compared with a single scan at 20 weeks'.
Methods: Using data from SCOPE, a prospective study of nulliparous pregnant women (N=2,665, 283 with SGA), we developed models for predicting SGA (birthweight <10th customised centile) based on fetal biometry and umbilical and uterine Doppler indices from 20- and 24-weeks'.
In 1,484 women with data on all variables, we assessed whether 24-week scan measures improved the performance of our previously published prediction model that uses questionnaire data from 15-weeks' and scan data from 20-weeks'.
Results: Using only data from 20-weeks', a model including abdominal circumference (AC) and umbilical and uterine Doppler resistance indices had an area under the curve (AUC) of 0.69 for prediction of SGA. A model including AC at 20- and 24-weeks' and mean uterine resistance index at 20- and 24-weeks' had an AUC of 0.73 ($p<0.001$ for difference in AUC) and a positive likelihood ratio (PLR) of 3.5 (95% 2.9-4.3) with a 10% false positive rate (FPR).
Our previously published prediction model combining clinical data collected at 15-weeks' with 20-week scan data had an AUC of 0.73 and a PLR of 3.3 (95% CI 2.5-4.4) with a 10% FPR. Addition of 24-week scan data to this model increased to AUC to 0.77 and the PLR to 4.0 (3.1-5.2) with a 10% FPR.
Conclusion: Two scans at 20- and 24-weeks' may result in modest improvement in the prediction of SGA infants compared with a single scan at 20-weeks'. Model performance with the two scans is similar to that obtained by combining clinical data with ultrasound data from 20-weeks'.

6.3 S PREVALENCE OF SMALL FOR GESTATIONAL AGE AND PRETERM DELIVERY IN LOW APP-A PREGNANCIES IN A DISTRICT GENERAL HOSPITAL

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Watford General Hospital, United Kingdom

Objectives: Determine the prevalence of small for gestational age (SGA) babies and preterm delivery associated with low pregnancy-associated plasma protein-A (PAPP-A), but normal combined screening in our local population.
Method: A retrospective observational study of all women opting for combined screening at West Hertfordshire Hospitals NHS Trust from August 2010 to November 2013 was performed. All women with PAPP-A less than 0.4 multiples of the median (MoM) were identified, along with the number of antenatal growth scans, birth weight and gestation at delivery.
Results: A total of 12,673 women opted for combined screening during the study period. Three hundred and ninety nine women were included in the study, and 29 chromosomal abnormalities, 12 miscarriages, 2 termination of pregnancy and 34 patients lost to follow-up were excluded.
Thirty women (9.3%) had SGA babies. Ethnic distribution in the SGA group was 73.3% Caucasian, 23.3% Asian and 3.3% African. Confounding factors were identified in 6 women (3 had gestational hypertension, 2 smokers and 1 previous history of low birth weight baby). No other maternal risk factors for SGA were found in the remaining 80% of women. In the SGA group, an average of 4 scans was performed per patient, compared to an average of 3 scans in our cohort. Gestational age at delivery was before 37 weeks in 31 out of the 322 pregnancies (9.6%). Two stillbirths were identified, of which one of the mothers was a smoker (40 weeks) and the other was an insulin dependent diabetic (38 weeks).
Conclusions: In our study population, the prevalence of SGA was 9.3% using a 5th centile (0.4 MoM) cut off for PAPP-A and 9.6% had preterm delivery.

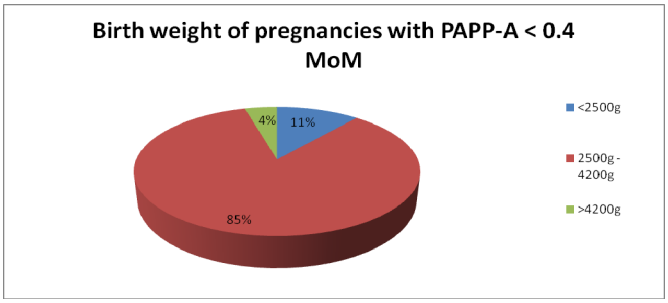

Figure 1: Birth weight outcome

6.4 S THE ROLE OF ANGIOGENIC FACTORS FOR FIRST TRIMESTER SCREENING OF FETAL ROWTH RESTRICTION

Francesca Crovetto, Stefania Triunfo, Fatima Crispi, Victor Rodriguez Sureda, Carmen Dominguez, Eduard Gratacos, Francesc Figueras.
BCNatal - Barcelona Center for Maternal-Fetal and Neonatal Medicine (Hospital Clínic and Hospital Sant Joan de Deu), IDIBAPS, University of Barcelona, and Centre for Biomedical Research on Rare Diseases (CIBER-ER), Barcelona, Spain

Objective: To assess if angiogenic factors could improve first trimester screening for the prediction of fetal growth restriction (FGR).
Methods: A nested case-control study drawn from a prospective first trimester cohort. The outcome was the development of FGR (birth weight <10th centile with Doppler abnormalities). Logistic regression-based predictive models were developed for the prediction of early and late FGR, subdivided for abnormalities of umbilical artery. The model included the *a priori* risk (maternal characteristics), mean arterial pressure (MAP), uterine artery (UtA) Doppler (11-13 weeks), and the measurement of the angiogenic factors (8-11 weeks): placental growth factor (PlGF) and soluble Fms-like tyrosine kinase-1 (sFtl-1), normalized by logarithmic transformation.
Results: Of the 9,167 participants, 248 (2.7%) were diagnosed as FGR, from which 43 fetuses (0.5%) were early, and 205 (2.3%) late FGR. Significant contributions for the prediction of early FGR were black ethnicity, chronic hypertension, previous FGR, smoking, together with MAP, UtA, PlGF and sFlt-1. A model achieved detection rates (DR) of 81% and 88% for 5% and 10% false positive rates (FPR), respectively (AUC: 0.96 [95%CI: 0.94-0.99]), and PlGF/sFlt-1 improved it by 26%. In those cases (49%) without preeclampsia (PE) DR was 81% at 10% of FPR. For late FGR, significant contributions were previous FGR, autoimmune disease, smoking together with MAP, UtA, PlGF and sFlt-1. The model achieved DR of 57% and 64% at 5% and 10% of FPR, respectively (AUC: 0.80 [95%CI: 0.75-0.84]), and PlGF/sFlt-1 improved it by 20%. In those cases (70%) without PE DR was 59% at 10% of FPR.
Conclusions: Angiogenic factors are essential for the prediction of FGR. For early FGR, even if the association with PE, the prediction in the first trimester is attainable. For the prediction of late FGR, not influenced by PE and difficult to achieve so early, angiogenic factors improved it substantially.

6.5 S PREDICTION OF SMALL FOR GESTATIONAL AGE INFANTS USING CLINICAL RISK FACTORS, BIOMARKERS AND ULTRASOUND DATA: FINDINGS FROM THE SCOPE STUDY

McCowan LME[1,3], Thompson J[2], Taylor RS[1], Baker P[3], Dekker G[4], Roberts C[4], Simpson N[5], Myers J[6], Kenny LC[7], North RA[8], on behalf of the SCOPE Consortium
[1]Dept of Obstetrics & Gynaecology, [3]Liggins Institute University of Auckland, New Zealand.

Background: Most small for gestational age (SGA) pregnancies are not recognised in the antenatal period and 40% of stillborn infants are SGA. We aimed to develop models to predict SGA infants, using clinical, biomarker and ultrasound data from the first 20 weeks' of pregnancy.
Method: 5628 nulliparous participants in the SCOPE study were interviewed at 15±1 weeks' and had an ultrasound at 20±1 weeks'; 46 candidate biomarkers were measured by Alere, San Diego at 15±1 weeks'. The cohort was divided into training (n=3735) and validation sets (n=1871). SGA was defined as birthweight <10th customised centile. Stepwise logistic regression was performed using clinical variables, then clinical combined with biomarker variables and finally combining these with ultrasound variables. Receiver operator curves were constructed and areas under the curve (AUC) calculated.
Results: 633 infants (11.3%) were SGA. Risk factors for SGA infants at 15±1 weeks' included: family history of coronary disease, maternal birthweight <3000g and 3000g to 3499g vs ≥3500g, taking >12 months to conceive, cigarette smoking, proteinuria, daily vigorous exercise and diastolic blood pressure ≥80 mmHg. Recreational walking ≥4 times weekly, rhesus negative blood group and increasing random glucose were protective. AUC for clinical factors was 0.66. Addition of biomarkers (PAPP-A & VEGFR-1) increased the AUC to 0.68 and addition of fetal measurements and uterine artery Doppler at 20±1 weeks' increased the AUC to 0.74.
Conclusions: A model combining clinical, ultrasound and biomarkers resulted in modest prediction of SGA infants. Biomarkers obtained at 15±1 weeks' resulted in minimal increases in AUC compared with clinical risk factors alone. This combined model for prediction of SGA in healthy nulliparous women does not perform sufficiently well to be applied in clinical practice.

6.6 S PlGF BEDSIDE TESTING IN STANDARD CLINICAL CARE: 6 MONTHS EXPERIENCE FROM A LARGE TEACHING HOSPITAL

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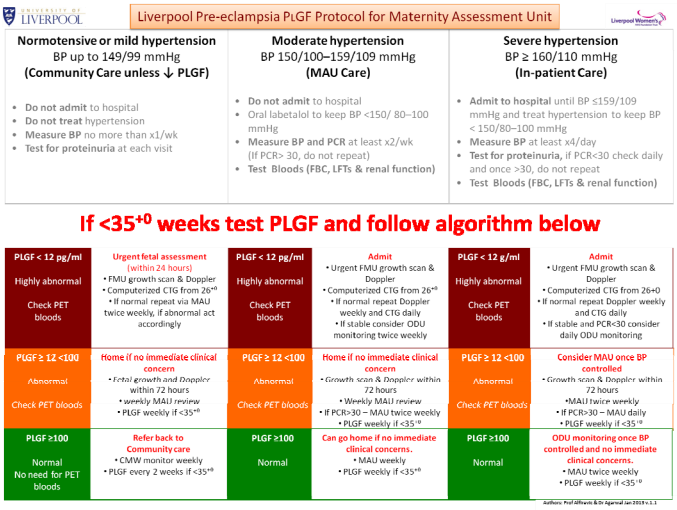
Objective: To evaluate the use of bedside Placental Growth Factor (PlGF) testing as part of standard clinical care for the management of hypertension <35 weeks.
Method: Patients managed with PlGF monitoring over a 6 month period in accordance with a clinical algorithm (see below) were identified and clinical outcome data collected.
Results: 49 women were managed with PlGF over the 6 month study period. 42% of women had a final diagnosis of preeclampsia; 82% with a PlGF <12 compared to 20-24% with higher measurements.
Overall 67% of women required caesarean section, increasing to 82% with PlGF <12. Gestation at birth was lower in women with low PlGF (32, 34 and 37 weeks for PlGF measurements of <12, 12-100 and >100 respectively).
Overall 35% of pregnancies were small for gestational age (SGA), but 72% of babies born to women with a PlGF <12 were SGA, whilst only 18% and 6% in the 12-100 and >100 groups. Babies born to mothers with a PlGF <12 required increased neonatal care (12.5, 0 and 0 days for PlGF <12, 12-100 and >100 respectively) with greater neonatal adverse outcomes (44%, 30% and 12% for PlGF <12, 12-100 and >100 respectively). There were few maternal adverse outcomes and these were evenly distributed throughout all PlGF groups.
Conclusions: Low PlGF (<12) is associated with SGA in a hypertensive population <35 weeks. There was also an increased incidence of neonatal morbidity and need for neonatal intensive care.
All women managed with PlGF monitoring remain at high risk of caesarean section, although the risk of maternal adverse outcome remains low.



Greater numbers are need to ensure the safety of PlGF based management as part of standard clinical care and so we have established the mapple@liverpool.ac.uk database to collate clinical outcome data for women managed with bedside PlGF.

