



UCL

EGA Institute for Women's Health '16th' Annual Conference 2021

Programme and Abstract Booklet

Friday 10th December 2021



BOOKLET CONTENT

Page	
3	<u>Directors Welcome</u>
4	<u>Report from Director, Women's Health Division UCLH</u>
5	<u>Programme</u>
8	<u>Speakers</u>
10	<u>Abstracts: Oral Presentations</u>
14	<u>Abstracts: Poster Presentations</u>
40	<u>Abstract: Medical Student Prize Talk</u>
41	<u>Acknowledgements</u>

Director's Welcome



I am delighted to welcome you to our second virtual conference - 'EGA IfWH '16th' Annual Conference 2021.

This time last year, I am sure we did not expect to be meeting virtually again a year later. But despite the ongoing pandemic and renewed concerns about Omicron, we are still providing excellence in research, education and clinical care towards our mission of better lives for women and babies across the world.

At this meeting we celebrate how staff have risen to the challenge of continuing to deliver research, for example in screening for ovarian cancer, fetal imaging, neonatal gene transfer and hypoxia, We hear about some new clinical services in complex pelvic mesh and pelvic congestion that are thriving despite the pandemic. We learn how COVID has impacted on reproductive health services and early pregnancy, and consider how to address inequalities in women's healthcare outcomes.

I would like to thank everyone who is taking part today – those of you who submitted abstracts, made video presentations of their posters, all of our invited speakers, our scientific review panels and session chairs, and everyone attending the meeting. My thanks go to the Conference Core Planning Committee and especially Sarah Mayhew, Aqsa Hjej-Andaloussi and Ian Waller who have made this conference happen. I hope that you enjoy the day.

I wish you all a well-earned break at Christmas and I look forward to the year ahead. It will again be filled with challenges and opportunity, but through our Institute team at UCL and UCLH I know that we can make a difference to women's health together.



Professor Anna David
Director of the UCL EGA Institute for Women's Health

You can keep abreast of activities within the Institute for Women's Health on our Facebook page and our Twitter account. [@UCL>IfWH](https://www.facebook.com/ucl.ega.ifwh)



Report from Clinical Director of WH Division, UCLH



**Mr Stuart
Lavery**

It's a real delight for me to participate in my second EGA Institute for Women's Health annual conference. Although we were all looking forward to meeting face to face, catching up with old friends and making new contacts, I think we all understand that the pandemic is still with us and it is entirely sensible and appropriate to prioritise the safety of our staff and guests.

Once again, we have a very high calibre of invited speaker that we hope will inform, educate and possibly even provoke us out of our intellectual comfort zones. All aspects of Women's Health will come under the spotlight at the conference. Of particular value is the contribution of our research fellows to this meeting. They represent the future of our specialty and it's impossible not to be impressed by the diversity and quality of the abstracts that have been submitted.

It is reassuring to know that the future of academic research into Women's Healthcare is in safe hands.

A handwritten signature in black ink that reads 'Stuart Lavery'.



IfWH '16th Annual Conference 2021
Friday 10th December 2021
Remotely – Via Zoom Link

08.45	Join Meeting	
09.00 – 09.15	Welcome and Highlights of the Day Professor Anna David, Director EGA IfWH and Mr Stuart Lavery, Clinical Director of Women's Health Division, UCLH	Presenters:
09.15 – 09.30	Update on the Faculty of Population Health Sciences, UCL Presenter: Professor Ibrahim Abubakar, Dean of FPHS	
09.30 – 11.00	SESSION 1: Screening for Ovarian Cancer Chairs: Dr Alex Gentry Maharaj and Dr Ojone Illah <ul style="list-style-type: none"> <i>The outcome of UKCTOCS: Where to now for Ovarian Cancer Screening?</i> – Professor Usha Menon, Professor of Gynaecological Oncology, MRC Clinical Trials Unit, UCL. <i>Where the role of ROCA might be for BRCA carriers</i> – Dr Adam Rosenthal, Consultant Gynaecologist at UCLH and Associate Clinical Professor at IfWH/UCL. <i>New approaches for Ovarian Cancer Screening</i> – Professor Martin Widschwendter, Professor for Cancer Prevention and Screening and Director of the EUTOPS Institute & Professor of Women's Cancer at IfWH/UCL 	
11.00 – 11.20	Coffee Break	
11.20 – 12.00	SESSION 2: DEBATE Chair: Professor Donald Peebles NICE guidance on BAME gestational age for induction <i>Do we support the early induction of Labour in Black and Ethnic Minority Women?</i> Speaker FOR the motion: Professor Philip Steer Emeritus Professor, Imperial College London Speaker AGAINST the motion: Dr Sonji Clarke Consultant obstetrician Guy's & St. Thomas' NHS Trust and Deputy Head, London School of Obstetrics & Gynaecology	
12.00 – 12.30	SESSION 3: EGA Hospital Charity Presentations Introduction by: Professor David Williams , Consultant Obstetric Physician UCLH & Trustee of EGA Hospital Charity & Professor Anna David , IfWH Director & Trustee of EGA Hospital Charity. <i>Anne Boutwood Travelling Fellowship to Malawi</i> Dr Roslyn Ghui , O&G Registrar, Mpilo Central Hospital/ST5 O&G, Severn Deanery, UK	

Recurrent stillbirth due to chronic histiocytic intervillitis: evidence for an alloimmune aetiology
Dr Emily Cornish, Clinical Research Training Fellow, UCL EGA IfWH

12.30 – 13.00

POSTER VIEWING – including live online Q&A Sessions

<https://www.ucl.ac.uk/womens-health/2021-ega-ifwh-16th-annual-conference-poster-abstracts>

13.00 – 13.45

LUNCH

13.45 – 14.45

SESSION 4: Early Career Researcher Presentations (2 Parallel Sessions)

Breakout Room 1 - Maternal & Fetal Medicine & Women's Cancer

Chairs: **Dr Rajvinder Karda & Dr Malcolm Scott**

1. *Validation of Advanced MRI Method for measuring fetoplacental oxygen saturation in a sheep model of human pregnancy* (**Dimitra Flouri**, Maternal & Fetal Medicine)
2. *Severe early onset fetal growth restriction (FGR) is a symptom of a maternal medical condition.* (**Katarzyna Maksym**, Maternal & Fetal Medicine)
3. *AAV gene targeting of natural regulatory element as a treatment for Dravet Syndrome* (**Juan Antinao Diaz**, Maternal & Fetal Medicine)
4. *Early detection of pancreatic ductal adenocarcinomas with an ensemble learning model based on a panel of protein serum biomarkers* (**Rocha Nene Nuno**, Women's Cancer)
5. *Investigating the diversity of biomarker patterns of expression using Ki67, p16 and E4 in young women diagnosed with CIN 2* (**Sabina Mistry**, Women's Cancer)

Breakout Room 2 - Reproductive Health & Neonatology

Chairs:

Dr Sioban Sengupta and Dr Jens Madsen

1. *SARS-CoV-2 infection in the first trimester and the risk of early miscarriage: a UK population-based prospective cohort study of 3041 pregnancies conceived during the pandemic.* (**Neerujah Balachandren**, Reproductive Health)
2. *Exploring Consent in Midwifery Practice* (**Rachel Martin**, Midwifery)
3. *Neural activity is acutely depressed following neonatal hypoxia-ischemia even in the absence of pronounced clinical encephalopathy* (**Kimberley Whitehead**, Neonatology)
4. *Evaluating the use of surfactant protein D (SP-D) as a diagnostic biomarker in COVID-19 patients treated with lung surfactant therapy.* (**Tania Castillo-Hernandez**, Neonatology)
5. *Outcomes at the limit of viability: network experience from 2005 to 2020* (**Rose Crowley**, Neonatology)

14.45 – 15.00

SESSION 5: Medical Student Prize Talk

Chair: **Dr Melissa Whitten, Consultant in Obstetrics and Maternal Fetal Medicine**

Obstetric outcomes among women with reactive hypoglycaemia at glucose tolerance test
Salsabeel Nasreen Kazi (Medical Student)

15.00 – 15.30

SESSION 6: UCLH WH Division: Audit and Quality improvement

Chair: **Dr Jo Modder, Consultant Obstetrician & Audit Lead WH Division, UCLH**

Outcomes from fetoscopic laser ablation for twin-twin transfusion syndrome: 5-year data
Mayya Vorona, Medical Student; **Lindsay Kindinger**, Subspecialty Trainee FMU & **George Attilakos**, Consultant Obstetrician

Pelvic congestion syndrome: a new service

Ghada Salman, Consultant Gynaecologist & **Dr Jocelyn Brookes** (Hon Associate Professor, Institute of Cardiovascular Sciences, UCL & Consultant Endovascular Radiologist)

#Ea15.30 – 15.45	Coffee Break (and oral judging)
15.45 – 16.30	<p>SESSION 7: Hot Topics (8 mins each topic) Chair: Mr Stuart Lavery</p> <ol style="list-style-type: none"> 1. <i>'Hertility Health</i> , Dr Helen O'Neill (Dept. Maternal & Fetal Medicine) 2. <i>The London Complex Mesh Centre</i>, Dr Sohier Elneil (Dept. Maternal & Fetal Medicine) 3. <i>The CAP-COVID Study</i>, Associate Professor Jenny Hall (Dept. Reproductive Health)
16.30 – 17.00	<p>SESSION 8: EGA KEY NOTE LECTURE Chair: Professor Anna David</p> <p><i>Tackling inequalities through research</i></p> <p>Professor Lucy Chappell (Professor of Obstetrics at King's College London and Chief Scientific Adviser for the Department of Health and Social Care (DHSC))</p>
17.00	<p>Closing Remarks and Prizes</p> <p>Presenter: Mr Stuart Lavery, Clinical Director of Women's Health Division, UCLH</p>

Debate Speakers

Professor Phillip Steer, Emeritus Professor, Imperial College London



Philip Steer is Emeritus Professor of obstetrics at Imperial College London, having been appointed Professor in 1989. He was a consultant obstetrician for 35 years, based at the Chelsea and Westminster Hospital from 1994, and at various times was the clinical director of maternity services and the level 3 neonatal unit.

He was Editor-in-Chief of BJOG – an International Journal of Obstetrics and Gynaecology - from 2005-2012, is now Editor Emeritus, and edits the 'BJOG on the case' series. He is currently an editor of 'High Risk Pregnancy – Management Options' with the fifth edition published by Cambridge University Press in 2018 and the 6th edition in preparation. In 2016 CUP also published the second edition of 'Heart Disease in Pregnancy' that he edits with Prof Michael Gatzoulis.

He has been President of the British Association of Perinatal Medicine and President of the Section of Obstetrics and Gynaecology of the Royal Society of Medicine. He is an honorary fellow of the College of Obstetricians and Gynaecologists of South Africa, and of the American Gynecological & Obstetrical Society.

He has published 147 peer reviewed research papers, 109 reviews and editorials and 66 book chapters/books. 23 of his research fellows have been awarded higher degrees. His particular interests are the pathophysiology of labour and maternal heart disease in pregnancy.

Dr Sonji Clarke (Consultant Obstetrician, Guy's & St. Thomas NHS Foundation Trust, and Deputy Head, London School of Obstetrics & Gynaecology)



Sonji Clarke is a consultant obstetrician and deputy head of the London School of Obstetrics and Gynaecology, and an honorary senior lecturer at King's College London. She has been a consultant for more than 10 years with special interests in perinatal mental health, substance misuse, and women who are pregnant with other complex social factors. She also has a special interest in Postgraduate and Undergraduate education, as well as an interest in multi-professional diverse leadership development.