6.7 K THIRD TRIMESTER BIOMARKERS FOR PREDICTION OF SMALL FOR GESTATIONAL AGE INFANTS: THE PELICAN STUDIES

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Small-for-gestational-age (SGA) infants are at increased risk of morbidity and mortality. Diverse aetiology and poor performance of current diagnostic tools make prediction of SGA challenging. Markers of placental dysfunction, a pivotal element of the complex aetiology, may improve prediction of this condition.
Our previous work evaluated maternal Placental Growth Factor (PlGF) in 625 women with suspected pre-eclampsia, demonstrating high sensitivity and negative predictive value (NPV) for the determination of pre-eclampsia requiring delivery within 14 days and delivery of an SGA infant (birthweight <1st centile). The use of revealed PlGF measurements in clinical practice is now being evaluated.
Our more recent work assessed the diagnostic accuracy study of PlGF and ultrasound parameters (estimated fetal weight (EFW) <10th centile, umbilical artery Doppler pulsatility index >95th centile and oligohydramnios) to predict delivery of an SGA infant <3rd customised birthweight centile (SGA-3) and perinatal outcome in 601 women with singleton pregnancies presenting with reduced symphysis fundal height (SFH) across 11 sites in UK and Canada.
For predicting delivery of SGA-3 (n=78), EFW <10th centile had sensitivity of 0.58 (95%CI 0.46 to 0.69) and NPV of 0.93 (0.90 to 0.95), PlGF < 5th centile had sensitivity of 0.37 (0.27 to 0.49) and NPV of 0.90 (0.87 to 0.93), and in combination, PlGF and EFW <10th centile had sensitivity of 0.69 (0.55 to 0.81) and NPV of 0.93 (0.89 to 0.96). The equivalent ROC areas were 0.79 (0.74 to 0.84) for EFW <10th centile, 0.70 (CI 0.63 to 0.77) for low PlGF, and 0.82 (CI 0.77 to 0.86) in combination.
In contrast to the previous findings demonstrating high sensitivity and NPV of maternal PlGF concentrations for prediction of SGA in women presenting with suspected pre-eclampsia, PlGF is no better than EFW <10th centile in determining delivery of an SGA infant in women presenting with reduced SFH.

7.1 S VALUE OF THE 32-34 WEEK ULTRASOUND IN THE DIAGNOSIS OF GROWTH RESTRICTED FETUSES BORN AT TERM

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Objectives: To test if biometry at the 32-34week ultrasound examination is predictive of full term fetuses with a birth weight less than 2500g.
Material and Methods: Assisted deliveries in the last 15 months (from March 1, 2013 to June 24, 2014) with fetuses more than 37 weeks whose birth weight was less than 2500g have been reviewed; the analyzed variables are: the ultrasound estimated weight of 32-34 week and weight at birth according to the percentile calculated using F.Figueras'curve (EJOGRM 2008).These data are also compared with a random sample of full term fetuses between 2501 and 3999 g born in the same year.
Results: There were 90 (2.14%) full term fetuses, with a birth weight below 3rd percentile. 21% of full term growth restricted fetus(GRF) were diagnosed during the 32-34 week ultrasound, but only 12% of fetuses with birth weight less than 2500 grams had a percentile ≤ 3 in 32-34week ultrasound. Due to this, 57% of full term GRF diagnosed in the 32-34week ultrasound had an early growth restriction. 55% of fetuses with birth weight less than 2500 g had a percentile < 50 in the 32-34week ultrasound, while in the sample of randomly selected fetuses with normal weight, only 4.6% had a percentile <50 (a statistically significant difference). In no one normal weight fetus, percentile < 25 of the 32-34 week had been calculated.
Conclusions: The 32-34week ultrasound is not very much predictive of full term GRF. It appears to be a relationship in those fetuses with a percentile <25th on that scan. The Hadlock formula in our hospital overestimates fetal weight. According to the results of our study, we propose to delay the 32-34week ultrasound to the 35 week to diagnose of late-onset intrauterine growth restricted fetuses.

7.2 S EFFECTIVENESS OF A POLICY OF ROUTINE ULTRASOUND SCANS IN THE THIRD TRIMESTER IN THE DETECTION OF SMALL FOR GESTATIONAL AGE BABIES

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Aim: To determine the diagnostic effectiveness of a routine third trimester scan for the detection of Small for Gestational Age babies at a tertiary care centre in India
Methods: Sonographic, obstetric and neonatal details of 490 pregnant women with singleton pregnancies considered low risk at first trimester booking were obtained and followed up through delivery. Fetal weight was estimated on the basis of Hadlock's EFW formula and recorded on Hadlock's EFW chart. Fetuses whose growth trajectory falls sequentially over several weeks are labelled as crossing centiles. Neonatal assessment and growth categorization was based on locally derived birth weight centiles, with small for gestational age (SGA) defined as <10th centile. The diagnostic effectiveness of antenatal scan based growth categorization was assessed against the neonatal assessment of SGA.
Results: The median gestational age at routine third trimester scan was 32 weeks (IQR 30-34 weeks). 43 (8.78%) of neonates were classified as small for gestational age at birth. The sensitivity, specificity, AUROC, false negative and false positive rates of third trimester scan reporting SGA was 10.5%, 98.4%, 0.54, 89.47% and 1.64% respectively. The sensitivity, specificity, AUROC, false negative and false positive rates of third trimester scan reporting crossing centiles was 12.8%, 95.7%, 0.57, 87.18% and 4.32% respectively. A scan result of SGA EFW, or crossing centiles, increased the probability of having a SGA baby from 8.2% to 36.5 % (95% CI: 15%, 65%) and 8.14% to 21 % (95% CI: 9 to 41%), respectively.
Conclusions: Current routine third trimester scan in a low risk population is highly specific but has poor discriminatory ability and a high false negative rate that limits its effectiveness as a routine screening tool for the detection of fetal growth restriction.

7.3 S ROUTINE THIRD TRIMESTER ULTRASOUND AT 32 *VS.* 36 WEEKS OF GESTATIONAL AGE IN THE DETECTION OF GROWTH RESTRICTION: RANDOMIZED TRIAL (ROUTE)

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Objective: To evaluate the effectiveness of routine third trimester scan at 32 vs. 36 weeks of gestation.
Methods: Study Design: Open-label parallel randomized trial (ROUTE study).
Setting: Single General Hospital covering a geographically well-defined catchment area in Barcelona, Spain, between May 2011 and April 2014.
Participants: Women at routine second trimester scan without adverse medical or obstetrical history and with a singleton non-malformed fetus.
Interventions: Routine third trimester scan at 32±1 or 36±1 weeks.
Main outcome measure: Detection rate of fetal growth restriction [FGR] (customized birthweight below the 10th centile) and severe FGR (customized birthweight below the 3rd centile).
Results: 1272 women were randomly allocated to 32-week scan and 1314 to 36-week scan. There were not significant differences in adverse perinatal outcomes between both groups. Severe FGR at birth was significantly associated with emergency caesarean section for fetal distress (OR 3.4; 95%CI 1.8-6.7), neonatal admission (OR 2.23; 95%CI 1.23-4.05), hypoglycaemia (OR 9.5; 95%CI 1.8-49.8) and hyperbilirubinemia (OR 9; 95%CI 4.6-17.6).
For a similar rate of false positives (8%), detection rate for severe FGR (45% vs. 61.4%; p=0.01)) was better at 36 compared to 32 weeks. The positive and negative likelihood ratios were 5.7 vs. 7.2 and 0.6 vs. 0.4, respectively.
Conclusions: In a low-risk pregnant population, routine scan at 36 weeks performs better than at 32 weeks for the detection of severe growth restriction at birth, which is associated with a number of adverse perinatal and neonatal outcomes.

7.4 S EFFECTINENESS OF DIFFERENT SERIAL SCAN POLICIES IN ANTENATAL DETECTION OF SGA BIRTHWEIGHT IN HIGH RISK PREGNANCIES

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Objective Previous delivery of a small for gestational age (SGA) baby is an accepted indication for increased surveillance in subsequent pregnancies. We sought to quantify the effectiveness of the various serial scan protocols which were in operation in our NHS Region.
Method The cohort consisted of 5281 singleton, normally formed pregnancies with a past history of one or more SGA births. Cases were categorised according to the number of serial scans ordered at the beginning of pregnancy. SGA birthweight was defined as <10th customised centile, and antenatal detection was based on one or more ultrasound estimated fetal weights (EFW) recorded as below the 10th centile.
Results The SGA rate in this group was 29.4%. The table shows the respective frequencies of various scan policies and detection rate if the birthweight was FGR.

No. of scans ordered	Proportion of pregnancies (%)	Median gestational age at scan (weeks)	Antenatal detection of SGA birthweight (%)
0	20.9	-	-
1	4.6	32	30.1
2	22.7	28 34	32.1
3	29.2	28 32 36	48.8
4	14.4	28 32 35 37	76.1
5+	6.1	28 30 32 35 37	84.1

Conclusion Antenatal detection rate is proportional to the number of investigations offered, and increases substantially with scans done at term. Performance of 1 or 2 scans seems not better than no scans at all. These findings raise doubt about the utility of routine single growth scans occasionally being advocated for screening in low risk pregnancies.

7.5 S ROUTINE VERSUS CONTINGENT THIRD TRIMESTER SCREENING FOR LATE FETAL GROWTH RESTRICTION

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Objective: To evaluate in an unselected population the performance of a contingency third-trimester scan for late fetal growth restriction (FGR) prediction based on the risk assessment at second trimester.
Methods: A prospective cohort was created of consecutive singleton pregnancies referred for routine first-trimester screening for aneuploidies. Data on maternal baseline characteristics, first and second trimester ultrasound biometries and uterine Doppler were modelled by logistic regression to estimate the risk of late FGR (defined as a birth weight below the 3rd centile or between the 3rd and 10th centiles plus abnormal Doppler before delivery). Based on this risk at second trimester, several contingency strategies selecting for a third trimester scan a 10%, 25% or 50% of the population were tested against a strategy of routine third trimester scan.
Results: A total of 2,696 women were included in the analysis, of which 145 (5.4%) developed FGR. At first trimester, a combination of *a priori risk based on maternal baseline characteristics* and uterine artery Doppler (*a posteriori* first trimester risk) yielded an area under the curve (AUC) of 0.75 (95%CI 0.7-0.79). At second trimester, the *a posteriori* first trimester risk combined with the second trimester abdominal circumference and uterine Doppler (*a posteriori* second trimester) yielded an AUC of 0.83 (95%CI 0.79-0.87). Under different strategies of contingent third trimester scan based on the second trimester *a posteriori* risk (selecting for third trimester scan a 10%, 25% or 50% of the population), the achieved predictive performances had AUC of 0.83(0.8-0.88), 0.87(0.82-0.91) and 0.9(0.86-0.93), respectively. Only the 50% contingency model had an AUC statistically equivalent to routine third trimester scan (p=0.13) [AUC of 0.91 (95%CI 0.88-0.95)].
Conclusion: A strategy of selecting a 50% of the population for third trimester scan based on the second trimester risk for late fetal growth restriction results in performance equivalent to routine third trimester scan.

7.6 S CHANGES IN FETAL DOPPLER INDICES AS A MARKER OF FAILURE TO REACH GROWTH POTENTIAL AT TERM

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Objective: To evaluate whether changes in the middle cerebral artery (MCA), umbilical artery (UA) and cerebroplacental ratio (CPR) Doppler indices at term might be used to identify those appropriate-for-gestational-age (AGA) fetuses that are failing to reach their growth potential (FRGP).
Methods: This was a retrospective cohort study of data obtained in a single tertiary referral center over a 10-year period from 2002 to 2012. The UA pulsatility index (PI), MCA-PI and CPR were recorded between 37+0 and 41+6 weeks within 14 days before delivery. The Doppler parameters were converted into multiples of the median (MoM), adjusting for gestational age, and their correlation with birth-weight (BW) centiles was evaluated by means of regression analysis. Doppler indices were also grouped according to BW quartiles and compared using Kruskal–Wallis and Dunn's post-hoc tests.
Results: The study included 11 576 term fetuses, with 8645 (74.7%) classified as AGA. Within the AGA group, fetuses with lower BW had significantly higher UA-PI, lower MCA-PI and lower CPR MoM values. Largefor-gestational-age (LGA) fetuses were considered as the group least likely to be growth-restricted. The CPR MoM < 5th centile (0.6765 MoM) in these fetuses was used as a threshold for diagnosing FRGP. Using this definition, in the AGA pregnancies the percentage of fetuses with
FRGP was 1% in the 75–90th BW centile group, 1.7% in the 50–75th centile group, 2.9% in the 25–50th centile group and 6.7% in the 10–25th centile group.
Conclusion: AGA pregnancies may present with fetal cerebral and placental blood flow redistribution indicative of fetal hypoxemia. Fetal Doppler assessment may be of value in detecting AGA pregnancies that are subject to placental insufficiency, fetal hypoxemia and FRGP. Future studies are needed to evaluate the appropriate threshold for the diagnosis of FRGP and the diagnostic performance of this new approach for the management of growth disorders.

8.1 S IMPACT OF ACCREDITATION TRAINING IN CUSTOMISED FETAL GROWTH ASSESSMENT ON STILLBIRTH RATES IN ENGLAND

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Objective To assess the effect that accreditation training in fetal growth surveillance and evidence-based protocols had on stillbirth rates in England.
Design Analysis of mortality data from Office of National Statistics.
Setting England including three National Health Service (NHS) regions (West Midlands, North East and Yorkshire and the Humber) which between 2008 and 2011 implemented training programmes in customised fetal growth assessment.
Population Live births and stillbirths between 2007 and 2012.
Main outcome measure Stillbirth.
Results There was a significant downward trend (p=0.03) in stillbirth rates between 2007 and 2012 in England to 4.81/1000, the lowest rate recorded since adoption of the current stillbirth definition in 1992. This drop was due to downward trends in each of the three English regions with high uptake of accreditation training, and led in turn to the lowest stillbirth rates on record in each of these regions. In contrast, there was no significant change in stillbirth rates in the remaining English regions and Wales, where uptake of training had been low. The three regions responsible for the record drop in national stillbirth rates made up less than a quarter (24.7%) of all births in England. The fall in stillbirth rate was most pronounced in the West Midlands, which had the most intensive training programme, from the preceding average baseline of 5.73/1000 in 2000–2007 to 4.47/1000 in 2012, a 22% drop which is equivalent to 92 fewer deaths a year. Extrapolated to the whole of the UK, this would amount to over 1000 fewer stillbirths each year.
Conclusions A training and accreditation programme in customised fetal growth assessment with evidence-based protocols was associated with a reduction in stillbirths in high-uptake areas, and resulted in a national drop in stillbirth rates to their lowest level in 20 years.

Gardosi J, Giddings S, Clifford S et al. Association between reduced stillbirth rates in England and regional uptake of accreditation training in customised fetal growth assessment. BMJ Open 2013 bmjopen.bmj.com/content/3/12/e003942.full

8.2 S THE GROWTH ASSESSMENT PROTOCOL (GAP): A NATIONAL PROGRAMME TO IMPROVE PATIENT SAFETY IN MATERNITY CARE

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Based on previous experience of the benefits of improved antenatal recognition of FGR, we put together a comprehensive programme to help maternity units and hospitals improve their performance. This included
1. Comprehensive staff training, and accreditation of local GAP trainers responsible for cascade training in each Trust; a competency document for peer assessment of knowledge of fetal growth surveillance and clinical application; e-Learning and test package to reinforce the initial training and to facilitate ongoing assessment; and online training and a competency log to internally monitor uptake within each Trust.
2. Template protocols and guidelines to standardise practice in the use of customised growth charts and referral criteria, which can be adapted in Trust based protocols, consistent with latest RCOG Green-top guidelines
3. Routine quarterly reporting of IUGR and antenatal detection rates to allow units to monitor their performance and benchmark against other units with similar demographics.
4. Calculation of customised birthweight centile by the GROW software to facilitate postnatal management and to aid audit of missed cases of IUGR to identify local issues and system errors relating to fetal growth surveillance.
5. Communication via nominated link persons from each speciality — a midwifery manager, an ultrasonographer and an obstetric/fetal medicine lead. They will provide local leadership assisting implementation of the GAP programme and strengthening the link with the GAP team, supporting implementation and feeding back on progress and action planning for the future.

From mid 2013 to September 2014, GAP has been implemented in 88 (52%) of the 168 hospital Trusts or Boards in England, Scotland, Wales and Northern Ireland, with a further 16% intending to do so soon, and another 11% who have expressed interest to proceed. We are working with NHS England to develop commissioning guidance which will ensure that all remaining hospitals adopt the same standard, evidence based approach.

8.3S THE ROLE OF SUPERVISION AND COMPETENCY ASSESSMENT IN IMPROVING FETAL GROWTH SURVEILLANCE

Carol Paeglis
Yorkshire and the Humber LSA, NHS England (to 2013)

Objective: To reduce the stillbirth rate in Yorkshire and the Humber, by optimising best midwifery practice through the mechanisms of the Local Supervising Authority and Supervision of Midwives.
Method: In recognition that there is a raft of published data, research and best practice in relation to Stillbirths and that whilst they are multi-factoral, 1 in 3 can be associated with substandard care; Yorkshire and the Humber Local Supervising Authority harnessed proactive and reactive Supervision of Midwives to spread best practice, to identify and rectify poor practice and to share the lessons learned from stillbirth reviews. One particular aspect was the production, publication and use of a Best Practice Competency Assessment Tool for the '*Assessment of Fetal Growth'* for all midwives to undertake which was verified as completed by their Supervisor of Midwives. The Best Practice Competency Assessment Tool was a document outlining the evidence base for best practice in relation to fundal height measurement and an assessment of the midwives' technique by an assessor. Completion rates of the Best Practice Competency Assessment Tool were included within the annual Local Supervising Authority audits to each Trust in Yorkshire and the Humber.
Results: ONS data demonstrates that the Yorkshire and the Humber stillbirth rate fell from 5.7 in 2011 (England rate 5.2) to 5 in 2012 (England rate 4.8). The first six months of 2013-14 Yorkshire and the Humber Local Supervising Authority data demonstrated a subsequent reduction to 4.8.
Conclusions: A statistically significant reduction in the Yorkshire and the Humber stillbirth rate between 2011 and 2012 occurred after the introduction of a range of mechanisms, including the completion of a Best Practice Competency Assessment Tool for the '*Assessment of Fetal Growth'* by all midwives in Yorkshire and the Humber. The stillbirth rate appears to have further reduced, based on Local Supervising Authority.

8.4 S IMPLEMENTING GROW IN A TERTIARY REFERRAL UNIT

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Customised grow charts were implemented in April 2012. Audit of growth referrals was undertaken within first 4 months (n=144) and then 18 months after implementation (n=812). Data evaluates number of referrals, reason for referral, proportion of growth restricted babies identified and birth outcomes.

The results of the 18 month audit will be presented. The presentation will highlight how to implement GROW in a large tertiary referral unit, impact on the service, lessons learned and how to build a sustainable service. Stillbirth data, with reference to proportion that are growth restricted will also be presented.

8.5 S SUCCESSES AND PITFALLS OF IMPLEMENTING GROW IN THE NETHERLANDS

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KNOV, The Netherlands

In The Netherlands, perinatal mortality rates are a source of concern. Fetal growth restriction (FGR) is one of the main contributors to perinatal mortality en morbidity. The national detection rates are low, and similar to figures presented in international literature.
To improve the detection of FGR, the Dutch organization of midwives (KNOV) developed a national guideline. After an extensive and structured literature study, we concluded that the GROW-program, developed in de West Midlands in England, was the most promising method to improve the detection rates of FGR with a relatively low false positive rate.
This lecture will be about the different strategies we use to implement this method in the country as a whole: introducing standardized fundal height measurements and the use of a customized growth chart as the national standard.
We will elaborate on the e-learning program and the hands-on training that we developed to train all midwives and other obstetric caregivers. Furthermore we will discuss the intensive (international) collaboration with midwives, obstetricians, ultrasound scanners, researchers and software developers to make GROW-Nl work for all care givers, and above all to provide better care for women and their babies.

8.6S THE NEW ZEALAND EXPERIENCE

Karen Richards, Joyce Cowan
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Approximately 3300 midwives work in New Zealand. They provide the majority of maternity care, either as lead maternity carer (LMC) under a continuity of care model from booking to 6 weeks postpartum, or as employed midwives. The majority of women in New Zealand have a midwife LMC. Some midwives practice within the district health boards (DHBs). GROW was introduced into NZ in around 2010, with training originally rolled out as part of compulsory education for registered midwives in technical skills workshops. The education was presented as part of a midwifery practice session discussing fetal wellbeing from a wider perspective so did not address use of GROW in detail or assess participants use of the tool.
Two New Zealand midwives with a research interest in fetal growth were invited to attend training at the Perinatal Institute in February 2014 and made a commitment to roll out training for maternity practitioners, including midwives, sonographers and obstetricians in New Zealand.
From spring 2014, DHBs were offered training nationally and response was very positive. 14 out of the 20 DHBs have enthusiastically accepted the initial offer, with workshops planned for 2015 to complete the roll out. Workshops have been multidisciplinary and response to education has been overwhelmingly favourable with several DHBs requesting further sessions to accommodate the high demand for places. Feedback from participants has indicated that the education has been beneficial and applicable to New Zealand practice. The multidisciplinary approach to workshops has generated positive interaction at the interface between maternity practitioners.
The issue of a national strategy for licensing, education and evaluation of GROW in New Zealand is being considered currently at Ministry of Health level.

8.7 S THE IMPACT OF DEPRESSION, ANXIETY AND STRESS ON FETAL GROWTH: FINDINGS FROM THE MERCY PREGNANCY AND EMOTIONAL WELL-BEING STUDY (MPEWS)

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Objective: Most studies investigating the effects of depression, anxiety and stress on fetal growth parameters via ultrasound measures have reported significant associations, however failed to measure maternal mental health and fetal growth parameters across multiple time points of pregnancy. This is important because maternal mental health or major stressors may be episodic or fluctuate during pregnancy. Stress appears to be a stronger predictor of fetal growth, suggesting the major drivers of fetal growth restriction are dysregulation of stress-related hormones seen in depression and anxiety, but this prediction requires testing. The present study aims to use a multi-measures/multi-methods approach and repeated measure design to investigate the relationship between maternal mental health and several indices of fetal growth.
Method: This study draws on data from the Mercy Pregnancy and Emotional Well-Being study being conducted in Melbourne, Victoria, Australia. 300 pregnant women recruited from the Mercy Hospital completed the SCID and repeated measures of Edinburgh Postnatal Depression Scale (EPDS) to measure depressive symptoms, the State-Trait Anxiety Inventory (STAI) to measure anxiety-related symptoms and the Stressful Life Events Questionnaire to measure stress. Biosamples have also been collected including blood and placenta samples. Sonographers conducted three ultrasound scans at approximately 14, 20 and 32 weeks gestation. Fetal growth parameters including estimated fetal weight, head and abdominal circumference, femur length and birth weight were recorded.
Results: Data on associations between maternal mental health and fetal growth are currently being analysed. However, preliminary analysis suggests that depression, anxiety and stress are strongly associated with one another over pregnancy, and principle components analysis suggests a single factor accounting for 71% of variance. Mixed models will be used to analyse repeated measures of fetal growth as predicted by levels and changes in maternal mental health.
Conclusions: Results will be discussed in the light of previous findings and study limitations.

8.8 S EARLY MUSIC PROGRAMS: AN OPTION TO SUPPORT NEURODEVELOPMENT IN HEALTHY AND GROWTH RETARDED BABIES FROM PRE- TO POSTNATAL LIFE?

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Clara Angela Foundation, Witten and Berlin, Germany

Music exists in the passage of time and cross-culturally. Some of its features are comparable to rhythmic elements in utero. Lullabies have been sung for centuries whereby the pure effect of music but also the emotional expression by the mother's voice, representing continuity from pre- to postnatal life, may be effective.
Stress and anxiety during pregnancy are associated with immediate and long-term effects on the fetus [1],[2].
Listening to relaxing music has been shown to decrease women's experience of stress, anxiety and depression [3].
While mothers listened to a melody via headphones, Zimmer already described a direct association of maternal relaxation and fetal response [4]. As mothers indicated to relax while watching a soap opera, Hepper reasoned that a change to an alert state when hearing this music might correspond to prenatally experienced relaxation rather than the sound itself [5].
In addition, the mother's voice has a *direct* impact on the developing brain. Prenates and newborns react to musical rhythms and thus orientate to the social world. Early acoustic impressions are essentially "musical" because words cannot be understood. Intimate contact between mother and baby combined with musical communication is thought to support neonatal development and to reduce morbidity. However, this hypothesis needs further evidence.According to the WHO health is understood as wellbeing that goes further than just an absence of suffering[6]. It is our goal, to investigate the hypothesis, that early exposure to music, vocal performance or dancing from the first trimester onwards and the continuation of musical experiences within the family will be effective in the prevention of cognitive delay of future generations preferably in children with risk factors such as poor growth. We still look for partners interested in creating and performing an international trial of music intervention from the first trimester to early infancy.