Sonji is a Fellow of the Royal College of Obstetrics and Gynaecology and the Higher Education Academy and has a Masters in Academic Practice. In 2018, she was honoured as one of the Top 70 NHS Women Leaders in London during the NHS 70 year celebrations by the London Women's Leadership Network.

Keynote Speaker

Professor Lucy Chappell

Professor Lucy Chappell FMedSci is the Chief Scientific Adviser for the Department of Health and Social Care (DHSC), with overall responsibility for the department's research and development, including the National Institute for Health Research (NIHR), the government's major funder of clinical, public health, social care and translational research.

Reporting to the Chief Medical Officer, the Chief Scientific Adviser provides science advice and analysis to ministers across the range of health topics and is involved in cross-government science policy.



Professor Chappell is Professor of Obstetrics at King's College London, Honorary Consultant Obstetrician at Guy's and St Thomas' NHS Foundation Trust and an NIHR Senior Investigator. She will undertake the Chief Scientific Adviser role on secondment into government, while continuing some of her clinical and academic work.

Abstracts

Oral Presentations

Presenter

Dimitra Flouri

Authors

Dimitra Flouri^{1,2}, Jack RT Darby³, Stacey L Holman³, Sunthara R Perumal⁴, Sebastien Ourselin², Anna L David^{5,6}, Janna Morrison³, Andrew Melbourne^{1,2}

Abstract

BACKGROUND:

Magnetic resonance imaging (MRI) techniques are increasingly providing information on placental function in vivo to support clinical decision-making. Preclinical models such as pregnant sheep allow invasive methods to validate MRI measurements. Non-invasive fetal oxygen saturation (FO₂) measurement would be clinically valuable in detecting fetal growth restriction (FGR). Here we use a multicompartment modelling of non-invasive placental MRI to estimate FO₂ and validate MRI FO₂ against invasively collected blood gas samples.

METHODS:

The study was approved by the Animal Ethics Committee of the South Australian Health and Medical Research Institute.

Non-pregnant ewes (n=10) were assigned to have most of their endometrial caruncles removed via carunclectomy (CX) under and recovered prior to mating. At 109-111 (Control=10, CX=10) and 139-141 (Control=4, CX=5) days gestation, ewes anaesthetised (induction: diazepam (0.3mg/kg) & ketamine (7mg/kg); maintenance: 2.5% isoflurane), and underwent MRI scan on a 3T Siemens Skyra Scanner. Diffusion-Weighted MRI performed at 7 b-values with echo time (TE)=72ms and T₂-relaxometry at 10 TEs at b-value=0 s.mm⁻². The dependence of FO₂ on the effective fetoplacental blood T₂ relaxation time is characterised by the Luz-Meiboom model.

RESULTS:

The linear relationship between blood gas and MRI solutions was significant for Controls ($y=1.64x-91.3$, $R^2=0.88$, $P=0.0002$), for CXs ($y=1.17x-54.3$, $R^2=0.60$, $P=0.017$) and when all animals were considered together ($y=1.37x-69.4$, $R^2=0.73$, $P<0.0001$). A strong correlation was observed between fetal descending aorta oxygen saturation measurements and MRI FO₂ in Controls ($r=0.94$, $P<0.0001$) and when all animals considered together ($r=0.85$, $P<0.0001$); and a medium correlation in CXs ($r=0.77$, $P=0.0003$).

CONCLUSION:

This study supports the use of multi-compartment placental MRI model in pregnancy using sheep as a model of human pregnancy. Results demonstrated a link between MRI FO₂ and reference fetal descending aorta oxygen saturation by catheterisation, supporting the possibility of using MRI for diagnosis of FGR associated with fetal hypoxia.

Presenter

Juan Antinao Diaz

Authors

Antinao Diaz, J. 1, Chilcott, E.1, Counsell, JR. 2, Schorge, S.3, Almacellas Barbanoj, A. 4, Lignani, G.4, Waddington, SN1, Karda, R1.

Abstract

BACKGROUND

Dravet Syndrome is an inherited childhood epilepsy mostly caused by a mutation in the SCN1A gene, which encodes the voltage-gated sodium channel NaV1.1. Patients suffer from generalized seizures, that can often evolve to status epilepticus, severe cognitive impairment and increased mortality. A natural expressing regulatory element controls the expression of endogenous SCN1A. Haploinsufficiency of SCN1A could be rescued by inhibiting this regulatory element by gene therapy, in turn allowing increased expression of the endogenous SCN1A gene.

METHODS

We designed several sequences targeting this regulatory element and cloned them into an AAV plasmid. We have tested the candidate sequences in N2a cells and assessed endogenous Scn1a expression by quantitative PCR. We then have selected 3 sequences to test in vivo.

We established a mouse model of Dravet syndrome to test the candidate sequences. One candidate AAV vector was administered to neonatal heterozygous Dravet and wild-type mice via either neonatal bilateral intracerebroventricular (ICV) injection or combination therapy of bilateral ICV and intravenous (IV) delivery. Mice survival was monitored.

RESULTS

Three of the designed constructs showed significant increases in endogenous Scn1a expression in N2a cells, ranging between 8 to 10 times baseline levels.

ICV & IV treated heterozygous mice showed 77.7% survival, bilateral ICV treated heterozygous mice showed 57% survival, whereas untreated heterozygous mice exhibited a 41% survival.

100% survival was observed for WT injected and uninjected mice.

CONCLUSION

Gene therapy on a naturally occurring regulatory element specific for Scn1a can provide a therapeutic treatment for Dravet syndrome and possible for other haploinsufficiency.

Presenter

Kasia Maksym

Authors

K. Maksym, A. David on behalf of EVERREST consortium

Abstract

BACKGROUND

Maternal health at the onset of pregnancy correlates with the development of pregnancy complications and the pregnancy outcome (Stephenson 2018). That includes development of the early onset fetal growth restriction (FGR) when condition is diagnosed before 32 weeks' gestation (Gordjin 2016). The aim of the study was to analyse maternal health during pregnancy and postpartum in early onset FGR cohort.

METHODS

Patients with singleton pregnancies at 20+0-26+6 weeks gestation with estimated fetal weight (EFW) <600g and <3rd centile and no known fetal abnormalities were recruited into EVERREST Prospective study in 4 European centres between March 2014 and January 2020. Data on pre-existing medical conditions was collected at enrolment and development of

pregnancy complications and diagnosis of new conditions recorded for pregnancy and postpartum for 134 patients.

RESULTS

61 out of 134 (46%) patients reported pre-existing medical condition at enrolment, most commonly essential hypertension (n=11), asthma (n=11) and hypothyroid (n=13). 37% perineal loss was noted in the cohort with no correlation with pre-existing maternal condition. For livebirths, gestational age at delivery and birthweight was significantly lower in the group with reported pre-existing medical condition (226 vs 208 days at delivery, $p < 0.05$; 1287g vs 937g, $p < 0.05$). 12 out of 134 (9%) patients were diagnosed with new medical condition after enrolment (during pregnancy or postpartum) including new diagnosis of fibroids, ulcerative colitis, hypercalcemia, SLE, chronic hepatopathy, coeliac disease and persistent hyperemesis. 14 out of 134 (10%) patients were admitted to High Dependency Unit in perinatal period.

CONCLUSION

Diagnosis of early onset FGR should prompt detailed evaluation of the maternal health as it can be a first sign of undiagnosed or worsening of pre-existing condition.

Presenter

Kimberley Whitehead

Authors

Whitehead K^a, Mistry N^a, Meek J^b

Abstract

BACKGROUND

In neonatal animal models, hypoxia-ischemia depresses neural activity, which disrupts experience-dependent synaptic plasticity. In human neonates, suboptimal school-age outcomes have been reported after perinatal hypoxia-ischemia even in the absence of pronounced clinical encephalopathy. In light of the animal work, this association could be mediated by depressed cerebral activity following the insult.

METHODS

We recruited infants who underwent clinical 9-channel EEG monitoring following perinatal hypoxia-ischemia and survived to hospital discharge. Infants were divided into i) mild/borderline clinical encephalopathy (n = 15, median 5 min Apgar: 6, median pH: 6.97), and ii) \geq moderate clinical encephalopathy sufficient to qualify for 72 hours of therapeutic hypothermia (n = 15, median 5 min Apgar: 5, median pH: 6.90).

We selected the first 11 minutes of artefact-free EEG during the 14 hours post birth, excluding any segments within 6 hours after phenobarbital administration or during seizures. We compared 0-35Hz power of the EEG to that of the EEG mean 22 hours post birth in a control group matched by gestational age, intensive care nursing, and EEG recording system (n = 8, median 5 min Apgar: 10, median pH: 7.28, who underwent monitoring for events later diagnosed as benign, e.g. myoclonus).

RESULTS

Infants with \geq moderate encephalopathy had lower power neural activity relative to controls ($p < .05$ all channels). Infants with mild/borderline encephalopathy also had lower power

neural activity relative to controls ($p < .05$ all channels), but higher power neural activity than the group with \geq moderate encephalopathy ($p < .05$ all channels except midline central).

CONCLUSION

Hypoxia-ischemia acutely depresses neural activity even in infants without pronounced clinical encephalopathy. Future work will review the synchronised video to examine how cerebral activity becomes organised by sensory input and sleep-wake state across the days following the insult, which both drive experience-dependent synaptic plasticity.

Presenter

Neerujah Balachandren

Authors

Balachandren N, Davies M, Hall J, Stephenson J, David A, Barrett G, O'Neill H, Yasmin E and Mavrelos D

Abstract

Background

In this study, we estimate the prevalence of early miscarriage among those who conceived during the SARS-CoV-2 pandemic, and determine whether SARS-CoV-2 infection in the first trimester of pregnancy is associated with an increased risk miscarriage before 13 week's gestation.

Methods

This is a nationwide prospective cohort study of pregnant women in the community recruited using social media between 21st May to 31st December, 2020. We recruited 3545 women who conceived during the pandemic and were less than 13 week's gestation at the time of recruitment.

We compared early miscarriage risk in women diagnosed with SARS-CoV-2 infection in the first trimester (Group A) v. risk in those who had no symptoms/diagnosis of SARS-CoV-2 and had no household contacts with symptoms/diagnosis of SARS-CoV-2 (Group B).

Results

Data for the primary outcome were available from 3041 women who completed their first trimester follow-up survey (3041/3545, 86%). The overall rate of self-reported miscarriage before 13 week's gestation was 8% (238/3041, 95% confidence interval (CI) 7-9).

Seventy-seven women reported a diagnosis of SARS-CoV-2 infection in the first trimester (3%, 77/3041, 95% CI 2-3). A total of 2669 women (87%, 2269/3041) had no symptoms or diagnosis of SARS-CoV-2 infection and no reported household contacts with symptoms/diagnosis of SARS-CoV-2. The rate of miscarriage before 13 weeks in Group A was 14% (11/77, 95% CI 6-22), and 8% in Group B (212/2660, 95% CI 7-9). After adjusting for age, BMI, ethnicity, smoking status and the number of previous miscarriages, the risk of early miscarriage was almost twice as high among women with confirmed SARS-CoV-2 infection compared to those with no infection (relative rate 1.925, 95% CI 1.101 to 3.367, $p = 0.022$).

Conclusion

The findings from this study suggest that pregnant women infected with SARS-CoV-2 in the first trimester are at a higher risk of early miscarriage. Further studies are warranted to evaluate a causal association.