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9.1 K MANAGEMENT AND FOLLOW-UP OF EARLY ONSET IUGR FETUSES

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Objective: To investigate the survival and morbidity at 7 years of age of growth restricted fetuses delivered on fetal indication before 30 gestational weeks.
Method: Since 1998, a proactive approach to the management of very preterm growth restricted fetuses has been practised at our level III perinatal centre. The decision to deliver is based on an integrated evaluation of umbilical artery flow velocity, ductus venosus flow pattern, umbilical venous pulsations, and fetal heart rate pattern. (low short-term variability, loss of variability, late decelerations). 42 SGA fetuses (fetal weight <mean-2 SD) with ARED flow in the umbilical artery were delivered via cesarean section alive at 24+4 to 29+5 weeks. The outcome (survival at 2 and 7 years, neonatal morbidity and development at 7 years) were compared to the background population of very preterm infants (n=371) and to AGA infants matched for gestational age and gender (n=42).
Results: The 2-year survival was 90% (background population, 87%) and the rate of cerebral palsy was 14% and 11%, respectively (n.s.). The only significant difference in morbidity was found for the chronic lung disease (65% vs. 37%) (1). At the follow-up at 7 years (n=34), the verbal and full scale IQ was lower in the IUGR group than in the matched controls ($p<0.01$) (2) and the respiratory function was more often impaired (3). There were no differences in the cardiac size and function; the microvascular dilatory response to acetylcholine was decreased, the aortic stiffness was decreased, and the aorta showed a higher distensibility (4).
Conclusions: There was a high survival of the actively managed very preterm IUGR fetuses. The morbidity at 2 years was not increased and the deficits in the neurocognitive and cardiovascular development at 7 years were not of such magnitude to refrain from the delivery on fetal indication.
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9.2 S EVALUATION OF THE ETHICS AND SOCIAL ACCEPTABILITY OF A PROPOSED CLINICAL TRIAL USING MATERNAL GENE THERAPY TO TREAT SEVERE EARLY-ONSET FETAL GROWTH RESTRICTION IN PREGNANT WOMEN

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Objective: The EVERREST programme proposes a clinical trial using maternal uterine artery vascular endothelial growth factor gene therapy to treat severe early-onset fetal growth restriction (FGR) in pregnant women. The ethical and social acceptability of the proposed clinical trial was evaluated as part of the programme.
Method: We conducted a literature review on the ethical and legal issues of highly experimental treatments in pregnant women. Semi-structured and qualitative interviews were conducted in several European countries with key stakeholders (disability groups, professional bodies and groups supporting families affected by pregnancy loss and FGR, n=34) and with women/couples who have experienced pregnancies affected by severe early onset FGR (n=24).
Results: The literature considered two main questions; whether it is ethical to treat a pregnant woman with a potentially risky treatment when she herself has no benefit from the treatment, and secondly, whether it is ethical to treat this condition of the unborn who may otherwise have died but with the treatment may be born with a serious disability. The review concluded that there was no ethical or legal objection to the intervention nor to a trial of this intervention.
The interviews also discussed the main areas of ethical concern, specifically the issue of acceptability of a treatment which, on the one hand, might reduce disability but, on the other hand, lead to a child, who might not have been born, being born with a serious disability. Overall, stakeholders and women/couples viewed the proposed trial in positive terms. Women were generally interested in participating in clinical trials where these conferred a potential benefit to their unborn child. The risk of disability of the premature child was a concern but not considered a major stumbling block for EVERREST.
Conclusion: Maternal gene therapy to treat severe early onset FGR appears to be ethically and socially acceptable.

9.3 K RESULTS OF THE TRUFFLE TRIAL

Christoph Lees on behalf of the TRUFFLE group
Imperial College London, UK

Objective: To determine the frequency of survival without neuro-impairment at 2 years of infants where early onset fetal growth restriction was detected. The trigger for delivery was based on one of 3 management strategies.
Method: Randomised controlled study in 20 European countries of women with a diagnosis of fetal growth restriction in singleton pregnancies 26-32 weeks. The trigger for delivery was abnormal short term variation on CTG, early ductus venosus changes or late ductus venosus changes ('a' wave at or below the baseline).
Results: The 2 year primary outcome data based on randomized group will be presented.
Conclusions: The data will inform management of early preterm fetal growth restriction.

9.4 K MANAGEMENT OF LATE ONSET IUGR

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There is a growing consensus that early and late-onset forms of intrauterine growth restriction (IUGR) must be dealt with as separate conditions, both from clinical and research perspectives. Early-onset IUGR is always a severe disease, highly associated with PE and abnormal placental implantation. Late-onset IUGR is rarely associated with PE and being far more prevalent than the early-onset clinical form it is responsible of a large proportion of perinatal deaths. Furthermore, the association of late-onset IUGR with poorer outcome is now well demonstrated and consequently the importance of its detection and proper management is increasingly recognized.
Follow-up: There is good quality evidence showing that compared with every two week monitoring, twice a week monitoring results in more induction without any improvement in the perinatal outcome. However, observational studies demonstrate that umbilical artery Doppler rarely becomes abnormal in late-onset IUGR and, therefore, other US and Doppler parameters have been proposed for the follow-up, including the growth velocity, the middle cerebral artery Doppler (both individually and combined with the umbilical artery Doppler in the cerebroplacental ratio) and the uterine artery Doppler. Although evidence from observational studies accumulates, there is not solid evidence regarding the beneficial impact of these additional parameters on the perinatal outcome.
Time of delivery: There is one large randomized equivalence trial comparing the effect of induction of labor beyond 36 weeks with expectant monitoring in pregnancies with suspected IUGR. The primary outcome was a composite measure of adverse neonatal outcome, and the secondary outcome was operative delivery. No significant difference was found in either outcome between study groups. The absence of difference in outcome between the two groups supports a strategy of induction of labour or conservative management, depending on the wishes of the woman.
Mode of delivery: Late-onset IUGR fetuses are at increased risk of fetal heart rate decelerations in labor, emergency cesarean section for suspected fetal compromise and metabolic acidemia at delivery. The offer of induction of labor with continuous monitoring is reasonable in term and near term fetuses SGA fetuses. Reported rates of emergency CS for suspected fetal compromise greatly vary from 6-45%, and several ultrasound and Doppler parameters before labor has been suggested as predictors of these adverse outcomes. However, there are no RCTs of mode of delivery in late-IUGR.

9.5 K FURTHER INSIGHTS FROM THE DIGITAT TRIAL & FOLLOW-UP

Sicco Scherjon [1], Sanne Gordijn[1], Saskia LeCessie [2], Linda van Wijk [1,3] and Kim Boers [4] on behalf of the

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Optimal treatment in IUGR at term is highly debated. The Disproportionate Intrauterine Growth Intervention Trial At Term (DIGITAT) compared in a nationwide study the effect of induction of labour with a policy of expectant monitoring for intrauterine growth restriction near term(1).
The randomised equivalence trial was performed between in pregnant women who had a singleton pregnancy beyond 36+0 weeks' gestation with suspected intrauterine growth restriction. 321 pregnant women were randomly allocated to induction and 329 to expectant monitoring. Composite adverse neonatal outcome was the same for the two groups (difference -0.8%, 95% CI -4.3% to 3.2%). It was concluded that patients who are keen on non-intervention can safely choose expectant management with intensive maternal and fetal monitoring; however, it is rational to choose induction to prevent possible neonatal morbidity and stillbirth.
Long term maternal health-related quality of life (HR-QoL), measured alongside the trial was also not affected by treatment allocation(2). No clinically relevant differences were found (SF-36, EuroQoL 6D3L, HADS, SCL-90) between allocated groups at baseline, 6 weeks postpartum and 6 months postpartum
We also evaluated which maternal or fetal markers (n=17) could identify at study entry IUGR fetuses who would benefit from early labour induction. The only potentially informative marker for inducing labour was maternal pre-pregnancy body mass index (BMI); the other prognostic markers seem unlikely to be helpful in identifying women who could benefit from labour induction(3)
Cost of both strategies were compared by documentation of resource utilization From a health care perspective, both strategies generated comparable costs: a cost difference of €111 (95%CI: €-1296 to 1641). Costs are lower, however, in the expectant monitoring group before 38 weeks of gestation and costs are lower in the induction of labour group after 38 weeks of gestation. So if induction of labour is considered to pre-empt possible stillbirth in suspected IUGR, it is reasonable to delay until 38 weeks, with watchful monitoring.

[1] Boers KE et al. BMJ. 2010;341:c7087; (2) Bijlenga D et al. Qual Life Res. 2011;20:1427-36. (3) Tajik P et al. EJOGRB 2014;172:20-5.(4) Vijgen et al SM EJOGRB 2010;170:358-63

10.1 K OVERVIEW OF NATIONAL PROTOCOLS FOR ASSESSMENT AND MANAGEMENT OF IUGR

Lesley McCowan
University of Auckland, New Zealand

This talk will present a review and comparison of existing national SGA guidelines

10.2 K PERINATAL IRELAND: PROTOCOL DEVELOPMENT AND IMPLEMENTATION

Julia Unterscheider, Fergal Malone - Department of Obstetrics and Gynaecology, The Rotunda Hospital, Royal College of Surgeons in Ireland, Dublin and Perinatal Ireland Research Consortium - www.hse.ie or www.rcpi.ie

Evidence-based clinical practice guidelines (CPGs) are designed as quality measures aimed at standardising and improving care for a defined population and specific clinical circumstances. Despite the large amount of published literature on ultrasound in the setting of FGR, there is a paucity of good quality evidence and no international consensus on optimal definition, management and timing of delivery. Guidelines need to be practical, applicable and pragmatic taking into account local factors, expertise and resources. They should summarise the published evidence in a succinct manner. While a systematic review summarises the evidence in detail, CPGs should interpret the evidence for the reader in a practical manner where key recommendations can be easily found.
This presentation will give an overview of the recently introduced Irish guideline on fetal growth restriction

10.3 S COST BENEFIT ANALYSIS OF RCOG GUIDELINES FOR THE INVESTIGATION AND MANAGEMENT OF THE SGA FETUS

Jason Gardosi
Perinatal Institute, Birmingham, UK

This presentation will summarise ongoing work to estimate the cost of implementing the new RCOG guidelines, focussing on potential benefits and required resources for scanning policies in pregnancies designated ‘high risk’.

11.1 K MACROSOMIA - DEFINITION, MANAGEMENT AND OUTCOME

Dharminthra Pasupathy
St Thomas Hospital, London, UK

Pregnancies complicated by higher than normal birth weight are associated with adverse outcomes causing significant short and longer term maternal and fetal morbidity. The population prevalence of macrosomia and large for gestational age (LGA) infants is increasing, primarily driven by rising rates of maternal obesity and impaired glucose tolerance. Improvements in pregnancy outcomes are limited by poor antenatal prediction of pregnancies at risk and limited interventions that may be available especially in women without gestational diabetes (GDM), who contribute significantly to the proportion of macrosomic infants (>80. These limitations may be due to the current definitions of macrosomia and LGA which do not distinguish between infants who are appropriately grown for maternal constitution with normal growth velocity from those which have exceeded their growth potential. This presentation will focus on current evidence, methods to improve characterisation and antenatal prediction of excessive fetal growth and also discuss the potential interventions that may impact clinical management.

11.2 S OBSTETRIC OUTCOMES AT TERM IN PREGNANCIES WITH LARGE FOR GESTATIONAL AGE BABIES

Dr David Bailey
Northland District Health Board, Whangarei, New Zealand

Objective: To investigate the association of delivery of a large for gestational age (LGA) term baby (>90th percentile) with adverse maternal and perinatal outcomes in a multi-ethnic New Zealand population where LGA, type 2 and gestational diabetes are common.
Method: This was a retrospective observational study of 61045 births at 37-42 weeks gestation in South Auckland, New Zealand 2001-2010. Height-weight measures were not available for most of the pregnancies, so birth weights were designated small (<10th percentile), normal (10-90th percentile) or large (>90th percentile) for-gestational-age using ethnic-specific gestation-related birth weight centile charts constructed from the CMDHB population using the GRAW methodology.
Results: Compared to pregnancies with normal birth weight, LGA was associated with significantly increased rates of caesarean section (CS), perineal trauma requiring repair in theatre and neonatal unit admission for both nulliparous and multiparous mothers. These findings persisted after adjustment for maternal age, ethnicity, deprivation, previous CS and diabetes. Antenatal stillbirth was significantly increased among multiparous women with birth weight >97th percentile, but this effect disappeared when diabetes was excluded.
CS in spontaneous labour was investigated in nulliparous women with single fetus and cephalic presentation. The CS rate increased progressively with birth weight above about 3.5 kg, which is close to the 50th percentile of the population at 40 weeks. However at 41-42 weeks gestation the CS rate was elevated across the birth weight range compared to 37-40 weeks.
Conclusions: LGA is associated with an increase in obstetric complications, but perinatal mortality is only increased with LGA and diabetes. Increased CS in prolonged pregnancy is not explained by birth weight alone

11.4 S RISK FACTORS FOR NEONATAL MORBIDITY IN LGA INFANTS

Vieira MC, Dib F, McCowan L, North R, Kenny L, Myers J, Dekker G, Walker J, Baker P, Poston L, Pasupathy D on behalf of the SCOPE consortium King's College London, London, United Kingdom

Objective: To identify clinical factors associated with neonatal adverse outcomes in LGA infants.
Method: Prospective cohort of nulliparous women recruited to the multicentre SCOPE study who delivered LGA (birth weight > 90th customized centile) infants at term. We compared maternal and fetal factors between LGA infants with and without neonatal morbidity. Neonatal morbidity was defined by severe neonatal morbidity (composite outcome comprised of ≥1: perinatal or infant death, grade II/III hypoxic ischemic encephalopathy, 5-minute Apgar score <4, cord arterial pH<7.0 and/ base excess <-15, neonatal seizures, neonatal ventilation>24 hours or admission to NICU>4 days) or any admission to neonatal care. Factors evaluated were maternal age; ethnicity; early pregnancy (15 & 20 weeks') - height, weight, BMI, BP, random glucose, smoking; fetal biometry at 20 weeks'; pregnancy outcome – gestational diabetes (GDM), pre-eclampsia; onset of labour and mode of delivery; gestational age at delivery (GAd) and birthweight. A multivariate model was developed from clinical factors identified from univariate analysis.

Results: In the SCOPE cohort, 8.7% (n=491) were LGA at term with a median birth weight of 4190g (IQR 3950-4440g). The incidence of LGA related neonatal morbidity was 11.8% of LGA (n=58). Factors associated with neonatal morbidity in univariate analysis were maternal obesity at 15 weeks (OR 2.3; 95%CI 1.2-4.4); random glucose (mmol/L) (OR 1.6; 95%CI 1.2-2.0) and no exercise at 20 weeks (OR 4.3; 95%CI 2.0-9.0); induction of labour (OR 2.1; 95%CI 1.2-3.7); and birthweight (/100g) (OR 1.1; 95%CI 1.1-1.2). In multivariate analysis only random glucose (mmol/L) (OR 1.4; 95%CI 1.1-1.9) and no exercise at 20 weeks (OR 4.1; 95%CI 1.8-9.2); induction of labour (OR 2.0; 95%CI 1.1-3.8); and birthweight (OR 1.2; 95%CI 1.1-1.3) were associated with LGA related morbidity.
Conclusion: There are maternal factors which are associated with neonatal morbidity amongst term LGA infants.

11.5 S CLINICAL PREDICTION OF FETAL OVERGROWTH IN PREGNANCIES COMPLICATED BY DIABETES

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[2]Southcoast Health System, Fall River, Massachusetts, USA

Objective: To develop a formula that incorporates widely available clinical factors to predict fetal overgrowth in pregnancies complicated by diabetes.
Methods: Data were derived from a cohort of patients enrolled in a collaborative diabetes in pregnancy program between 2010 and 2012. The primary outcome was fetal overgrowth defined as a birth weight ≥ 90th customized percentile. A logistic regression model predicting fetal overgrowth was created using a stepwise selection algorithm that incorporated clinical factors available in the first 20-30 weeks of pregnancy. Each of the factors included in the final multivariable model was assigned a weight based on its beta coefficient. The sum of weights yielded a fetal overgrowth index for each pregnancy analysed.
Results: The cohort included 275 singleton gestations, of which 51 (18.5%) were complicated by fetal overgrowth. The derived fetal overgrowth index included five clinical factors. Area under the receiver operating characteristic curve (AUC) for the index was 0.87 (95 % confidence interval [CI] 0.78-0.94). An alternative model that included five clinical factors available in the first 20 weeks of pregnancy yielded a fetal overgrowth index with an AUC of 0.79 (95% CI 0.70-0.87). Cut-points were selected that identified a “high risk” index range that has a positive predictive value of 84% and a “low risk” index range that has a negative predictive value of 95%. The majority of patients in our cohort (66%) had a “low risk” index while 9% had a “high risk” index. Approximately one-third of the remaining 25% of pregnancies with an “intermediate risk” index were complicated by fetal overgrowth.
Conclusion: This new fetal overgrowth index that incorporates five clinical factors provides a means of predicting which pregnancies complicated by diabetes are at highest risk of fetal overgrowth and thereby serves as a tool for targeting the allocation of healthcare resources and treatment individualization.

11.6 S INSULIN GROWTH FACTORS AND THEIR BINDING PROTEIN EXPRESSION IN PREGNANCIES AFFECTED BY DIABETES AND OBESITY

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Objective: The insulin–like growth factors 1 and 2 (IGF1 and IGF2) are known to play an important role in placental and fetal growth. We sought to investigate whether the placental expression of IGF and their binding proteins (IGFBPs) is altered in women delivering small for gestational age (SGA; birth weight <10th percentile for gestation) and large for gestational age (LGA; birth weight >90th percentile for gestation) neonates compared to those delivering appropriate for gestational age (AGA) neonates.
Methods: We included 73 pregnant women with singleton pregnancies; 37 with AGA, 16 with SGA and 20 with LGA neonates. Placental samples were obtained at delivery and stored at -800C. Laboratory techniques involved RNA extraction, cDNA preparation, gel electrophoresis for confirming the product size, real time PCR for gene expression and western immunoblotting for protein analysis.
Results: Compared to AGA group, placental expression of IGF1 gene was found to be significantly lower in SGA neonates ($p<0.01$) but no different in the LGA group. There was no difference in placental IGF2 expression between the groups. Placental IGFBPs 1, 2, 3, 4 and 7 expression was significantly higher in SGA neonates while IGFBPs 1, 2 and 3 were significantly down-regulated in the LGA group (both $p<0.01$). We show for the first time the presence of IGFBP7 in term placenta.
Conclusions: The placental expression of IGFs and their binding proteins differ in fetal growth disorders. We have found placental gene expression of IGFBP1, 2 and 3 to be inversely correlated with birth weight. Whether these alterations cause FGR or are an associated finding requires further investigation.

1.1 P MEASUREMENT OF EARLY CHILDHOOD OBESITY IN CHILDREN BORN SGA VS. AGA

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Objective: The Fetal Origins of Adult Disease Hypothesis suggests that fetal life, and fetal growth, are associated with long-term changes in metabolism that impact chronic disease risk. As they grow older, children born small for gestational age (SGA) are more often underweight compared with children born appropriate for gestational age (AGA). Further, studies have suggested that, relative to their AGA peers, SGA children have a reduced amount of lean body mass and a higher percentage body fat for a given body mass index (BMI). However, research on the performance of childhood obesity metrics in the SGA population is scant, especially among younger children among whom the impact of fetal growth may be most relevant. We used data from the Follow-Up Development and Growth Experiences Study (FUDGE, 1997-99) to compare obesity and adiposity in 54-month-old children who were born SGA (n=288) and AGA (n=137) in Atlanta, Georgia.
Method: Adiposity was assessed using BMI, triceps-, and subscapular-skinfold-thickness (TST, SST). For each metric, normal weight was defined as being in the 5 - 85% and overweight/obese as being in the top 15% according to CDC norms.
Results: Overall, the prevalence of overweight/obesity was higher in AGA children compared with SGA children for all three obesity metrics (BMI: 27.7% vs. 9.7%, TST: 8.0% vs. 3.8%, SST 10.2% vs. 6.9%), though the relative prevalence differed by metric. Further, among children with a normal BMI, TST and SST Z-scores in SGA children were similar to (and minimally higher than) those in AGA children (TST: -0.67 vs. -0.78, SST: -0.60 vs. -0.63).
Conclusions: These findings suggest that children born SGA may have, on average, more adipose tissue than children born AGA. The use of skinfold thickness metrics, rather than relying only on BMI, may provide a better picture of early childhood obesity in the SGA population.

1.2 P THE CONTRIBUTION OF SOFT TISSUE TO BIRTHWEIGHT

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Objective: To determine the contribution of fetal soft tissue to birthweight in an exercise intervention study in overweight women.
Method: Women recruited to an exercise in pregnancy study (IMPROVE) in Auckland, New Zealand were offered serial ultrasound scans from 24 weeks of pregnancy. These included 3D limb volume data sets to measure limb circumference and partial limb volume of the thigh and upper arm using the method described by Lee (2008). Separate measurements of muscle and fat were also measured. The last measurements for the above parameters before delivery were compared with fat distribution estimates from postnatal DXA scans at age 2 weeks.
The arm and leg fat measured on DXA utilised the whole limb compared with just thigh and upper arm utilised in the ultrasound models.
Data are presented on the women who have delivered and had both DXA and ultrasound scans (n=37).
Statistical analysis was by multiple linear regression analysis.
Results: Soft tissue parameters on the last scan at36 (+/- 2) weeks' that were significantly associated with birthweight were abdominal circumference (p=0.002), arm circumference (p=0.007) and arm fat circumference percentage (p=0.009).
When ultrasound limb fat percentage at 36 weeks' and fat percentage on DXA scans at 2 weeks of postnatal age were compared there were significant linear relations for both the leg and trunk fat measurements in spite of the 6 week interval between the scan and DXA scan and that ultrasounds were of the upper limb and DXA was on the complete limb

Table: Comparison of ultrasound and DXA measurements

Ultrasound at 36 wks	DXA at 2wks of age	P value
Thigh fat vol %	Leg fat %	0.03
Thigh fat circ %	Leg fat %	0.05
Abd Circ %	Trunk fat %	0.04

Conclusion: Soft tissue is an important contributor to birthweight that is not often measured in the fetus. Assessment of limb soft tissue may be a better predictor of fetal adiposity than abdominal circumference. Ultrasound estimates of fetal adiposity may help to determine the influence of exercise in pregnancy when the trial is finished.

Reference: Lee W, Balasubramaniam M, Deter RL, Hassan S, Gotsch F, Kusanovic JP, Goncalves LF, Romero R. (2009). "Fractional limb volume: a soft tissue parameter of fetal body composition. Validation, technical considerations, and normal ranges during pregnancy." Ultrasound Obstet Gynecol 33: 427-440.

1.3 P ASSESSMENT OF INTRACRANIAL STRUCTURE VOLUMES IN FETUSES WITH GROWTH RESTRICTION BY MEANS OF THREE-DIMENSIONAL ULTRASOUND USING THE EXTENDED IMAGING VIRTUAL ORGAN COMPUTER-AIDED ANALYSIS METHOD.

Ana Carolina Rabachini CAETANO (MD); Ana Cristina Perez ZAMARIAN (MD); Edward ARAUJO JÚNIOR (PhD); Rafael Oliveira CAVALCANTE (MD); Carolina PACHECO (MD); Antonio Fernandes MORON (PhD); Luciano Marcondes Machado NARDOZZA (PhD)
Department of Obstetrics, Paulista School of Medicine – Federal University of São Paulo (EPM-UNIFESP), São Paulo-SP, Brazil.

Objective: To assess the volume of the fetal head, the frontal region of the brain, the cerebellum and the relationship between the frontal brain and fetal head through the three-dimensional ultrasonography using the eXtended Imaging Virtual Organ Computer-aided Analysis (XI VOCAL) method in fetal growth restriction (FGR) comparing them with appropriate for gestational age fetuses. To assess intra-and interobserver repeatability of the method.
Methods: We conducted a prospective cross-sectional study in 125 singleton pregnancies between 24 and 34 weeks, divided into 3 groups (controls, restricted below the 3rd percentile and restricted between percentiles 3 and 10). For the estimation of fetal weight, we used Hadlock 4 formula. To measure the volumes of the fetal head, the frontal region of the brain and cerebellum, we used the XI VOCAL method with delimitation of 10 sequential plans. For evaluation and comparison of volume measurements of brain structures in the three groups we used ANOVA and the Tukey multiple comparisons method. Regarding the repeatability of the method the intraclass correlation coefficient (ICC) and Bland-Altman were used.
Results: We have observed a statistical significance difference between the volumes of brain, frontal region, cerebellum and the relationship between the frontal region and fetal head of fetuses with estimated weight < 3th and controls, with $p<0.001$, $p<0.001$, $p=0.002$ and $p=0,008$; respectively. We have observed a good intra and inter-observer repetibility to fetal brain, frontal region and cerebellum volumes with ICC 0,998, 0,997, 0,997, 0,999, 0,997 and 0,998; respectively.
Conclusion: The volumes of the fetal head, the frontal region of the brain, cerebellum and relationship frontal region/fetal head measured by three-dimensional ultrasound using the XI VOCAL method are reduced in fetuses affected by FGR in relation to the appropriate weight for gestational age. There was excellent intra-and interobserver repeatability in all volumes evaluated.

1.4 P AN AUDIT FOLLOWING IMPLEMENTATION OF CUSTOMISED GROWTH CHARTS IN A TERTIARY UNIT

Renuka Sekar and Candy Kwan
Royal Brisbane and Women's Hospital, Australia

Objective: To assess compliance in using customised growth charts since implementation in our unit. Has this improved earlier detection of SGA babies thus improving outcomes?
Design: Retrospective cohort study in the general hospital population over the first 3 months after implementation of customised growth charts
Setting: Royal Brisbane and Women's Hospital, Brisbane, Australia
Methods: A preliminary review of sixty babies born between 26th June 2014 and 9th July 2014 from the general population were classified as small for gestational age (SGA), normal for gestational age (normal) or large for gestational age (LGA) by two standards: customised percentiles which account for height, booking weight, ethnicity, parity and infant sex) and standard percentiles (Australian population growth curves from Kitchen et al, 1983). Perinatal mortality rates were compared between births before and after implementation of customised growth charts.
Results: At birth, only 2 (3.33%) babies were identified as SGA using standard percentiles, whereas 7 (11.67%) were identified as SGA using customised percentiles. 5 (8.34%) additional babies were identified as SGA using customised percentiles. SGA could have been identified antenatally using customised growth percentiles in 2 of those 5 births. From the sixty pregnancies, there were 433 encounters where fundal height or estimated fetal weights were noted. Of these, only 98 (22.6%) encounters were plotted on a customised growth chart. The perinatal mortality rate for the 3 months leading up to implementation of customised growth charts was 1.73% compared to 0.76% over the 3 months post-implementation.
Conclusions: In the population studied, customised birth weight percentiles detect more SGA babies than standard percentiles. Customised growth charts may help identify more SGA babies antenatally to reduce both perinatal mortality and morbidity although to date, its utility is limited by low compliance.