Presenter

Nuno Nené

Authors

Nuno R. Nené^{1,*}, Alexander Ney², Tatiana Nazarenko^{1,3}, Oleg Blyuss^{1,4,5}, Harvey E. Johnston^{1,6}, Harry J. Whitwell^{1,4,7,8}, Eva Sedlak¹, Aleksandra Gentry-Maharaj⁹, Eithne Costello¹⁰, William Greenhalf¹¹, Ian Jacobs^{1,12}, Usha Menon⁹, Justin Hsuan², Stephen P. Pereira², Alexey Zaikin^{1,3,4,13}, John F. Timms¹.

Abstract**Background**

Earlier detection of pancreatic ductal adenocarcinoma (PDAC) is key to improving patient outcomes, as it is mostly detected at advanced stages which are associated with poor survival. Developing non-invasive blood tests for early detection would be an important breakthrough. The primary objective of the work presented here was to use a unique dataset, that is both large and prospectively collected, to quantify a set of 96 cancer-associated proteins and construct multi-marker models with the capacity to accurately predict PDAC years before diagnosis.

Methods

The data is part of a nested case control study within the UK Collaborative Trial of Ovarian Cancer Screening and is comprised of 219 samples, collected from a total of 143 post-menopausal women who were diagnosed with pancreatic cancer between approximately 1 and 70 months after sample collection, and 248 matched non-cancer controls. We developed a stacked ensemble modelling approach to achieve robustness in predictions and, therefore, improve performance in newly collected datasets.

Results

With a pool of 10 base-learners and a Bayesian averaging meta-learner, we predicted PDAC status with an AUC of 0.91 (95% CI 0.75 - 1.0), sensitivity of 0.92 (95% CI 0.54 - 1.0) at 90% specificity, up to 1 year to diagnosis, and an AUC of 0.85 (95% CI 0.74 - 0.93) up to 2 years to diagnosis (sensitivity of 0.61, 95% CI 0.17 - 0.83, at 90% specificity). These models also used clinical covariates such as hormone replacement therapy use (at randomization), oral contraceptive pill use (ever) and diabetes status.

Conclusion

We demonstrated how using a stacked ensemble approach which relies on a panel of cancer-associated proteins and clinical covariates outperforms state-of-the-art multi-biomarker combinations previously applied in PDAC early detection. Further developments in the selection of base-learners from available code libraries should further enhance the predictive capacity of the method.

Presenter

Rachel Martin

Authors

Martin R., Nicholls J., Ni Y., Harris J., Lanceley A.

Abstract**Background**

Montgomery v Lanarkshire Health Board described the concept of 'materiality' of risk, shifting the focus of consent and risk disclosure from what a healthcare professional

deems suitable to what a 'reasonable' patient may find significant. Little is known about midwives' knowledge of MAX. 300 WORDS consent and whether Montgomery has had an impact on

midwifery practice. This study explored midwives' knowledge and understanding of the consent process.

Methods

A cross-sectional online anonymous survey was conducted using an exploratory research design. The survey was disseminated via social media to midwives practising in the United Kingdom. Both quantitative and qualitative data were collected. Descriptive statistics were used to analyse a subsection of the quantitative data.

Results

The final sample consisted of data from 395 participants who work within the NHS. 9% of participants reported that consent does not need to be voluntarily obtained. When discussing risk, 91% of participants thought women should be informed of all risks, whilst 26% thought that women should be informed of some risks. Most participants were 'sure' that their discussions of consent with women meet current legal requirements. Participants rated themselves highly in their competence to gain consent and their confidence at judging the importance of risk to an individual pregnant person. Gaps in knowledge of consent were observed in participants that rated themselves highest in 'sureness' of meeting legal requirements, competence to consent and confidence at judging importance of risk

Conclusion

Fundamental gaps in midwives' knowledge of legal consent were identified. Participants demonstrated uncertainty regarding risk disclosure and discussion of alternative care options. Participants generally rated themselves highly in their consenting practices, despite lacking in basic knowledge of legal consent, revealing a discrepancy between midwives' self-perceptions and their actual knowledge.

Presenter

Rose Crowley

Authors

Crowley, R, Dyet, L, Huertas-Caballo, A

Abstract**Background:**

The 2019 publication of the British Association of Perinatal Medicine (BAPM) Framework on Extreme Preterm Birth has reignited discussion about the ethics of attempting to resuscitate babies born at the limits of viability. Central to this debate is our understanding of their survival rates and risk of neurodevelopmental impairment.

Methods:

The outcome of all births at 22 or 23 weeks gestation in hospitals within the North Central London Neonatal Network between 2005 and 2020 was reviewed. Survival in Labour Ward (LW), during neonatal unit (NNU) admission and to 2 years of age was calculated. Health and developmental outcomes at 2 years were classified according to the National Neonatal Audit Programme framework.

Results:

219 babies were born at 22 or 23 weeks gestation. At 22 weeks (n=49), 63% of babies died in LW, 24% died on NNU and 12% survived to discharge, with no evident improvement during the time period studied. All survivors had severe impairment in multiple categories at 2 years. At 23 weeks (n=170), 11% of babies died in LW, 33% died on NNU and 55% survived to discharge. At 2 years, 64% of survivors for whom data was available had no or mild/moderate impairment only. The subset of babies born at 23 weeks weighing less than 500g (n=28) had a survival rate to NNU discharge of only 21%.

Conclusions:

Knowledge of local outcome data can inform shared decision-making between parents and obstetric and neonatal teams when preterm delivery is imminent. Our data indicates better survival rates than those quoted by BAPM in babies born at 23 weeks. However, we found higher rates of death and severe disability in those born at 22 weeks, for whom initiation of intensive care may not be appropriate.

Presenter

Sabina Kaur Mistry

Authors

S Mistry¹, K Tjandraprawira¹, M de Koning², H van den Munckhof², Rosenthal¹, D Jenkins², N Wilkinson¹,

Abstract

Background

CIN 2 is considered high grade precancer, but many spontaneously regress and treatment may lead to problems in pregnancy. The diagnosis of CIN 2 is subjective as it includes productive and transforming lesions.

Methods

We studied 41 routine CIN 2 cases confirmed by four expert pathologists. All biopsies were graded for immunohistochemical expression of biomarkers Ki67 (cell proliferation), P16 (hrHPV E7 transforming gene expression) and HPV E4 gene expression (completion of productive HPV life cycle). In 27 cases the LLETZ was delayed by 4 months or more. P16 and Ki67 were graded according to published criteria with grade 1 being diffuse staining of the lower third, grade 2 above the lower third, and grade 3 from two-thirds to full thickness. Spotty superficial staining by Ki67 associated with HPV replication was noted. HPV E4 staining was graded as negative (0), focal (1) or extensive (2).

Results

Mean age was 29.6 years. For 27/41 cases followed: 20 (74%) regressed and seven persisted/progressed. Most CIN 2 heterogeneously expressed biomarkers. A "spotty" pattern of Ki67 mega-nuclei represented productive HPV infection. Of regressing cases 8/20 scored ≤ 1 with P16 and Ki67 with 7 negative for E4 in worst areas, 11 scored 2 for P16, mostly with spotty Ki67 expression; four expressed E4. One case scored 3 for P16 and Ki67 and was negative for E4. All seven persistent/progressive cases were persistently positive for hrHPV: 7 scored ≤ 2 for P16, and 7 ≤ 2 for Ki67; four expressed E4.

Conclusions

This study demonstrates the complex expression of Ki67, P16 and E4 with variable expression in mixed grade lesions and a high rate (74%) of short-term spontaneous regression. P16 immunoreactivity was not always associated with progression.

CIN2 in young women warrants formal trials of biomarkers with conservative management.

Presenter

Tania Castillo-Hernandez

Authors

Castillo-Hernandez T, Madsen J, Clark H

Abstract

Background:

Patients with 2019 coronavirus disease (COVID-19) caused by severe acute respiratory distress syndrome coronavirus 2 (SARS-CoV-2) present severe respiratory symptoms progressing to acute respiratory distress syndrome (ARDS). Upon infection, SARS-CoV-2 destroys cells expressing the ACE2 receptor including alveolar type II cells (AT2) found in the alveolar-capillary barrier. AT2 cells secrete pulmonary surfactant, a complex of lipid and surfactant proteins (SP-A, SP-B, SP-C, SP-D). Surfactant therapy, mainly composed of SP-B and SP-C, has been successful in treating lung disease in preterm babies.

This study, part of two clinical trials repurposing surfactant therapy in adult ventilated COVID-19 patients, aims to determine whether the level of SP-D in samples from COVID-19 patients can be potentially used as a biomarker for lung integrity and to identify any potential SP-D degradation.

Methods:

Enzyme-linked immunosorbent assay (ELISA) was used to quantify SP-D concentration in patient plasma and tracheal aspirate samples. Western Blotting was used to identify any protein degradation in plasma samples.

Results:

SP-D concentration in serum was 10-20 times higher in patients ventilated for COVID-19 than in healthy volunteers. Additionally, the concentration of SP-D in plasma has shown to be 10-100-fold higher than in tracheal aspirates. Furthermore, degraded fragments of SP-D were detected at a higher ratio than intact SP-D in plasma of ventilated patients. This ratio has shown to be correlated with dose administration of surfactant therapy.

Conclusions:

Increased serum SP-D and decreased tracheal aspirate SP-D from ventilated COVID-19 patients suggested leakage of pulmonary surfactant into the bloodstream caused by damage to the alveolar-capillary barrier in diseased lungs. The ratio of degraded vs. intact SP-D found in the plasma was correlated with surfactant administration. These results indicated that levels of SP-D in plasma and tracheal aspirates together with the ratio of degraded and intact SP-D in the plasma might become novel biomarkers for COVID-19 progression.

Abstracts

Poster Presentations

Presenter

Anjana Lakshmi Narasimhan

Authors

Siassakos, D, Jaufuraully, S

Abstract

Objectives: Brachial plexus injury (BPI) can occur in neonates during childbirth. BPI can have a debilitating impact upon quality of life and is highly litigated. The focus has therefore turned to prevention, with literature suggesting that caesarean section (CS) is protective against BPI and should be considered for those at high-risk. However, although rates of caesarean section are rising, the incidence of BPI is increasing worldwide. This study aims to explore if there are cases of BPI post CS in the literature, and whether there is evidence to support BPI occurring during a difficult CS.

Methods:

Systematic literature review of Medline, EMBASE, and PubMed Central. Search terms used were 'brachial plexus injury' and 'shoulder dystocia'. Papers identifying BPIs that occurred after CS were extracted and risk factors were identified.

Results:

62 papers with BPI after CS were extracted, with 35 providing clinical details. Many cases with BPI after CS in the literature, with sufficient clinical detail, occurred in the presence of risk factors for potentially difficult delivery. These included malpresentation, macrosomia, obstructed labour, fetal distress, and failed instrumental delivery.

Conclusions:

This study highlights that CS isn't necessarily protective against BPI. It is questionable whether the studies identified could support that persistent and/or severe BPI after CS can occur with the forces of nature alone (expulsion). More research needs to be conducted to identify women at risk for BPI and explore prevention strategies. Clinicians should be mindful that such injuries can occur during CS and be diligent when performing this procedure.

Presenters

Anna Marsh – Lead Midwife for Antenatal Clinic

Gurth Fernando – Assistant General Manager - EGA

Elizabeth Eddershaw – General Manager for Maternity and Neonatology

Authors

Marsh, A., Fernando, G. and Eddershaw, E.

Abstract

BACKGROUND

Antenatal classes are an integral element to midwifery practice and a woman's journey to parenthood (NICE 2021) with links to reduced maternal stress, caesarean section rates and use of epidural anaesthesia (Ferguson et al., 2012; Hong et al 2021). During the COVID-19 pandemic, traditional large classes became unsafe and were immediately stopped. In response to this, UCLH introduced YouTube videos and, following a service evaluation, subsequent midwife-led Zoom sessions.

METHODS

Phase 1 – An online questionnaire was sent to pregnant women via their healthcare app to evaluate their experience of the new YouTube videos and their Antenatal education preferences.

Phase 2 – A second online questionnaire to evaluate the new Zoom Question and Answer classes alongside the videos sent to all class attendants. Ethics approval was considered but not required as this is a service evaluation project.

RESULTS

Phase 1 – 23 respondents. 15 had watched the videos, with 12 finding them informative. 19 stated that they wanted an additional interactive element with midwives. 10 women responded with freetext answers of topics that they would like covered.

Phase 2 – 45 respondents. 39 agreed that Zoom sessions were needed alongside videos. 38 felt able to ask their questions via Zoom, with 4 disagreeing and 2 stating they neither agreed nor disagreed. 38 found it easy to use, 1 neither agreed nor disagreed and 5 disagreed.

CONCLUSION

During the pandemic, women at one hospital have found Zoom Antenatal Question and Answer sessions alongside YouTube videos an acceptable source of Antenatal Education. YouTube videos as standalone were not found to be adequate. Without sufficient data from analysis of pre-pandemic face-to-face Antenatal classes, the relevance is limited to long-term applicability and more research is recommended into midwives' experience of providing online classes, content and into women's' perceived knowledge gain.

Presenter

Annette Thwaites

Authors

Thwaites, A, Hall, J, Barrett, G, Stephenson, J

Abstract

BACKGROUND

Women undergoing in vitro fertilisation (IVF) are an increasingly heterogeneous group with a range of subfertility factors and reasons other than subfertility. We aim to better understand the contraceptive needs of women after successful IVF to improve delivery of services and prevent unplanned, rapid-repeat pregnancies in this group.

METHODS

A qualitative study of views of women who have had spontaneous pregnancies after successful IVF was conducted in September 2020. Purposive and snowballing sampling methods were used with participants recruited from social media and peer networks. The sample consisted of 21 UK interviewees, having a range of spontaneous pregnancy outcomes after successful IVF, including single and multiple livebirth, miscarriage, ectopic pregnancy and termination of pregnancy. The framework analysis method was used in NVivo12.

RESULTS

Contraceptive choices were subject to a complex interaction of influencing factors including i) beliefs in own subfertility, ii) desire for more children and iii) views on contraception. After IVF pregnancy, most women used no or ineffective contraception before their next pregnancy. Spontaneous pregnancy was not universally welcomed, and the inter-pregnancy intervals were often short. After subsequent spontaneous pregnancy, use of contraception and the most effective methods remained low. Women associated aspects of the IVF process with a sense of personal failure, reinforcing their self-belief in subfertility. These beliefs often persisted despite spontaneous pregnancy. Other specific barriers to contraception use included lack of knowledge of the likelihood of spontaneous pregnancy, contraceptive inexperience and inherent incentives towards shorter inter-pregnancy intervals.

CONCLUSION

The contraceptive needs of women having IVF pregnancies are real and being overlooked. Fertility services should provide accurate information on the risks of subsequent spontaneous pregnancy in this population and further research is required to better estimate this risk. Maternity and community healthcare professionals must address women's perceptions of their fertility to engage them in contraception counselling.

Presenter

Ariel Finkielstein

Authors

Finkielstein, A1, Panichi, D2, Castillo-Hernandez, T1, Watson, A3, Schlosser, A4, Holmskov, U4, Sorensen, G4, Kemp, M5, Madsen J1, Kramer, B2 and Clark, H1

Abstract

Background: Premature babies have low levels of SP-D and may develop RDS, which correlates with increased risk of neonatal chronic lung disease. A surfactant therapy with whole length native SP-D was shown to decrease inflammation in a pre-term ventilated lamb model of neonatal RDS (Sato et al., 2010), and a recombinant fragment of human surfactant protein D (rfhSP-D) was shown to have anti-inflammatory effects in a mouse model (Knudsen et al., 2007). We therefore hypothesized that surfactant treatment including rfhSP-D would decrease ventilator-induced inflammation similarly to full-length SP-D.

Methods:

Pre-term lambs were delivered by caesarean section, ventilated and treated intratracheally with surfactant only (N=8) or surfactant and additional rfhSP-D, at 1.5 mg/kg three times (N=16). Arterial blood gas measurements and blood samples were collected at 15 and 30 minutes, and then hourly up to 5h. Lambs were sacrificed to obtain tissue samples and bronchoalveolar lavage (BAL). Total RNA was extracted from lung tissue and gene expression of key inflammatory cytokines was determined by qRT-PCR. The levels of rfhSP-D in serum and BAL were measured by ELISA. The levels of inflammatory cytokines were determined by multiplex (Luminex).

Results:

We confirmed the presence of rfhSPD by ELISA in plasma and BAL from rfhSP-D treated lambs. We found rfhSP-D

treatment lowered gene expression of pro-inflammatory cytokines in the lungs and circulating levels of protein in plasma. Monocytes, lymphocytes and neutrophils in BAL showed a downward trend in the rfhSP-D treated group. Finally, lung physiological variables showed an improvement in lung compliance, modified ventilation index and peak inspiratory pressure in the rfhSP-D-treated groups consistent with reduced lung inflammation.

Conclusion:

In a lamb model of neonatal RDS, rfhSP-D showed similar anti-inflammatory properties to those previously reported for the full-length SP-D molecule.

Presenter

Arwa Almutlaq

Authors

Arwa Almutlaq, Sioban Sen Gupta, Rabi Odia, Xavier Gonzalez.

Abstract

BACKGROUND

MicroRNAs (miRNAs) are small non-coding genes that play a fundamental role in regulating gene expression post-transcriptionally. Little is known about miRNA in preimplantation embryo as a whole body. To have an overview of the biological pathway's activity in this stage of embryonic development, we here investigate the gene expression profile of miRNAs in fair quality embryos that are ready to implant.

METHODS

MiRNAs were extracted from 120 surplus embryos, which were consented and donated for research purposes from 46 couples. Using

the high throughput Next generation sequencing (NGS) technique, we captured and quantified the miRNAs expressed in each sample. Normalization of gene reads, and other statistical measures were all conducted using R and R studio. Gene ontology and pathway annotation were executed using miRPathDB 2.0 and Reactome, respectively.

RESULTS

A total of 2497 miRNAs genes were detected with an overall 9,388,791 reads. Pathway annotation, with experimental evidence, showed six critical biological processes that are expected to be highly regulated by miRNAs in blastocysts. These are: gene expression and transcription regulation which includes regulation by TP53 and RUNX family, FOXO transcription and post transcriptional protein modification like deubiquitination and PTEN regulation. Cell cycle and cell death processes were also influenced by the detected miRNAs showing a possible controlling function of the first two cell cycle phases (G1 and S), the genes associated with Cyclin A, D and E events, apoptosis, and oncogenic induced senescence. Moreover, genes involved in signalling and cellular responses such as AKT, NOTCH, ESR and tyrosine kinases along with genes regulating the immune response like interleukins and cytokines were highly implicated.

CONCLUSION

Understanding the post-transcriptional regulation of gene expression in preimplantation embryos may help us to clarify the unknown reasons for miscarriage and IVF failure, which will enhance the reproductive treatments.

Presenter

Bryony Stoneman

Authors

Bryony Stoneman, Andreia Goncalves

Abstract**Background:**

Recommended changes in policy have come into place in maternity services in the UK aiming to improve women's experiences, their health outcomes and their babies. Previous policy changes did not make women feel that their experiences of choice were improved, and the issue has only been officially re-highlighted in recent years following the National Maternity Review (NHS England, 2016). A large amount of research exists looking into the experiences of choice in the intrapartum period, yet minimal research is available that delves into women's perceptions of choice antenatally. In the current political climate, it is important to understand what they are, why women may feel this way and what changes need to take place to hand control back to women about their own pregnancies.

Objectives:

To examine women's perceptions of choice during decision making in their antenatal care.

Methods: A systematic review of the literature.

Results:

Twelve papers were selected for review after eligibility screening and results were presented in a thematic synthesis format. Multiple factors influence the way women receive information and whether they feel able to partake in decision-making. These includes restricted information from healthcare professionals, the power of clinical professions, societal norms and expectations, women's own demographics and an uncomfortableness with taking responsibility. Women who were looked after by caseloading midwives were more likely to perceive that they had the ability to access choice.

Conclusions:

The results align with the findings of the National Maternity Review (NHS England, 2016), and it is advised that the recommended policy changes be supported in each NHS Trust. These results also highlight the need for further research into the subject, including an in-depth study with a large sample of diverse women, examining their experiences. Authors also suggest for it to be looked at alongside audits for future policy changes.

Presenter

Catherine Stewart

Authors

Stewart, C., Hall, J.

Abstract**Background**

Utilisation of maternal healthcare is vital for improving maternal and neonatal mortality rates. Furthermore, the continuum of care (COC), defined as the integrated delivery of antenatal, delivery and postnatal care, has been shown to be particularly important. Sub-Saharan Africa has the highest neonatal and maternal mortality rates in the world and significant improvements in the utilisation of the COC are urgently needed. The barriers preventing women accessing

care need to be better understood for effective strategies to be successfully implemented.

Methods

4,244 pregnant women from the Mchinji District of Malawi were interviewed at home between March and December 2013. The overall utilisation of maternal healthcare was calculated from the integrated use of antenatal, delivery and postnatal care, combining all three services into one outcome variable. Univariate and multivariate ordered logistic regressions were performed based on a conceptual hierarchy to determine the factors associated with the utilisation of maternal healthcare in the Mchinji District.

Results

Utilisation of maternal healthcare in Mchinji District was inadequate, with only 24% of women receiving the recommended package. Being further from a healthcare facility (OR 0.2, 95%CI 0.04-0.96) and previous experience of miscarriage (OR 0.64, 95%CI 0.50-0.82) or abuse (OR 0.81, 95%CI 0.69-0.95) reduced utilisation, whereas being in the richest 20% (OR 1.33 95%CI 1.08-1.65), having a planned pregnancy (OR 1.3, 95%CI 1.11-1.51) or more control over decisions (OR 1.09, 95%CI 0.80-1.49) increased utilisation.

Conclusions

Women who live over 5km from a healthcare facility, who fall within the poorest socio-economic group, who are experiencing an unplanned pregnancy, who have experienced a previous miscarriage, who have no control over their healthcare decisions or who have experienced abuse have an increased risk of low utilisation of maternal healthcare. Extra attention should be paid to these high-risk groups when designing strategies to improve utilisation of maternal healthcare.

Presenter

Ellie Chilcott

Authors

Chilcott, E. 1, Antinao Diaz, J. 1, Moore, M.2, Counsell, J.R. 3, Schorge, S., Waddington, S.N. 1, Karda, R. 1

Abstract**Background:**

Dravet Syndrome is a paediatric form of epilepsy caused primarily by mutations in the SCN1A gene. Dravet Syndrome manifests around 6 months of age as refractory seizures, hyperactivity, autistic-like behaviour and increased mortality. SCN1A expression is regulated by a natural, regulatory element. Haploinsufficiency of SCN1A could be rescued by inhibiting this regulatory element by gene editing, allowing increased expression of the endogenous SCN1A gene.