1.5 P AUDIT: THE ESSENTIAL LINK TO EVALUATION OF CUSTOMISED GROWTH CHARTS IN CLINCAL PRACTICE

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University Hospitals of Coventry and Warwickshire NHS Trust, United Kingdom

Objective: To evaluate the effectiveness of customised growth charts in the identification and management of SGA foetuses within the Trust, as despite using charts for a number of years the detection rate had not increased significantly and below the regional average.
Method: An audit was undertaken of 50 SGA cases, the cases were identified from a database, where all births are recorded, current practice was to identify SGA if the birthweight plotted below the 10th centile on the customised chart
A profprma was designed to ask specific questions regarding:

- Were there predisposing risk factors
- Was SGA was suspected and detected antenatally
- What antenatal investigations were initiated
- Any intrapartum complications
- Delivery details
- Calculation of birthweight centile

Results: When birthweight centiles were calculated - 11 cases were not actually SGA, and 7 had been recorded as missed SGA. Early involvement of senior staff demonstrated appropriate management and expedited delivery. Midwives referred appropriately based on fundal height measurements
In the cases where SGA was not detected, often antenatal surveillance was Inappropriate i.e. no scans when antenatal risk factors present or serial scans stopped after 36 weeks. If scans undertaken after 36 weeks estimated fetal weights were not calculated In 2 cases where SGA had been identified and increased fetal surveillance was imitated the need for early delivery was not recognised and the pregnancies continued to post maturity, with satisfactory birth outcomes but centiles calculated as 0.
Conclusions: Involvement of senior staff is essential to plan management when IUGR is recognised
Customised birthweight centiles aid clear identification of SGA cohort. Estimated fetal weights aid detection and provide information for appropriate management
When IUGR has been identified clear management plans should be documented within the pregnancy notes. Audit should be undertaken annually to ensure recommendations have been implemented into practice.

1.6 P ANTENATAL DETECTION OF SMALL FOR GESTATIONAL AGE BEFORE AND AFTER INTRODUCTION OF CUSTOMISED GROWTH CHARTS: EXPERIENCE OF A LARGE TEACHING HOSPITAL

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Objectives: Liverpool Women's Hospital introduced customised fetal growth charts in 2012. We present comparison of detection rates, and pregnancy outcome, of small for gestational age (SGA) pregnancies (<5th centile) from before and after implementation.
Method: Retrospective analysis of all births in 2011 and a prospective audit of births in a single month in 2014. All singleton deliveries with a birthweight <10th centile using population based charts were identified from hospital records; customised birthweight centiles were produced for this group. Only those with a customised birthweight <5th centile were included in further analysis. SGA was deemed to have been identified if there was an entry in the medical records of SGA, growth restriction, oligohydramnios, reduced fetal movements, hypertension or preeclampsia.
Results: There were 444 cases of SGA (<5th customised) born in 2011, 5.5% births. In April 2014 there were 44 cases of SGA, 6.9% births. There was a significant improvement in detection of SGA between 2011 and 2014, from 149/444 (33.5%) to 22/44 (50%) p=0.032. In 2014 customised growth charts were implemented in 35/44 (79.5%) of the SGA cases. Customised charts were used in all the identified cases of SGA (22/22), but only 13/22 of the non-identified cases, giving the GROW charts an SGA detection rate of 62%.
In both audits there was a higher induction rate in the SGA detected vs. undetected group (2011 RR=3.70, 95%CI 2.78-4.91 and 2014 RR=2.42,95%CI 1.26-4.26). In 2011 there was a higher Caesarean section rate in the identified group (RR=1.4 95%CI, p=0.04), this did not reach significance in 2014 (50% vs 36%).
Conclusions: Our data show an improvement in detection of SGA with implementation of customised growth charts. The small sample size in 2014 limits the comparability of pregnancy outcomes, but given the increased obstetric intervention with SGA detection this warrants further investigation.

1.7 P DIAGNOSIS OF FETAL GROWTH RESTRICTION ON TWIN PREGNANCIES, USING DIFFERENT FETAL GROWTH STANDARDIZED FORMULAS

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Method: retrospective study of twin births occurred in our hospital during the last four years. Variables: fetal weight percentile obtained using Hadlock's formula (1984),which is included in our ultrasound equipment packages, and percentile obtained by using Clinic Barcelona Hospital's multiple III TM gestational percentile calculator (Figueras, 2000), an specific formula for twin pregnancies. Both fetal weight percentile were compared.
Results: total number of births during the past four years was 13037, 329 of them were twin deliveries (2.52%). Using Hadlock's formula, for singletons pregnancies, in 48'9% of them at least one fetus had an estimated fetal weight below the 10^{th} percentile for gestational age, and in 34% of them, both fetuses had. Furthermore, 30'4% of the pregnancies had an estimated fetal weight below the 3^{rd} percentile for gestational age in at least one fetus and 15'1% in both of them. However, if we use Figueras formula, designed specifically for twin pregnancies, we found that only 16'4% of the pregnancies had an estimated fetal weight below 10^{th} centile in at least one fetus, and 6'3% below 3^{rd} percentile. The incidence of selective fetal growth restriction in one of the two fetuses was 94% below 10^{th} centile and 85% below 3^{rd} percentile.

Conclusion: Right diagnosis of fetal growth restriction on twin pregnancies needs to use specific standardized formulas.

1.8P INCIDENCE OF FETAL GROWTH RESTRICTION IN PRETERM AND TERM PREGNANCIES

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Objective: the aim of the study was to asses de incidence of fetal growth restriction in preterm (delivery ≤ 37 weeks) compared to term pregnancies (delivery > 37 weeks)
Method: retrospective study of the deliveries occurred in our hospital during three years. Twin pregnancies were excluded. Variables: number of deliveries, gestational age at delivery, birth weight and its percentile. Clinic Barcelona Hospital's III TM growth centile (singletons) calculator (Francesc Figueras) was used.
Results: number of deliveries in that period was 9968; 1611 of them were preterm and 8357 at term. The overall incidence of inadequate fetal growth, defined as a weight below 10^{th} centile for gestational age, in both groups jointly was 7.5%, and 3.9% of them were below 3^{rd} percentile. Considering the group of preterm deliveries, in 404 cases (25%) birth weight was $<10^{th}$ centile and in 234 (14.5%) $<3^{rd}$ percentile. On the other side, in the group of those ones that exceeded 37 week, 344 cases (4%) had a birth weight below 10^{th} centile and 161 (1.9%) below 3^{rd} percentile. Comparing both groups, it was noted that incidence of fetal growth restriction was higher in preterm deliveries, with a statistically significant difference ($p < 0.001$). Furthermore, 78% of preterm deliveries of a growth restricted fetus were diagnosed during pregnancy, while at term deliveries, only 22% were diagnosed.
Conclusion: the incidence of fetal growth restriction on fetuses born below 37 weeks is higher than on those born at term, possibly due to an increased diagnosis, leading to deliver those pregnancies.

2.1 P AMNION DISRUPTION SEQUENCE: A NEW PERSPECTIVE ON THE PATHOLOGICAL MECHANISM.

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Objective : To examine the placentae in a series of amnion disruption sequence (ADS) cases for HPV infection.
Methods: The placentae from 7 cases (gestational ages 13, 17, 19, 23, 26, 27 and 37 weeks gestation) were examined from the Otago Placenta Study and case records at Dunedin Hospital from 2006 to 2014.Four ADS cases showed the classical fetal consequences, two cases consisted of intrauterine ultrasound and pathologically detected amnion chorion separation, and one case consisted of ultrasound detected, but not pathologically confirmed amnion bands. Placental histopathology, HPV immunohistochemistry (clone K1H8,Dako, Glostrup, Denmark) and in situ hybridisation (GenPoint™ Amplified Signal Detection System Cocktail) for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68 were performed.
Results: Six of the ADS placentae showed HPV L1 IHC positivity and four cases in-situ hybridisation positivity for high risk HPV, including the amnion epithelium. In three of the high risk HPV positive cases a histopathological sclerosing villitis was present. The ultrasound detected, but not pathologically confirmed, ADS case did not have a villitis, and was negative for IHC and GenPoint assays.
Conclusions: These findings suggest that development of amniotic band disruption sequence is associated with HPV infection of the placenta.

2.2 P THE IMMUNOHISTOCHEMICAL DETECTION OF HPV L1 CAPSID PROTEIN IN THE PLACENTA AND MATERNAL CERVICAL SMEAR HISTORY

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Objective: To determine the correlation of the immunohistochemical detection of HPV L1 capsid protein in the placenta and fetal growth restriction (FGR), preterm delivery, and cervical smear results.
Methods: A cross sectional study of 120 singleton placentae collected for the ethically approved Otago Placenta Study from 2009 to 2014, in Dunedin New Zealand, comprised 36 pre-term cases, 38 idiopathic fetal growth restriction cases (FGR, ≤5th personalised growth centile (PGC), as determined by the Gestation Network Calculator for NZ), 33 normal term pregnancies >10th PGC, and 12 stillbirths for which no cause was found following full post mortem by a perinatal pathologist. Known maternal or fetal medical conditions were excluded. For ninety of these cases a cervical smear had been performed within 7 years prior to the index pregnancy and results were available from the National Cervical Screening Register. A randomly selected centrally located transmural section of placenta was subject to HPV antibody (clone K1H8,Dako, Glostrup, Denmark) which reacts to major capsid protein of HPV-1, in HPV types 6, 11, 16, 18, 31, 33, 42, 51, 52, 56 and 58. Cases were scored positive if either the decidua or villous trophoblast were positive.
Results Overall 64 % (77/120) of cases were positive for HPV L1 in the placenta using L1 HPV IHC. In the premature delivery group 75% were HPV L1 positive, and in the FGR group 71% were HPV L1 positive. Of the 19/90 women with a positive HPV-related smear result within seven years of the index pregnancy, 89% (17/19) were HPV L1 positive, whereas 6% (2/19) were HPV L1 negative. This is a statistically significant correlation χ^2 (2, N=90)=6.75, p=0.03.
Conclusion: These results suggest HPV L1 IHC detection in the placenta is associated with pregnancy complications, and cervical HPV infection. Multivariate analyses adjusting for confounding variables are progressing in a larger cohort.

2.3 P HISTOPATHOLOGY OF TREATED CHRONIC HISTIOCYTIC INTERVILLOSITIS

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Objective: To present the histopathological features of untreated and treated chronic histiocytic intervillositis (CHI).
Method: Four placentae from six consecutive pregnancies were examined histopathologically from a 31yr old P0G6 woman. CHI was diagnosed in her fifth pregnancy which was growth restricted and an intrauterine demise at 20 weeks. In the sixth pregnancy, a regime of oral daily prednisone 20mg from conception to 20 weeks, oral daily aspirin 100mg from conception onward, and daily subcutaneous enoxaparin 40mg from six weeks onward, was instituted..
Results: Three pregnancies demonstrated CHI histopathologically, but the diagnosis was missed in the first two pregnancies. The first live born fetus was delivered at 35 weeks gestation with personalised growth centile of 15, in the sixth treated pregnancy. Minimal intervillous and perivillous fibrin was present in the treated liveborn placenta compared to the previous three placentae. The histiocytic infiltrate was also reduced but not eliminated.
Conclusions: CHI is diagnosable in first trimester miscarriage following D&C, and increasing awareness of this entity in the D&C specimen by pathologists will provide the opportunity for earlier pregnancy treatment. This treatment regime appears to prevent intervillous fibrin accumulation, lower histiocyte count, and improve fetal growth.

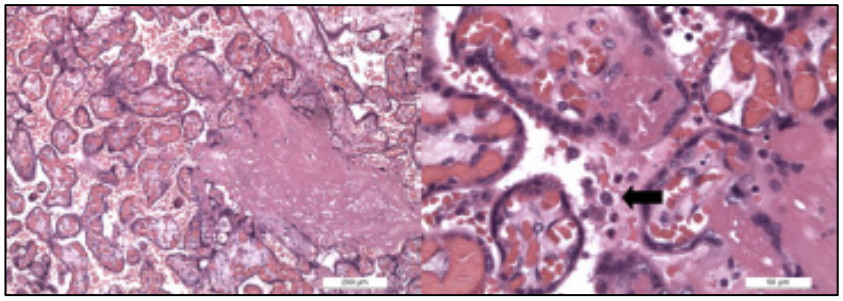

Figure 1: Treated placenta at 35 weeks gestation with only one area of fibrin found in six transmural sections (left, low power) and scattered intervillous histiocytes (right high power).