Methods:

Guide RNA constructs targeting the regulatory element specific for mouse *Scn1a* were cloned into an AAV gene therapy vector backbone and tested in vitro. Baseline editing efficiency was determined in HEK293T cells by editing a control, luciferase gene. Neuron-like, Neuro2a cells were transiently transfected with these gene editing plasmids and assessed for increases in *Scn1a* expression by quantitative PCR. Separately, an in vivo model of Dravet Syndrome was characterised. The candidate AAV gene editing vector was

administered to neonatal heterozygous Dravet Syndrome and wild-type mice via injections into the brain ventricles.

Results:

Editing of the luciferase gene led to a 38% reduction of expression in vitro. Five guide RNA constructs targeting the regulatory element significantly increased endogenous Scn1a expression in vitro (1.54-1.97-fold change above baseline). AAV-treated heterozygous DS mice exhibited 85% survival at 30 days old, relative to 75% untreated animals and 100% of injected wild type mice. Interestingly, a caveat of this model is the mortality of heterozygous mice drops to 30% at 100 days; consequently long-term assessments are on-going.

Conclusion:

Gene editing of this naturally occurring regulatory element specific for Scn1a could be a therapeutic strategy for Dravet Syndrome by increasing endogenous Scn1a expression. The technology described here could provide a general approach for other diseases of haploinsufficiency for which similar regulatory elements are found..

Presenter

Georgia Graham

Authors

Graham, G. Hall, J.

Abstract

Background:

Family planning (FP) is essential for reducing unintended pregnancies and encouraging wider birth spacing. This is particularly important in Malawi where unplanned pregnancies are closely associated with maternal and neonatal mortality, and contraceptive services remain poor despite the increase in contraceptive prevalence rate. Indeed, restrictions to accessibility and availability make the correct use of user-dependent contraceptives difficult to achieve. By using minimally demanding methods like the implant or Intrauterine device (IUD) this can be avoided, however, individual and societal barriers inhibit the widespread use of such methods.

METHODS

A secondary analysis of data collected from the Mchinji District of Malawi in 2012 using binary logistic regression to assess the factors associated with 6-month post-partum implant or IUD use. A conceptual hierarchical model of the determinants of post-partum implant and IUD use was developed. Multivariable logistic regression was then performed to explore their combined influences on implant and IUD use and identify women in need of additional FP interventions.

RESULTS

Upon bivariate analysis, implant and IUD use was associated with mother's age, mother's education, postnatal marital status, distance to health facility, asset category, father's occupation, sexual abuse, pregnancy intention and postnatal check-up discussions of FP. These variables, plus father's education and live child number, were considered for the conceptual hierarchy. The multivariable analysis found that mother's age, distance to health facility, asset category, pregnancy intention, and live child number were associated with post-partum implant and IUD use. The effect of asset

category was mediated through reproductive characteristics.

CONCLUSION

This research suggests women <18 and >30, living further from a health facility, with a lower wealth index, weaker views on pregnancy intention and a low number of children should be targeted for post-partum FP interventions.

Presenter

Georgina Brown

Authors

Brown G, Madsen J, Clark H

Abstract

Asthma is an inflammatory disease that can be triggered through contact with allergens. It is one of the most common chronic diseases with more than 300 million cases worldwide. Allergens such as pollen and fungi are presented by dendritic cells, activating the adaptive immune system, and stimulating a Th2 CD4+ T cell response. The inflammatory cytokines released contribute to mast cell degranulation upon further contact with the allergen. Surfactant protein A and D (SP-A and SP-D) are innate immune molecules that bind to non-self glycoproteins. They have been found to have multiple functions in the immune system, including aggregating and opsonising pathogens, lysing bacteria, and immunomodulatory effects on other cells such as macrophages, dendritic cells, and T-cells. A recombinant form of SP-D has been developed that has been shown to maintain many of the immunomodulatory effects of the full-length protein. Surfactant proteins have been found to have anti-allergy properties, preventing histamine release, and suppressing an inflammatory response from dendritic cells. Surfactant proteins have been shown to have a role in modulating the pulmonary allergic response, however how they exert this influence is not fully understood. This PhD project will address research questions related to this mechanism. A co-culture of mast and dendritic cells will be established to create an in-vitro model of pulmonary inflammation. This model will be validated using techniques such as microscopy and flow cytometry. The crosstalk between the cells, and how surfactant proteins effect this, will be investigated by mass spectrometry and RNA analysis. This will allow the cytokines produced to be analysed.

This project presents the opportunity to research the anti-inflammatory roles of surfactant proteins, providing the groundwork for their possible use as a treatment for allergic asthma in the future. This could potentially alleviate the chronic inflammation characteristic of allergic asthma.

Presenter

Hannah Yusuf

Authors

Yusuf H,2,5 Stokes J,1 Whitten SM,1-2 SiassakosD.1-4

Abstract

BACKGROUND

Current research suggests women with a previous intrauterine fetal death (IUFD) are more likely to have a repeat IUFD than women with a previous live birth. Such risks range from a 2 to 20-fold increased risk. Despite this, there is limited research regarding the management and outcomes of subsequent

pregnancies. No single figure has been reported in the literature of the chances of a woman having a healthy subsequent pregnancy after IUFD, only of complications.

METHODS

A retrospective study was conducted at University College London Hospital between March 2019 and April 2021. Obstetric outcomes of women with a previous intrauterine fetal death after 16 weeks' gestation were investigated. Outcome data included birth outcome, obstetric and medical complications, gestational age and birth weight and mode of delivery. Those who had healthy subsequent pregnancies were compared with those who experienced adverse outcomes.

RESULTS

Ninety-six women with subsequent pregnancies after a history of IUFD > 16 weeks were identified. Seventy-nine percent of women delivered a baby at term, without complications. Overall, two women had repeat IUFDs (2.1%), two (2.1%) women delivered babies with fetal growth restriction. Those with adverse outcomes in their subsequent pregnancies had a greater incidence of pre-eclampsia ($p=0.033$) and fetal growth restriction ($p=0.028$) in previous pregnancies compared to those with healthy outcomes.

CONCLUSION

There is generally favourable outcome in pregnancy following IUFD. Four in five women had a healthy subsequent pregnancy. This is a very reassuring figure for women when contemplating another pregnancy, particularly if cared for in a specialist clinic.

Presenter

Janina Schellenberg

Authors

Schellenberg1 J., Aughwane2 R., David2 A., Maksym2 K., Flouri1 D., Mufti2 N., Melbourne1 A.

Abstract

BACKGROUND

Placental insufficiency causes fetuses to have dangerously low oxygen levels^{2,3,4}. Measuring placental function is done indirectly via fetal growth and Doppler ultrasound⁶ rather than investigating the presence of chronic hypoxia^{5,7}.

Quantitative MRI model fitting⁸ can determine properties which gives information about placental function such as perfusion and blood saturation^{2,9}. This could identify pregnancies affected by placental insufficiency.

METHODS

Written consent was provided by all subjects and data anonymised. Subject MRI data was acquired with a 1.5T Siemens Avanto under free breathing. The voxel resolution was 1.9x1.9x6mm. Data was acquired as a combination of 7 b-values and 9 echo-times. Lobular and placental segmentation was performed for FGR and control cases ($n=6$, itk-Snap). The growth-restricted data was grouped into pregnancies with normal Doppler's, uterine artery PI>95thcentile, uterine and umbilical artery PI>95thcentile ($n=2$ per group). DECIDE model fitting computed multi-parametric maps (MATLAB).

Average mean and FWHM with standard deviations were calculated. Significance testing was used for FGR and controls (t-test).

ANOVA testing determined differences between lobular and wholeplacenta segmentations.

RESULTS

Cases with raised uterine and umbilical Doppler exhibit significant differences for whole-placental average fetal T2 (control= 520.2 ± 275.5 ms, raised uterine and umbilical Doppler= 887.5 ± 579.1 ms, two-way t-test rejects null hypothesis with test statistic= -2.1498). No significant differences were found between the lobular segmentations and whole-placenta ROIs of the FWHM or mean of placental properties (eg. ANOVA for fetoplacental perfusion fraction: p -value= 0.0513 , critical value= 4.09 , $p<c$).

CONCLUSION

MRI parameters showed no difference for the FWHM or mean of lobules and whole-placenta ROIs. Results of lobular and wholeplacental segmentations agree. The low number of cases and variability of segmented lobules limits this study. Additional cases could show more differences between appropriately developing and growth-restricted pregnancies. This could determine differences between properties of lobules and whole-placenta segmentations. Nonetheless, the data shows significant differences for fetal T2 values for fetuses with raised uterine and umbilical Doppler.

Presenter

Kavita Prashar

Authors

Prashar, K

Abstract

BACKGROUND

Evidence supporting fetal surgery to correct antenatally diagnosed spina bifida has resulted in fetal surgery being offered as routine therapy to parents. Fetal surgery is not without risk, however, and potential parents are faced with the possibility of maternal and fetal demise during surgery. There are few policies available which provide guidance for both clinicians and parents on how to approach this scenario. This study aimed to determine current policy and practice for anticipated emergent fetal delivery (EFD) during fetal surgery in all Centres where this surgery is undertaken.

METHODS

This study used survey methodology to explore policies and practices in place for fetal, maternal and neonatal resuscitation, EFD and fetal death during fetal surgery. The survey was emailed to 47 Centres globally where fetal surgery for spina bifida is performed.

RESULTS

Responses were obtained from 22 Centres (47%). Most Centres have policies in place supporting fetal resuscitation (75%), EFD (50%) and fetal death (58%). Fewer Centres (37%) reported policies for maternal resuscitation. Only 2 Centres included parents in the development of these policies. The gestation that Centres would attempt neonatal resuscitation following EFD varied from 22+0 to >29 weeks.

CONCLUSION

The requirement for global consistency in practice requires all clinicians involved in coordinating fetal surgery for spina bifida

to be educated on how to approach and discuss the scenario of EFD with patients. All clinicians should seek to obtain informed written consent to perform these procedures.

Presenter

Kelly Harvey-Jones

Authors

Harvey-Jones, K1, Lange F2, Bale G2, Meehan C1, Avdic-Belltheus A1, Torrealdea F3, Sokolska M3, Golay X4, Bainbridge A3, Robertson N1, Tachtsidis I2, Mitra S1

Abstract

Background:

Neonatal encephalopathy (NE) remains a significant global health problem. A need exists for a cot-side biomarker for early stratification of severity and prediction of neurological outcome. Broadband near-infrared spectroscopy (BNIRS) monitors changes in mitochondrial metabolism (oxCCO) and cerebral oxygenation (HbD). Wavelet semblance (reactivity index) between BNIRS variables can measure cerebral autoregulatory disturbance at 48h of life during therapeutic hypothermia and predict outcome. A novel monitoring platform with BNIRS and diffuse correlation spectroscopy (DCS) can continuously monitor mitochondrial metabolism, oxygenation and cerebral blood flow (BFI). We hypothesised that optical metabolic and haemodynamic wavelet reactivity indices early after hypoxic ischaemic (HI) injury in a preclinical model will relate to outcome.

Methods:

BNIRS-DCS monitoring was performed in 19 newborn piglets after induced HI injury. Insult severity simulated moderate HI (7 piglets) and severe HI in 7 piglets, with 5 controls. Reactivity indices were calculated as mean oxCCO-HbD and BFI-HbD semblance over one hour of monitoring, 1h post-insult using wavelet analysis. All animals had MRI/proton MR spectroscopy in a 3T scanner 6hrs post-insult. Thalamic Lac/NAA 0.39 was used as cut-off threshold for neurological outcome along with Thalamic TUNEL+ cell count on brain histology.

Results:

Both oxCCO-HbD (metabolic reactivity) and BFI-HbD semblance (vascular reactivity) correlated with thalamic Lact/NAA ($p=0.009$, $r^2=0.353$ $p=0.057$, $r^2=0.234$ respectively) and thalamic TUNEL histology ($p=0.056$ and 0.020). Both oxCCO-HbD and BFI-HbD semblance were significantly different between groups based on insult severity ($p=0.046$ and 0.002) and neurological outcome using thalamic Lac/NAA threshold 0.39 ($p=0.002$ and 0.025).

Conclusions:

Early optical markers of metabolic and vascular reactivity following HI insult assess injury severity and predict neurological outcome in an animal model of NE. These findings need to be validated further in a clinical study and are potentially significant for clinical decision making, early prognostication and as an assessment tool for future clinical trials of emerging neuroprotectants.

Presenter

Konstantina Tetorou

Authors

Konstantina Tetorou, Claudia Sisa, Sigrun Lange, Mariya Hristova

Abstract

BACKGROUND:

Hypoxic-ischaemic encephalopathy (HIE) is a leading cause of child mortality and morbidity. The only currently available treatment for neonatal hypoxia-ischaemia (HI) is therapeutic hypothermia which has limited effectiveness and application. Thus, there is a need for alternative therapies for neonatal HI brain damage. HI strongly up-regulates Signal Transducer and Activator of Transcription 3 (STAT3) in the immature brain. We have previously shown that neuronal or astroglial STAT3-deletion reduce cell death, tissue loss, microglial and astroglial activation in a postnatal day 7 (P7) HI mouse model, suggesting detrimental effect of STAT3 in neonatal HI. Moreover, pre-insult STAT3-blockade at tyrosine 705 (Y705) with JAK2-inhibitor WP1066 reduces microglial and astroglial activation to a more moderate degree, but similarly to the cell-specific deletions. The P7 mouse is considered slightly pre-term, while the P9 corresponds to term when compared to the human fetus. Therefore, we aimed to investigate whether inhibition of STAT3 phosphorylation at Y705 will provide neuroprotection in the P9 mouse similarly to the P7 model. We hypothesized that pharmacological STAT3 Y705 inhibition immediately post-HI will provide neuroprotection in the neonatal P9 mouse.

METHODS:

We subjected P9 mice to unilateral carotid artery ligation and 60min hypoxia, and then treated them with different doses of WP1066, compared with non-treated controls.

RESULTS:

WP1066 treatment reduced brain tissue loss, cell death, microglial and astroglial activation and protected myelination at a dose of 80µg/g body weight, however doses of 40µg/g and 160µg/g were not neuroprotective.

CONCLUSION:

STAT3 is a crucial factor in neonatal HI-brain damage and the immediate post-HI inhibition of its phosphorylation with a dose of 80µg/g WP1066 reduces inflammation, tissue loss and cell death. The application of WP1066 as a neuroprotective agent in the regulation of STAT3 phosphorylation may be a promising new strategy in neonatal HIE..

Presenter

Lily Hutton

Authors

Hutton L., Nicholls J., Khan Z., Neiman S. & Lanceley A.

Abstract

Background

Episiotomy is a surgical incision of the vaginal wall and perineum, performed by health care professionals (HCP) in 1 in 7 births. Informed consent to surgery of any description, including episiotomy, is a legal requirement and is fundamental to effective medical practice. The landmark legal case of Montgomery represents a shift from a doctor-assessed standard of what information should be disclosed to a patient making a decision requiring their consent, to a patient-centred standard in which an individual woman's values and preferences are fully recognised. There is some evidence that

consent processes on the labour ward in general do not align with the law or professional practice guidance. However little is known about how HCPs gain consent for episiotomy.

Methods

Ethical approval from the Health Research Authority was gained (REC 17/YH/0212) and a semi-structured interview topic guide was developed for the one-on-one interviews which lasted between 20-45 minutes. The participants were 7 doctors and 10 midwives who worked at an inner-city NHS Foundation Trust Hospital. Interviews were audio recorded, transcribed, and thematically analysed using Braun & Clarke's 6-phase approach.

Results

Consent to episiotomy is not always meeting the current legal and professional standards of consent. Four key themes were identified: professional conflict in honouring women's autonomy; minimising women's choices; expressed acquiescence with clinical judgement and professional practice and the law.

Conclusion

Our findings indicate that healthcare professionals do not always implement consent practices which accord with legal and professional requirements. We suggest that consenting women for an episiotomy is an area of professional practice that needs further scrutiny and should be a training priority for healthcare professionals.

Presenter

Maria Ivan

Authors

Ianosev, C-S2, David, AL1,2

Abstract

Background:

Congenital uterine abnormalities affect up to 1% of all pregnant women and are associated with late miscarriage and preterm birth. A unicornuate uterus appears to confer a high risk of complications although there is limited prospective data on which to base advice to women.

Methods:

This is a 10-year prospective study of pregnant women diagnosed with unicornuate uterus who underwent antenatal surveillance in the UCLH Preterm Birth Clinic (2011 – 2021) after the first trimester.

Results:

Out of 47 women identified, 43 had complete outcome data. All women had a livebirth. The preterm birth rate was 14% (95% CI [5.3%, 27.9%]). The median gestational age at delivery was 38w6d (+/- 2w3d, interval range [30w0d, 41w4d]).

Nearly one-fifth of patients (18%, 8/43) underwent a preterm birth intervention due to identification of a short cervical length (7%, 3/43 cases) or a history of preterm birth/late miscarriage (11%, 5/43 cases). Cervical cerclage was performed in 7 cases (16% (7/43) and 1 patient (2%) received vaginal progesterone pessaries. The spontaneous preterm birth rate amongst patients receiving a preterm birth intervention was 50% (4/8 cases).

Renal tract abnormalities were identified in 28.5% (12/42, 1 missing data). The presence of a renal tract abnormalities was not associated with a positive urine culture or an increased risk

of spontaneous preterm birth when compared with patients who had normal renal anatomy.

Women who had undergone surgery for a rudimentary horn (14%, 6/43 cases) were no more likely to deliver spontaneously preterm if they had undergone the surgical removal or preservation of the rudimentary horn (16.7% vs 13%, Fisher's exact test $p=1$). Similarly, there were no significant differences in the median gestational age at delivery across different types of unicornuate uteri: rudimentary horn present vs isolated unicornuate uterus (median 39w0d, $p = 0.529$).

Conclusion:

Our results indicate a good pregnancy outcome of women with unicornuate uterus, even in women who underwent prophylactic preterm birth interventions. The sample size was small which limits the strength of some conclusions. We propose a national UK study using the UK Preterm Birth Network.

Presenter

Michele Robinson

Authors

Robinson M, Yasmin E, Davies M

Abstract

Background:

Fertility preservation (FP) for women with cancer is well established, however FP for women with benign conditions that may threaten fertility is not well represented in FP clinics, accounting for 8-13% of indications for FP.^{1,2} Recent guidance has emphasised the importance of recognising benign conditions as indications for FP.^{3,4}

Methods:

Audit of clinic database between August 2019 and April 2021.

Results:

We examined the database for FP consultations and identified 23 women with non-malignant conditions who had discussions on FP. 48% had gynaecological conditions which may require fertility limiting surgery. These included ovarian cysts (dermoid or borderline) and endometriosis. 45% of these women undertook FP. The reasons for declining treatment included young age (14), intention to conceive naturally, or opting for surveillance. 35% had medical conditions requiring gonadotoxic treatment or stem cell transplant, including multiple sclerosis, sickle cell anaemia and SLE. Two women with Langerhans histiocytosis and Rosai-Dorfman disease were planned for chemotherapy. All of these women accepted FP treatment, however one was declined after MDT discussion, due to increased thrombosis risk. 17% were women with conditions which risk premature ovarian insufficiency (POI) including Fragile X carrier status, Turner syndrome, polyglandular autoimmune endocrinopathy, and NR5A1 mutation carrier status. 75% of these patients underwent treatment.

Conclusion:

Women with benign conditions account for 9% of the referrals to our FP clinic. They may benefit from counselling regarding FP, which is often less considered than for oncological patients, due to a lack of information from medical teams. Each indication must be carefully considered to reduce risks of

complications. More long term data to further understand the risks and benefits of FP in benign conditions are required.

Presenter

Nada Mufti

Authors

Mufti, N1,3, Ebner, M3,4, Patel, P8, Aertsen, M9, Gaunt, T2,8, Humphries, PD8, Bredaki, FE2, Hewitt, R7, Buter, C.7, Sokolska, M5, Kendall, GS1,2, Atkinson, D6, Vercauteren, T3,4, Ourselin, S3,4, Pandya, PP2, Deprest, J1,10, Melbourne, A3,4, David, AL1,10

Abstract

Background:

Reliable diagnosis of airway patency in fetuses with tracheal-aryngeal obstruction is crucial for Ex-Utero Intrapartum Treatment (EXIT) procedure surgical planning. Fetal MRI requires ultrafast acquisition of thick 2D slices to mitigate effects of unpredictable fetal motion whilst maintaining a high signal-noise-ratio. This can result in data with limited geometric integrity, complicating accurate diagnosis. We present a case-series of fetuses with upper airway obstruction in which MRI super-resolution reconstruction (SRR) of the trachea was performed, evaluating the clinical potential of novel MRI technology.

Methods:

SRR of the trachea was performed on seven cases from University College London Hospital. This involved rigid motion correction of acquired 2D slices combined with robust outlier detection to reconstruct an isotropic high-resolution volume. SRR volumes, 2D MRI, and paired data were blindly assessed by three radiologists in three experimental rounds.

Results:

Airway patency was correctly diagnosed in 4 out of 7 cases (57%) using 2D MRI in comparison to 2 out of 7 cases (29%) when using SRR alone or paired 2D MRI and SRR. Radiologists were more confident ($p=0.026$) assessing airway patency using 2D MRI compared to SRR. Anatomical clarity was higher using SRR ($p=0.027$) or paired data ($p=0.041$) in comparison to 2D MRI. Radiologists were able to detect further anatomical details like head and neck involvement using paired images compared to 2D MRI ($p<0.001$). There was no difference in time for assessment using 2D MRI, versus paired imaging. Cognitive load, assessed by the NASA Task Load Index, was increased using paired or SRR data in comparison to 2D MRI.

Conclusion:

Fetal 2D MRI used alongside SRR of the trachea provides comprehensive anatomical information which is beneficial for EXIT surgical planning. Additional validation is necessary to support SRR fidelity and limitations of rigid motion-correction for reconstructing non-rigidly deforming anatomy should be taken into account.

Presenter

Natasha Liou

Authors

Natasha Liou, Rajvinder Khasriya, Catherine Chieng, Qingyang Kong, Anna David, James Malone-Lee, Artur Yakimovich, Harry Horsley

Abstract

Background

Women are disproportionately affected by urine infections. Urine microscopy, where a microscopist visually identifies cellular content in urine, is arguably the most accurate test to diagnose infections. Machine learning (ML) is a powerful tool that has increasingly become a useful adjunct to clinical care. We demonstrate the application of image-based ML to identify urinary cells from microscope images.

Methods

Patients with lower urinary tract symptoms were recruited from an outpatient clinic over a two-month period. Urine samples were assessed on-site using brightfield microscopy. Weak annotation was applied to segment informative foreground (e.g. bacteria) from background (e.g. debris) and produce binary masks for ML training. FIJI was used for optimisation and particle analysis. DICE score was used to assess the ML model's accuracy in predicting cells. Exploratory data analysis was used to perform cluster analyses, and one-way ANOVA tests to compare morphometric features.