2.4 P NORMAL VALUES OF BRAIN- THYMUS WEIGHT RATIO IN NON-IUGR PERINATAL DEATHS

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Objective: Thymus weight reflects fetal/neonatal wellbeing. Similarly to the liver, the thymus shrinks in response to intrauterine malnourishment, but also to other causes of stress e.g. intrauterine infection. Pathologists use thymus weight as an indicator of chronic stress, but interpretation may be difficult if the gestation is uncertain or the baby is SGA. Brain:liver weight ratio is an accepted indicator of fetal growth as brain growth is maintained in IUGR at the expense of other organs, but is not always reliable when used in isolation. We sought to determine the normal values of brain:thymus weight ratio as part of a project to improve the pathological identification of IUGR in stillbirths.
Method: Normally grown intrauterine, intrapartum, or neonatal deaths over 22/40 gestation with body weight >25th centile (237 cases) were extracted from our MSaccess Database of >5000 autopsies. Cases with moderate or severe maceration (205), limited examination (168), abnormalities (149) and neonates surviving more than 2 days were excluded. This left 130 cases to analyse.
Results:

Category by centile/ B/L ratio:	No	Br/Liv ratio ± SD	Br/Thy ratio ± SD
BW >25th	130	2.84±0.91	46.7±29.5
BW>25th and B/L<4	115	2.6±0.64	44.4±22.7
25th<BW<90th	108	2.9±0.90	47.1±30.4
25th<BW<90th and B/L<4	95	2.66±0.60	44.1±22.8
22-23/40 >25th &B/L<4	7	2.60±0.64	89.3±39.8
25-28/40 >25th &B/L<4	13	2.64±0.63	59.1±14.4
29-32/40 >25th & B/L<4	14	2.80±0.46	59.2±23.0
33-36/40 >25th & B/L<4	16	2.50±0.75	41.2±16.2
34-40/40 >25th & B/L<4	46	2.53±0.67	32.6±12.0
41-42/40 >25th & B/L<4	19	2.70±0.61	36.1±10.3

BW=birth weight; L=liver; B=brain

Conclusion: Brain/thymus weight ratio in this group of normally grown fetuses appears to lie in a narrow range and we suggest at <32/40 ~70 marks the upper limit of normal, whilst at >32/40 ~50 is appropriate. Further evaluation is planned to assess the efficacy of these cut-offs in identifying and analysing cases of IUGR.

2.5 P EVALUATION OF ANGIOGENIC FACTORS COMBINED WITH DOPPLER PARAMETERS IN HEALTHY CONTROLS AND FETAL GROWTH RESTRICTION.

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Objective: Assessing the angiogenic factors levels and the Doppler parameters in healthy controls and fetal growth restriction (FGR).
Methods: This case-control study included 66 patients with diagnosis of FGR and 64 healthy pregnancies at 24-41 weeks of gestation. For both groups, maternal circulating concentrations of angiogenic factors of soluble fms-like tyrosine kinase-1 (sFlt-1), soluble endoglin (sEng), adiponectin, A Disintegrin and Metalloproteinases (ADAM-12), pregnancy-associated plasma protein-A (PAPP-A), Angiopoietin-2 (ANGI-2), vascular endothelial growth factor (VEGF), placental protein 13 (PP13) and Transforming growth factor-β (TGF-β) were assayed by ELISA method and uterine artery (UtA) by Doppler studies were performed. Logistic regression was applied to analyze relationships between angiogenic factors and Doppler parameters.
Results: Concentrations of sFlt-1, sEng, PAPP-A were significantly higher in FGR pregnancies than controls ($p<0.0001$, $p=0.02$ and $p=0.03$, respectively), but concentration of ADAM-12, ANGI-2 ($p=0.05$ and $p<0.0001$) were significantly lower in FGR diagnosed than controls. Increased sEng concentrations were correlated with abnormal UtA Doppler in FGR. Adiponectin and TGF-β were not associated with any analyzed parameters.
Conclusion: Fetal growth restriction showed increased serum levels of sFlt-1, sEng and PAPP-A with levels of ADAM-12 and ANGI-2 decreased. Moreover, a positive association between elevated concentrations of sEng and changing impedance of UtA Doppler were observed.

2.6 P PLACENTAL T2* IN NORMAL PREGNANCY AND IN TWO CASES OF FETAL GROWTH RESTRICTION

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Objective: To investigate placental T2* in uncomplicated pregnancy and in two cases of fetal growth restriction (FGR) due to placental insufficiency.
Methods: Placental T2* was estimated in 24 uncomplicated pregnancies (gestational week 24 to 40) and in two extreme cases of FGR. In FGR cases ultrasound Doppler examination demonstrated redistribution of fetal blood flow indicating light fetal hypoxia (case 1, gestational week 30+3) and severe hypoxia and acidosis (case 2, gestational week 24+5). Placental T2* measurements were performed using a gradient recalled echo sequence with multiple readouts at 16 different echo times. T2* value was calculated using a non-linear fitting algorithm. The linear correlation between T2* measurements and gestational age was estimated by Pearsons correlation coefficient.
Results: (figure 1): In normal pregnancies the mean T2* was 81.3±28.1 ms and a negative linear correlation between T2* and gestational age was found (R^2 =0.68, $p<0.001$) with a decline of 4.8 ms per week. In the FGR cases the placenta appeared darker in the T2*-weighted MR image and the T2* was 29.6 ms and 27.0 ms respectively.
Conclusion: In normal pregnancies placental T2* decreases with gestational age. This finding reflects a combination of: (1) A morphological maturation of the developing placenta as previously demonstrated by placental T2 measurements and (2) A decrease in placental oxygenation as pregnancy advances. In the FGR cases the T2* was reduced suggesting abnormal placental morphology and reduced placental oxygenation. Placental T2* measurement has the potential to become a non-invasive test of placental morphology and oxygenation in FGR pregnancy.

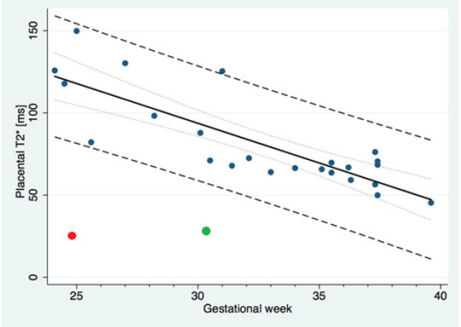

Figure: The linear relation between placental T2* in normal pregnancies (Blue dots) and gestational week. Thick line is ordinary least squares fit ($P<0.001$. $R^2=0.68$). Dotted lines indicate 95% confidence interval while dashed lines indicate 95% prediction interval. Green dot: case 1, Red dot: case 2.

2.7 P THE IMPACT OF SCREENING FOR SMALL-FOR-DATES FETUS USING LOW MATERNAL PREGNANCY ASSOCIATED PLASMA PROTEIN-A

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The first trimester combined screening test was introduced in our Trust in 2010. Across the four maternity units in the Trust, there had been no uniform decision on the management of low level of pregnancy associated plasma protein-A (PAPP-A) reported from the test. At the Oldham unit where there was local fetal medicine input, patients with low PAPP-A levels had been offered uterine artery Doppler and serial growth scans since 2012. We examined the outcome of this cohort of patients. The publication of the Royal College of Obstetricians and Gynaecologists Greentop Guideline No. 31 ("The Investigation and Management of the Small-for-Gestational-Age Fetus") in 2013 had highlighted the importance of low PAPP-A level in predicting small-for-gestational-age fetus. This has also prompted the authors to assess the potential impact of implementing this practice across the Trust, which total around 10,000 deliveries annually.
Patients with low PAPP-A were identified retrospectively from the ultrasound scan appointment records. The findings of their ultrasound scans and pregnancy outcome were recorded from the Picture Archiving and Communication System (PACS) and electronic maternity records respectively. Analysis was performed to estimate the cost implications of making this practice trust wide.
Only a total of 65 patients were identified with low PAPP-A over the two-year period due to the low uptake (40%) of combined screening in our unit. A number of adverse pregnancy outcomes were identified and will be discussed.
Our findings confirmed those of published literature on the effect of low PAPP-A and pregnancy outcome. Although our analysis showed additional cost largely incurred by the additional ultrasound sessions, the correlation between low PAPP-A levels and adverse pregnancy outcome was evident. Every effort should be made to ensure additional surveillance is in place for these women and fetuses in accordance with the RCOG guidelines.

2.8 P RELATIONSHIP BETWEEN NUCLEATED RED BLOOD CELL COUNTS AND OBSTETRIC AND NEONATAL OUTCOMES IN SMALL-FOR-GESTATIONAL-AGE FETUSES WITH NORMAL UMBILICAL ARTERY DOPPLER

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Objective: Because identification of small-for-gestational-age (SGA) fetuses with true milder forms of growth restriction cannot be determined by umbilical artery Doppler, other parameters associated with perinatal complications have been proposed. The present study aims to evaluate obstetric and neonatal outcomes in pregnant women with SGA fetuses after 35 weeks depending on the nucleated red blood cell (NRBC) count in umbilical cord blood.
Method: The NRBC count per 100 white blood cells in umbilical cord blood was collected from 61 pregnant women with small-for-gestational-age fetuses and normal umbilical Doppler. These were divided into two groups: NRBC> = 10 (trial, n = 18) and NRBC <10 (control, n = 43). Obstetric and neonatal outcomes were compared between groups. The umbilical artery pH, blood gases and base excess were also evaluated. Data was compared using the chi-square, Fisher exact test and Mann-Whitney test, and it was considered the significance level of 5%.
Results: The median nucleated red blood cell per 100 white blood cells was 25.0 ± 13.5 in the study group and 3.9 ± 2.2 in the control group. The group NRBC> = 10 has shown higher rates of cesarean delivery (51.2 x 83.3%, p = 0.01), fetal distress (0 x 50%, p <0.01) and pH <7.20 (11.8 x 42.9%, p = 0.02). Birth weight was observed significantly lower in the group NRBC> = 10 (2062 x 2309 g, p <0.01) as well as weight percentile for gestational age (2.4 x 5.1, p = 0.04). No neonates had <7 5-min Apgar score. There were no diferences between the groups in terms of arterial gases and bases excess.
Conclusions: In small-for-gestational-age fetuses and normal umbilical Doppler, the NRBC counts above 10 per 100 leukocytes in umbilical cord blood was able to identify higher risk for cesarean delivery, fetal distress and acidosis at birth.

3.1 P DEVELOPING A THERAPY FOR SEVERE EARLY ONSET FETAL GROWTH RESTRICTION: THE CHALLENGES OF DESIGNING A MULTINATIONAL PHASE I/IIA CLINICAL TRIAL PROTOCOL

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Objective: The EVERREST project aims to carry out a phase I/IIa safety/efficacy trial of maternal vascular endothelial growth factor gene therapy for severe early onset fetal growth restriction (FGR) at four centres (UK, Germany, Sweden, Spain). The lack of early phase obstetric research protocols and practice differences across the centres highlighted the need for a systematic approach to develop the clinical trial protocol.
Method: The individual elements contributing to a diagnosis of severe early onset FGR were compared across the four centres. We reviewed criteria for grading adverse events in clinical trials for their coverage of pregnancy-related events.
Results: The consortium agreed standard fetal biometry. Using gestational reference range biometry from four cohorts (1-4) we determined that Hadlock formula $Log_{10}EFW = 1.326 – 0.00326\ AC \times FL + 0.0107\ HC + 0.0438\ AC + 0.158\ FL$ (5) consistently gave the highest estimated fetal weight (EFW) for a given set of biometry. The Marsal gestational reference range for EFW (6) was the most appropriate for the relevant clinical trial gestational age range (20-26 weeks). Of the two methods used by the centres for assessing change in EFW with time, the Swedish method of percentage weight deviation (7) gave a shallower gradient, identifying those fetuses that had the slowest growth. We found no internationally recognised criteria to grade most pregnancy-related adverse events in phase I clinical trials.
Conclusions: Careful analysis of differences in the assessment of fetal growth has allowed consensus agreement of inclusion criteria for a phase I/IIa clinical trial protocol in severe early onset FGR. The EVERREST consortium will now develop adverse event grading criteria for obstetric phase I trials.
customised growth charts remains high.