Results

826 images were obtained from 100 patients, and 36,733 cells identified. The ML workflow produced an initial DICE score of 61.5% (95% CI 60.8-62.2). Optimisation resulted in a DICE increase to 80.8% (95% CI 80.7-80.9%). 7 clusters were identified, and representative cluster centroids were visually confirmed to be distinctly separate biological cells, all of which are common markers of infection. ANOVA test confirmed each cluster to be significantly different in surface area ($F = 51.156$, $p < .0001$) and circularity ($F = 60.575$, $p < .0001$).

Conclusion

We demonstrated the application of image-based ML to identify cells from microscope images and achieved an accuracy over 80%. We identified 7 significantly distinct clusters which appeared to correlate with visual examination. We now aim to leverage more advanced ML techniques and anticipate the model will be capable of identifying cells with even greater accuracy. This state-of-the-art model could be easily translatable to a point-of-care test to diagnose urine infections.

Presenter

Naz Shagufta

Authors

Shagufta. N

Abstract

BACKGROUND:

Surfactant Protein D (SP-D), found in surfactant, is an innate immunity protein with immuno-modulatory properties and is important in the clearing of airways viruses. Low or absent levels of levels of SP-D in lung lavage has been observed in patients with chronic obstructive pulmonary disease (COPD) and asthma with excessive exacerbations and in the premature babies and has been linked with levels of inflammation in the lung. Human rhinovirus (HRV) and respiratory syncytial virus (RSV) has been linked with exacerbations in adults with COPD and asthma and is also a problem in preterm infants. A recombinant fragment of human SP-D (rfhSP-D) has been developed and shown to have the same anti-inflammatory properties as native full-length SP-D and is currently in the

process of being tested in a “first in man” safety phase I trial in spring 2021.

METHODS:

The aim of my PhD project is to investigate the interaction of rfhSP-D with HRV and RSV in detail and evaluate where in the timeline of a viral infection, SP-D therapy might have the best impact. My project will use various methods including Western Blot, Co-Immunoprecipitation, ELISA, Surface Resonance Plasmon with recombinant viral surface proteins and in vitro and in vivo infection models where outcomes will include viral titres and level of cytokines.

RESULTS: Just started on my PhD project so results yet to come.

CONCLUSION:

This information could be useful in evaluating if rfhSP-D has a potential to be developed as an antiviral agent against HRV and/or RSV.

Presenter

Radha Graham

Authors

Radha Graham¹, Nicola D MacDonald¹, Krithika Murali ², Shah-Jalal Sarker³, Rowan Miller^{1,4}, Susana Banerjee², John Butler², Sara Stoneham¹, Jonathan Shamash⁴, Viola Liberale¹, Daniel M Berney⁴, Michelle Lockley^{1,5}, Claire Newton^{6,7*}

Abstract

Background:

We aimed to describe current surgical practice in the management of stage 1 ovarian germ cell tumours and oncological outcomes. These tumours are rare (1-2% of all ovarian malignancies), and there are no interventional trials in this field.

Methods:

All consecutive patients with stage 1 primary ovarian germ cell tumours treated in four major UK gynaecology oncology centres over 12 years were assessed.

Results:

Eighty-six patients were followed-up for 4.4 years (median, IQR 4.3). Overall survival estimates were 96.6% (OS, 95% CI 91.9-100%) at 5 years, and event free survival 81.8% (EFS, 95% CI 72.5-92.3). The majority (93%,n=80) had fertility-sparing surgery, which was not associated with higher rates of recurrence or death than non fertility-sparing approaches. Surgery was most commonly via laparotomy (n=66, 76.7%). Surgical route was not associated with significant difference in OS or EFS. Assessing the use of surgical staging, 42 (48.6%) patients underwent staging procedures, with equivalent rates between histological subtypes. Peritoneal biopsies were taken in eleven patients (12.7%), omental assessment in 40 (46.5%) and lymphadenectomy 10 (11.6%). There was no significant difference in EFS in patients who underwent any form of staging procedure (83% in staged (95% CI 71-98%) versus 84% (95% CI 72-98%) in unstaged). Assessing EFS in patients undergoing surveillance alone without adjuvant therapy, there was no difference in recurrence in staged patients (37% 10/27) (EFS 72% (95% CI 54-97%) versus unstaged (16% 5/31) EFS 92% (5 year CI 81-100%). The majority of unstaged patients not receiving adjuvant treatment had immature teratoma or dysgerminoma histology (87.1% (27/31).

In patients with immature teratoma, outcomes of unilateral cystectomy only (n=9) and unilateral salpingo-oophorectomy (n=29) were compared, with no significant difference in death, recurrence or residual disease.

Conclusions:

In patients undergoing surveillance alone, the absence of surgical staging did not impact upon disease free or overall survival, and may be acceptable in a subset of patients. If ovarian cystectomy is performed for immature teratoma and malignancy subsequently identified, observation rather than completion surgery may be an alternative management strategy.

Presenter

Rose Maloney

Authors

Maloney, R1, Whitten, SM2,3

Abstract

Background:

Sex workers (SWs) are vulnerable to stigma and discrimination, partly driven by criminalisation of sex work, with punitive laws increasing risk of harm. Migrants and LGBTQ+ people are particularly vulnerable, with intersecting identities creating increased opportunity for discrimination. SWs have a high burden of sexually transmitted infection (STIs) and a greater risk of mental illness and domestic violence. Research suggests SWs struggle to access healthcare.

This work aimed to explore barriers which impact upon SWs access to healthcare, and to conduct a service review of current provision of care for SWs in London.

Methods

This was a mixed methods study:

- Literature review exploring mechanisms, barriers and facilitators for SWs access to healthcare.
- Online service review of London-based healthcare for sex workers, utilising online search strategies, reviewing for inclusivity, accessibility, range of support available, and overarching aims and ethos.

Results:

Literature review: 15 peer-reviewed and 9 pieces of grey literature were included. Stigma, breaches of confidentiality from healthcare professionals (HCPs) and low-privacy healthcare settings created barriers to seeking care. Peers were essential to empower SWs to access healthcare. Service review: Four NHS clinics and seven charities were identified. Services had varying perspectives on the nature of sex work, with charities often viewing it as inherently exploitative; this impacted whether they took a harm-reduction approach or prioritised ‘exiting’ sex work. Not all services promised confidentiality and non-judgemental attitudes to service users, and not all services referred SWs to further care.

Conclusion:

Person-centred, non-stigmatising care is essential for SWs; current services do not always meet this. Services must offer a wider range of health services, beyond just STIs. Sex workers are an underserved population, with healthcare and legal environments which limit access to care. A ‘best practice’ matrix may be useful for service providers to consider when developing their services.

Presenter

Sania Latif

Authors

Latif S, Davies M, Lavery S, Mavrelou D, Yasmin E

Abstract**Background:**

Childhood cancer survival has improved greatly, leading to a growing population of girls at risk of premature ovarian insufficiency. Fertility preservation (FP) in the adolescent group represents unique challenges - physiological, medical, social and psychological - as this is a stage of substantial growth and change. Oocyte cryopreservation (OC), ovarian tissue cryopreservation (OTC) and ovarian transposition (OT) are key techniques applicable in this population. Response to OC in adolescence has not been well studied. We report our clinical experience in managing girls undergoing FP.

Methods:

A retrospective study of girls < 18 years attending a specialist unit for FP between 2016 - 2021. Data was retrieved from a prospectively managed database.

Results:

A total of 57 girls aged < 18 years (10-17 years) were referred, 23% (13/57) had previously received chemotherapy. Indications for FP included malignancy, immunological disorders, benign haematological disorders, recurrent ovarian cyst surgery and gender reassignment treatment. 60% (34/57) did not proceed with FP, OTC was performed in 19% (11/57), OC in 16% (9/57) and OT in 7% (4/57). In the OC group, AMH was 7-28 pmol/L, AFC 7-36, and random-start with GnRH analogue trigger used in 78% (7/9). Number of cryopreserved oocytes was 10-45 and number of MII oocytes 8-35. There were no complications in any cycle, including the 55% (6/9) performed for haematological malignancy. In those who did not proceed with FP, reasons included patient choice 56% (19/34), being medically unfit 18% (6/34) and no gonadotoxic risk identified 9% (3/34). Parental consent in under 16's was obtained.

Conclusions:

This is the largest case series published in this population. FP in adolescent girls is associated with unique medical and ethical challenges, affecting treatment planning, decision-making, and consent. Services treating treating under 18s need to undertake an individualised assessment and provide all modalities of FP (OC, OTC, OT).

Presenter

Silvia Vignola

Authors

S. Vignola¹, C. Cavalli^{1,2}, V. Azzaretto^{1,2}, V. Donadono¹, R. Napolitano^{1,3}, P. Pandya^{1,3}

Abstract**Background:**

The ultrasound assessment of fetal biometry and fetal growth is an essential component of antenatal care which can substantially contribute to the correct management of the pregnancy. Moreover, the acquisition of standard fetal biometry planes is one of the trainees' first approach to fetal ultrasound in teaching modules. Therefore,

it is important that this assessment is accurate and reproducible. Our study aims to assess the reproducibility of ultrasound measurements for fetal biometry, using a focus point (FP) for the acquisition of the relevant plane.

Methods:

80 women with singleton normal pregnancies were recruited at University College London Hospital between 18 and 37 weeks. Planes to calculate head circumference (HC), abdominal circumference (AC) and femur length (FL) were obtained twice by sonographers with different experience, blind to each other, the first time asking to obtain the plane referring to a standard image, the second time using the FP: a unique landmark that once identified, the sonographer is asked to rotate the probe along the 3 axes (x, y, z) to acquire the relevant plane keeping the FP in view (cavum septum pellucidum for HC, 2/3 of the umbilical vein for AC and one of the two diaphysis for FL). Sonographers were in training or with > 3000 scans experience. Intra- and interobserver reproducibility were assessed using Bland-Altman plots calculating mm and %.

Results:

Overall reproducibility was good with 95% confidence intervals (CI) <8%. Reproducibility was higher using the FP compared with acquiring the plane without using the FP, regardless of sonographer seniority (95% CI <4% versus <6% for intra- and <7% versus <8% for interobserver reproducibility respectively).

Conclusions:

Fetal biometry reproducibility is higher with the use of FP for plane acquisition regardless of sonographer experience. We propose this method to be used for clinical practice and training.

Presenter

Sonia Johnson

Authors

Petrovic, M1; Johnson, S2, Whitten, M3, Siassakos, D4.

Abstract**Background**

1 in 267 pregnancies end in stillbirth and gestational diabetes confers a 3-fold increased risk which continues at lower thresholds. Congenital pneumonia accounts for 10-38% of stillbirths with no identified risk factors in 83% of cases. The aim of this retrospective case review is to investigate a relationship between congenital pneumonia and diabetes in pregnancy at lower thresholds, through abnormal placental histopathology.

Methods

Congenital pneumonia cases were retrieved from clinical databases and experts in February 2021. Presence of glucose dysmetabolism serum markers or risk factors indicative of diabetes and infection triggers were compared between true congenital pneumonia ('no MSAF') and a control ('MSAF'). Histopathologies were analysed for fetoplacental lesions.

Results

33 cases were eligible including 4 perinatal mortalities. 88.9% had ≥1 diabetic risk factor, 56% ≥1 glucose dysmetabolism marker out of which 44% were potentially undiagnosed and 75% had ≥1 infection trigger. 'No MSAF' had increased

diabetic risk factors (70.4%;P=0.156) and markers (40%;P=1.000) which were nonsignificant. Infection triggers were weakly increased in cases with risk factors (73.1%;P=0.123; 'No MSAF' 65.2%; P=1.000) and not different in dysmetabolism markers (37.5%;P=0.649), except for 'No MSAF' (46.2%;P=0.497). 3 out of 4 perinatal mortalities had fetoplacental lesions and similar characteristics.

Conclusion

Congenital pneumonia was not strongly associated with diabetes in pregnancy when comparing 'MSAF' subgroups. Lethal cases suggest there may be a link in babies with fetoplacental lesions but insufficient placental data was available. Work is needed to improve histopathology referrals and reporting prior to re-testing the hypothesis using a matched control group without pneumonia.

Presenter

Tatiana Nazarenko

Authors

T. Nazarenko, H. J. Whitwell, O. Blyuss and A. Zaikin

Abstract

BACKGROUND

A representation of complex data in the form of a network, i.e. a graph with nodes and edges, is a powerful tool to visualise data structure, clusters and communities, and all other interdependencies. Parenclitic and synolitic networks provide a powerful and relatively new way to coerce multidimensional data into a graph form, enabling the application of graph theory to evaluate features.

METHODS

To compare different network approaches alongside more traditional machine-learning algorithms, we performed a substantial analysis using both synthetic data with a priori known structure and publicly available datasets used for the benchmarking of ML-algorithms.

RESULTS

We have successfully applied network analysis to a number of multidimensional data, e.g. to predict a severity of COVID-19 patients following the analysis of high-throughput proteomic data. Moreover, a comparison of different network approaches has shown that the main advantage of parenclitic and synolitic networks is their resistance to overfitting (occurring when the number of features is greater than the number of subjects) compared to other ML approaches. Secondly, the capability to visualise data in a structured form, even when this structure is not a priori available, allows for visual inspection and the application of well-established graph theory to their interpretation, eliminating the "black-box" nature of other ML approaches.

CONCLUSION

The quality of the synolitic network algorithms as a classifier is higher for those datasets where the sample size is small in comparison with the features size. Using this advantage we have recently applied this approach to the analysis of proteomics data from a large cohort of CoVID-19 patients.

Presenter

Vaishali Kiridaran

Authors

Kiridaran, V, Bailey, J, Chawla, M

Abstract

Background:

Many South Asian women face difficulties accessing sexual health services due to faith and cultural taboos. Therefore, there is a need to understand South Asian women's attitudes towards and experiences with sexual health service provision to recognise how healthcare providers can develop culturally appropriate initiatives and facilitate equality of access.

Methods:

Thirteen semi-structured interviews with South Asian women over the age of 18 and living in the UK were conducted and video-recorded online. Interviews explored participants' experiences of accessing sexual health services, including discussions around contraception, smear tests and STI tests. Thematic analysis was used to analyse the data.

Results:

Five themes were identified: 1) Interactions with healthcare professionals: Participants were often met with judgement and a lack of partnership from clinicians. 2) Stigma and shame: Many participants felt shame in accessing services and discussing their sexual health. 3) Confidentiality concerns: Many participants conceal their sexual activity and expressed concerns around the confidentiality of services. 4) Accessibility of sexual health services: Long waiting times and poor availability of services created a sense of panic. 5) Information provision: Due to limited knowledge around sexual health and local sexual health services, participants stated a need for better provision of information.

Conclusion:

This research highlights the cultural and social factors that underpin engagement with sexual health services. Formal training in cultural competence for service providers may facilitate a greater understanding of cultural issues pertinent to the South Asian community. Service providers should collaborate with community-based organisations to develop culturally appropriate initiatives.

Presenter

Vera Donadono

Authors

Donadono, V.¹; Ambroise Grandjean, G.^{2,3,4}; Stegen, M.¹; Collin A.³; Bertholdt, C.^{2,3}; Casagrandi, D.^{1,5}; Morel, O.^{2,4}; Napolitano R.^{1,5}

Abstract

Background: Obstetricians rely on fetal biometry to make decisions regarding the antenatal care and delivery plan. Unfortunately access to training in ultrasound is still limited not only because of lacking resources, but because of a missing comprehensive structured training programme. In this study we aim to assess the intra- and interobserver reproducibility of fetal biometry measurements obtained by trainee (junior) and experienced sonographers (senior) in the contest of two training programmes in obstetric ultrasound.

Methods:

This was a prospective study on 192 women recruited ensuring an even distribution throughout gestation (18 to 41 weeks), at University College London Hospital (UCLH), UK (87 cases) and

at Maternité Regionale Universitaire de Nancy (MRUN), France (105 cases). Measurements for head circumference (HC), abdominal circumference (AC) and femur length (FL) were obtained twice by junior and senior sonographers, blind to their own and each other's measurements. Differences between and within sonographers were expressed in mm and as a percentage of fetal dimensions. Reproducibility was assessed using Bland-Altman plots.

Results:

Reproducibility was overall high with 95% confidence intervals (CI) within <6% for intra-observer and <8% for inter-observer reproducibility. Intraobserver reproducibility was lower within junior than senior sonographer measurement for HC (95% CI: <4% vs. <3%) and FL (95% CI: <6% and <5%). Intraobserver reproducibility was similar between the two centres/training programmes (AC 95% CI: <6%). Cumulative interobserver reproducibility in both centres was similar to the reproducibility within a single site (95% CI: <5%, <8%, <7% for HC, AC, FL respectively).

Conclusions:

Reproducibility of fetal biometry measurement was high in centres with structured training programmes regardless of sonographer experience. Reproducibility was higher in sonographers who completed the training.

Presenter

Vikram Talaulikar

Authors

Malgorzata Bochno, Vikram Talaulikar, Françoise Shenfield and Melanie Davies

Abstract

Background:

Infertility or ovarian insufficiency can result from medical therapies, and in addition female fertility declines with age. Oocyte cryopreservation can be utilised to preserve fertility potential. We sought to study the knowledge and attitudes of doctors in a teaching hospital towards discussing fertility and oocyte cryopreservation.

Methods:

A cross-sectional online survey (containing 17 questions) was conducted between 2017 to 2020 among clinicians in University College London Hospital. Participants included 82 doctors from several clinical specialties. 57% of the respondents were female. The survey data was analysed to verify sample characteristics, clinicians' knowledge about female fertility and IVF success rates, and clinicians' attitudes towards fertility preservation.

Results:

Virtually all respondents (98%) felt that a doctor treating female patients in the reproductive age-group should initiate discussions about implications of illness and treatment on their fertility. 90% of doctors felt that there is a need for a specialist pathway for them to be able to refer patients for fertility discussion or fertility preservation. 3 out of 4 doctors felt that discussing the natural decline in fertility with age should be a part of routine clinical care - like cervical smear testing or contraceptive advice with a GP or Gynaecologist. 75% of respondents felt that educating women about such issues helps them make informed reproductive decisions.

Conclusion:

As this is a single centre survey conducted at one university teaching hospital, it limits the generalisability of the findings. However, the survey result indicates a need to establish a clear and 'easy to access' referral pathway for specialist clinicians who wish to refer women for appropriate fertility consultation and/or counselling. Most survey participants indicated a need to promote informed reproductive decision-making among patients. Efforts are therefore needed to help specialist clinicians provide comprehensive fertility education to all women, while respecting their individual choices.

Presenter

Xulin Foo

Authors

Foo X., Burt E., Lavery S., Yasmin E., Davies M.

Abstract

Background:

Gender incongruent individuals undergoing gender-affirming hormone treatment (GAHT) may face infertility. Evidence on fertility after testosterone use is limited, but is not known to cause irreversible infertility. Testosterone causes amenorrhoea and polycystic ovarian morphology¹. Medical bodies such as the Endocrine Society recommend fertility preservation (FP) counselling before GAHT². Our study describes the experience and uptake of FP by oocyte cryopreservation in trans-males at our centre.

Methods:

We conducted a retrospective study of trans-males referred for FP between July 2013 and January 2021. Demographic data, GAHT use, treatment funding and outcomes were obtained from electronic records.

Results:

Gender incongruence (GI) formed 7.5% (45/598) of our FP clinic attendances. Patients were referred via Paediatric Endocrinology (26/45;57.8%), GP (12/45;26.7%) and the Gender Identity Development Service (7/45;15.6%). Median age was 16 years (range 13-45 years) at referral and 17 years (range 14-45 years) at presentation. The average clinic waiting time was 141 days (range 11-1087 days). Patients were on GnRH analogues (23/45;51.1%), GnRH analogues and testosterone (8/45; 17.8%), contraceptives for menstrual suppression (7/45;15.6%), or testosterone alone (1/45;2.2%). Following counselling, 44.4% (20/45) did not proceed with treatment for the following reasons: no intention to be biological parent (7/20;35%), absence of funding (5/20;25%), concerns about interrupting GAHT (3/20;15%), not the right time (1/20;5%), medically unfit (1/20;5%), not Gillick-competent (1/20;5%), and moved away (1/20;5%). Funding was approved in 56% (14/25).

Conclusions:

Referral for fertility discussion for GI followed various routes. FP uptake rate was 24.4% (11/45), which is higher than described in previous studies^{3,4}. This may be explained by better access to funding. In those who declined FP, majority cited genetic parenthood not being important; whether decisions around fertility and parenthood change later merits further study. FP counselling need not be restricted to pre-GAHT, but can be conducted post-GAHT. There is need for more consistent referrals.



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Medical Student Prize Talk

Obstetric outcomes among women with reactive hypoglycaemia at glucose tolerance test

Salsabeel Nasreen Kazi (Medical Student)

Co-authors: Rehman S, Kindinger L, Siassakos D, Wallis N & Whitten M

Some women experience "reactive hypoglycaemia" (RH) during oral glucose tolerance test (OGTT) screening for gestational diabetes (GDM). RH can be defined as a 2-hour plasma glucose value which is lower than the fasting value. In the non-pregnant population, RH is associated with early insulin resistance (impaired first-phase secretion) and diabetes. However, its significance and impact on obstetric outcomes is poorly understood as studies are limited, heterogeneous and define RH differently.

The aim was to assess the obstetric outcomes of women with RH during an antenatal OGTT, defined as a 2-hour plasma glucose lower than the fasting value. This was a cross-sectional study of 1063 antenatal women attending University College London Hospital for an OGTT between April 2019-July 2020. The outcomes were compared across three groups: RH, GDM and controls.

In the sample, 301 women had RH, 450 had GDM, and 312 had a normal OGTT (controls). Mean birth weight was greatest in the RH group (3355 ± 539 g) compared to both the GDM (3208 ± 575 g, $p=0.0002$) and control groups (3298 ± 522 g). Relative to controls, RH had higher rates of polyhydramnios (7.8% vs 3.9%, $p=0.03$), abdominal circumference >95th centile (11% vs 5.1%, $p=0.005$), small-for-gestational age infants (5.3% vs 2.4%, $p=0.048$) and neonatal oxygen desaturation (1.3% vs 0%, $p=0.04$). Compared to GDM, RH babies were more likely to have ambiguous genitalia (2.5% vs 0.4%, $p=0.01$). The RH group had the highest rates of chorioamnionitis (4.6% vs GDM 2.7% vs controls 1.9%), wound infection (5.3% vs 3.6% vs 2.9%, respectively) and gestational hypertension (12.3% vs 10.5% vs 10.6%, respectively). Stillbirths were observed in the GDM and RH groups only (RH $n=1$, GDM $n=3$, controls $n=0$).

In this sample, women with RH were at risk of adverse outcomes usually associated with insulin resistance and diabetes.



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