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3.2P AN INTERGRATED MODEL WITH CLASSIFICATION CRITERIA TO DIFERENTIATE LATE ONSET FETAL GROWTH RESTRICTION VS, SMALL FOR GESTATIONAL AGE

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Department of Maternal-Fetal Medicine, ICGON, Fetal and Perinatal Medicine Research Group, IDIBAPS, Hospital Clinic - Universitat de Barcelona, Barcelona, Spain.

Objectives: The objective of this study was to develop an integrated model with the best performing criteria to classify late-onset, small-for-gestational age (SGA) fetuses as either fetal growth restriction (FGR) or low-risk SGA, according to their risk of adverse outcome.
Methods: Cohort of 509 pregnancies with suspected SGA fetus eligible for trial of labor was recruited prospectively, and data on the perinatal outcome recorded. A predictive model for the occurrence of emergency cesarean delivery for non-reassuring fetal status or neonatal acidosis was constructed using the Decision Tree Analysis algorithm (SPSS 19.0), with predictors: maternal age, body mass index, smoking, primiparity, gestational age at delivery, labor onset, estimated fetal weight (EFW), umbilical artery pulsatility index (PI), mean uterine artery (UtA) PI, middle cerebral artery PI, and cerebroplacental ratio (CPR).
Results: An adverse outcome occurred in 134 (26.3%) cases. The best performing combination to define FGR was the presence of CPR < 10th centile, a mean UtA PI > 95th centile or an EFW < 3rd centile. The algorithm showed a sensitivity, specificity, positive and negative predicted value for adverse outcome of 82.8% (95% CI 75.1%-88.6%), 47.7% (95% CI 42.6%-52.9%), 36.2% (95% CI 30.8%-41.8%) and 88.6% (95% CI 83.2%-92.5%), respectively. Positive and negative likelihood ratios were 1.58 and 0.36.
Conclusions: Our model could be used as a diagnostic tool to discriminate late-onset FGR from low-risk SGA pregnancies in the population of suspected SGA, to rule out the risk of adverse outcome.

3.3 P DOES SECOND TRIMESTER UTERINE ARTERY DOPPLER SCREENING MODIFY PERINATAL OUTCOMES?

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BCNatal | Barcelona Center for Maternal Fetal and Neonatal Medicine Hospital Sant Joan de Déu and Hospital Clínic, University of Barcelona Spanish Maternal & Child Health Network Retic SAMID
BARCELONA-SPAIN

Objective: To determine whether routine uterine artery Doppler assessment during second trimester ultrasound modifies the evolution of pregnancy by means of perinatal outcomes
Method: Prospective case control analysis of 830 patients undergoing second trimester ultrasound evaluation at our hospital in a one year period randomly selected for either uterine artery Doppler assessment or not.
Patients were divided into two groups, followed up until delivery in our hospital and perinatal outcome details were recorded. Results from both groups are compared
Results: We found in the group of patients that underwent Doppler screening 3.9% of IUGR 3.4% PE and as adverse perinatal outcomes recorded, delivery < 34wks 1.2%, APGAR <7 (1") 3.9%, NICU admission 5.2%, being the main pathology reported neonatal RDS 3.2%
The group not undergoing Doppler assessment had the following results: 4.3% of IUGR, 2.6% PE and as adverse perinatal outcomes recorded, delivery < 34wks 1.7%, APGAR <7 (1") 3.9%, NICU admission 3.3%, being the main pathology reported also neonatal RDS 2.7%
These results were not proven to be statistically significant
Conclusions: As we found very similar results in both groups we conclude that uterine artery Doppler assessment is a useful tool for predicting obstetrical complications and adverse perinatal outcomes only when performed in a specific population bearing certain risk factors that predispose them to present these clinical features.

3.4 P EMERGENCY CAESAREAN DELIVERY PERFORMED BECAUSE OF A NONREASSURING FETAL HEART RATE, ON A TERM PREGNANCY WITH A NOT DIAGNOSED GROWTH RESTRICTED FETUS. ON PURPOSE OF TWO CLINICAL CASES

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Objective: to analyse two cases of late-onset intrauterine growth restriction, fortuitously diagnosed at the time of delivery, in order to provide some experience for similar clinical cases.
Method: review of the medical history of two cases.
Results: Case 1: a 37 year old nulliparous with a pregnancy obtained as a result of an in vitro fertilization. No other medically relevant complaints reported. At 37 weeks of gestation, the patient came to emergency department because of not perceiving fetal movements. The fetal heart rate (FHR) assessment was nonsreassuring: baseline rate 180 beats per minute (bpm) with no accelerations, absent variability and recurrent variable decelerations. An ultrasound examination was performed, showing a fetus in a cephalic presentation, amniotic fluid volume and placenta both normal. Estimated fetal weight was 2300 gr. Doppler velocimetry of umbilical artery was normal but middle cerebral artery shows an increased flow because of hemodynamic redistribution. During ultrasound examination, no fetal movements were noted. Because of all of that, emergency cesarean delivery is performed. Newborn was a boy, birth weight 2180 gr (1^{st} percentile), Apgar test 7/10, pH=7'15.
Case 2: a 22 year old nulliparous with no medically relevant complaints. At 37 weeks of gestations, the patient came to emergency department because of abdominal pain. Urinalysis was normal. No cervical dilatation or effacement was found. FHR assessment was nonreassuring: baseline rate 155 bpm, no accelerations and minimal variability with recurrent atypical variable decelerations. Emergency cesarean delivery is performed because of nonreassuring FHR. Newborn was a boy, birth weight 1945 gr (<1^{st} percentile), Apgar test 8/10, pH=7'1.
Conclusions: omission of 35-36 weeks ultrasound examination in low risk pregnancies, underdiagnosed late-onset intrauterine growth restriction, with its increased morbidity.

3.5 P DIFFERENTIAL PLACENTAL EXPRESSION OF INSULIN LIKE GROWTH FACTORS AND THEIR BINDING PROTEINS IN PREGNANCIES AFFECTED BY GROWTH DISORDERS

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Objective: The insulin–like growth factors 1 and 2 (IGF1 and IGF2) are known to play an important role in placental and fetal growth. We sought to investigate whether the placental expression of IGF and their binding proteins (IGFBPs) is altered in women delivering small for gestational age (SGA; birth weight <10th percentile for gestation) and large for gestational age (LGA; birth weight >90th percentile for gestation) neonates compared to those delivering appropriate for gestational age (AGA) neonates.
Methods: We included 73 pregnant women with singleton pregnancies; 37 with AGA, 16 with SGA and 20 with LGA neonates. Placental samples were obtained at delivery and stored at -80^{0}C. Laboratory techniques involved RNA extraction, cDNA preparation, gel electrophoresis for confirming the product size, real time PCR for gene expression and western immunoblotting for protein analysis.
Results: Compared to AGA group, placental expression of IGF1 gene was found to be significantly lower in SGA neonates ($p<0.01$) but no different in the LGA group. There was no difference in placental IGF2 expression between the groups. Placental IGFBPs 1, 2, 3, 4 and 7 expression was significantly higher in SGA neonates while IGFBPs 1, 2 and 3 were significantly down-regulated in the LGA group (both $p<0.01$). We show for the first time the presence of IGFBP7 in term placenta.
Conclusions: The placental expression of IGFs and their binding proteins differ in fetal growth disorders. We have found placental gene expression of IGFBP1, 2 and 3 to be inversely correlated with birth weight. Whether these alterations cause FGR or are an associated finding requires further investigation.

3.6 P INTRAUTERINE GROWTH RESTRICTION OR SMALL-FOR-GESTATIONAL-AGE FETUS DIAGNOSIS IN TWIN PREGNANCY DEPENDING ON WHETHER IT IS THE FIRST OR THE SECOND TWIN.

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Objective: The study of the incidence of fetal intrauterine growth restriction (IUGR) or small-for-gestational-age (SGA) in twin pregnancies is more common on the first or on the second twin.
Method: Twin births were analyzed in our hospital over a period of 4 years. Coprimary end points: birth weight, birth weight percentile, gestational age and sex. Multiple gestational percentile calculator TM III of Barcelona Clinic Hospital was used (Francesc Figueras).
Results: The total amount of births over these four years was 13017, from which a 2,52 percent were twins (329).
The incidence of fetuses with a percentile lower than 10 on twin pregnancies was sixteen percent, and six percent were lower than percentile 3.
If we consider this incidence of each fetus independently, seven percent out of the first twins and ten percent out of the second twins would have an incidence lower than percentile 10 (non-significant result).
Three percent and five percent out of first and second twins, respectively, would be lower than percentile 3 (non-significant result).
However, out of the 57 fetuses with a percentile lower than 10, sixty percent was present on the second twin and forty percent on the first one ($p < 0,05$). And out of the 24 fetuses with a percentile lower than 3, sixty-two percent was present on the second twin and thirty-eight percent on the first one ($p = 0,07$).
If we consider fetal sex, we do not encounter any differences in the incidence of SGA or IUGR fetuses.
Conclusions: Intrauterine growth restriction in our hospital is more frequent on the second twin.

3.7 P ROUTE OF DELIVERY IN GROWTH RESTRICTED FETUSES BORN AT TERM

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Objectives: The aim of the study was to compare the route of delivery of growth restricted fetuses born at term versus normal weight fetuses born above 37 weeks of gestation

Material and Methods: Assisted deliveries in the last 15 months (from March 1, 2013 to June 24, 2014) with fetuses more than 37 weeks old whose birth weight was less than 2500 g have been reviewed; the analyzed variables are: spontaneous, operative vaginal deliveries, cesarean deliveries and newborn Apgar test. These data are also compared with a random sample of full term fetuses between 2501 and 3999 g born in the same year.
Results: The percentage of full term fetuses with a birth weight below 3rd percentile was 2.14% of total deliveries.
The percentage of spontaneous, operative vaginal deliveries, cesarean deliveries in fetuses with intrauterine growth restriction was respectively 58.89% (N = 53), 6.67%(N = 6),34.4% (N = 31),compared to 58%, 22%, 20% for the sample of fetuses with normal weight. A statistically significant difference was found just between the operative vaginal deliveries.
48% of cesarean deliveries in fetuses whose birth weight was less than 2500 g were scheduled, similar to the rate of scheduled caesarean deliveries in the general population (42%).
In growth restricted fetuses at term 33.3% of operative vaginal deliveries were spatula, 16.67% forceps and 50% vacuum, while in fetuses with normal weight 25% were spatula, 50% forceps and 25% vacuum.
We identified only 6 cases with 1ºminute Apgar test ≤7 in newborn with intrauterine growth restriction, while in the sample of normal weight fetuses no cases with 1ºminute Apgar ≤7were identified.
Conclusions: The route of delivery in fetuses <2500g is fundamentally spontaneous.
These fetuses don´t have a higher rate of cesarean deliveries statistically significant compared to normal weight fetuses.
However, operative vaginal deliveries´ number is reduced in fetuses with intrauterine growth restriction.

3.8 P OBSTETRIC COMPLICATIONS AND ADVERSE PERINATAL OUTCOMES CORRELATED WITH UTERINE ARTERY DOPPLER ASSESSMENT DURING SECOND TRIMESTER OF PREGNANCY

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Objective. To determine how the assessment of the uterine artery Doppler during the second trimester correlates with the development of certain obstetrical complications and adverse perinatal outcomes as well as its correlation with certain risk factors.
Method. Prospective case control analysis of 414 patients undergoing second trimester ultrasound evaluation at our hospital in a one year period, randomly selected for uterine artery Doppler assessment. The mean pulsatility index was calculated and considered pathological when >95th percentile for the correspondent gestational age. Patients were followed up until delivery in our hospital. Risk factors for preeclampsia and IUGR were recorded for posterior correlation as were adverse perinatal outcomes. Only statistically significant results are reported.
Results. In the pathologic uterine Doppler result group 19% developed IUGR, 11,9% PE, 4.9% delivered at < 34 weeks and 12.5% had APGAR <7 (1").
In the normal uterine Doppler group 2.2% developed IUGR, 2.4% PE, 0.8% delivered at <34weeks and 3% had APGAR <7 (1").
The intensity of association to each outcome was estimated with Cramer's V coefficient getting the following results: 0.158 for PE, 0.265 for IUGR, 0.111 for <34wk delivery and 0.146 for APGAR <7 (1").
From the risk factors considered for correlation we found statistical significance in relation to maternal age >35 y/o for PE (intensity from 0.112 to 0.202 when correlated with abnormal Doppler); obesity for PE (intensity from 0.181 to 0.367); hypertension for PE 0.43; nulliparity only significant when correlated with abnormal Doppler (for PE intensity 0.322, IUGR 0.337) and previous history of PE (intensity of 0.166 for PE and 0.152 for IUGR).
Conclusions. Uterine artery Doppler study improves the follow up of patients with higher risk of developing specific obstetrical complications and may be a tool to better assess the impact of certain risk factors involved in the gestational outcome.

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