ID: 74  
**TITLE:** THE POPULATION OF CIRCULATING EXTRACELLULAR VESICLES DRAMATICALLY ALTERS AFTER VERY PREMATURE DELIVERY - A PREVIOUSLY UNRECOGNISED POSTNATAL ADAPTATION PROCESS?  
**AUTHORS:** Daniel O’Reilly1,6, Karl Egan1,2, Oscar Burke1, Angharad Griffiths3, Elaine Neary3, Alfonso Blanco1, Paulina Szklianna1, Patricia Maguire1, Naomi McCallion3,5, Fionnuala Ní Áinle1,2,4  
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**CONTENT:**  
Following birth, the transition from intrauterine to extrauterine life is associated with major physiological changes, including the clearance of lung liquid and the closure of the ductus arteriosus. Many pathological processes linked with mortality and serious morbidity in preterm infants start at this time. Extracellular vesicles (EVs) are small subcellular particles released by all known cell types and readily detectable in large numbers in all biological fluids. EVs are heterogeneous in size and origin, consisting of exosomes (endosomal origin, 30-150 nm), microvesicles (plasma membrane-derived, 50-1000nm), and apoptotic bodies (500-2000 nm). They are linked with a wide variety of processes including coagulation and cell-cell communication, and it has been hypothesized that they may affect lung disease and other preterm morbidities. It is however unknown whether circulating EVs can change during this extrauterine transition period.  

Preterm neonates were recruited through the Department of Neonatology at the Rotunda Hospital, Dublin, Ireland. Written informed consent was obtained from the parents of all participants. Blood collection was performed during routine phlebotomy. Platelet free plasma was prepared by double centrifugation at 3000g for 10 minutes. 15x Day 1 of life and 14x days 3 of life plasma samples were available from preterm neonates, 8 of which were matched Day 1 (D1) and Day 3 (D3) samples. EVs were quantified and characterised by both nanoparticle tracking analysis (NTA) and flow cytometry.  

NTA and Flow Cytometry were utilised to demonstrate significant difference in EV populations between D1 and D3 of life with differences in size and concentration with EVs in both 0-200nm range (D1; 4.0 ± 2.5 x 107/µl vs. D3; 7.2 ± 4.4 x 107/µl; p = 0.03) and the 100-900nm range (D1; 1.1 ± 0.3 X 106/µl vs. D3; 4.2 ± 3.2 x 106/µl, p = 0.0009) becoming significantly different. D3 samples were characterised by a unique population of homogenous particles 100-300nm in size with unique side scatter properties suggesting a potential change in membrane or internal composition of EVs during the transition period. We assessed the levels of platelet EVs (CD41+/Annexin V+), a marker of platelet activation. The percentage of CD41+/Annexin V+ EVs significantly decreased from D1 to D3 (D1; 6.5 ± 4.9 % vs. D3; 2.4 ± 1.9 %, p = 0.007), suggestive of a platelet activation event during transition.  

In this study, we clearly demonstrate that the extrauterine transition period is characterised by major changes in plasma EVs. These changes include an increase in the levels of EVs, a change in the composition of EVs, and a reduction in the percentage of platelet-derived EVs. The physiological or pathophysiological causes of the changes need to be further elucidated.  

**COI:** None Declared
ID: 84
TITLE: DO BILIRUBIN/ALBUMIN (B/A) RATIOS CORRELATE WITH UNBOUND BILIRUBIN LEVELS IN PRETERM INFANTS?
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CONTENT:
Unbound bilirubin (UB), which is bilirubin not bound to albumin, can pass the blood-brain barrier and has been considered is a sensitive marker for bilirubin encephalopathy. However, UB levels is not used clinically to assess an infant’s risk for developing bilirubin neurotoxicity in areas outside of Japan. Assessment is usually done using the ratio of total bilirubin /albumin (B/A) levels, which has been shown to theoretically correlate with UB. We have previously reported a strong correlation between the B/A ratio and UB concentrations in serum of newborns ≥35 wks’ gestation (Sato Y, et al., y = 1.35x - 0.089, R2= 0.88, p < 0.0001) ; however, in preterm infants, the binding capacity of albumin to bilirubin is weak, and thus the usefulness of B/A ratio is unclear. Therefore, in this study, we correlated B/A ratios and UB concentrations in newborns <35 wks’ gestation.

Serum UB concentration was measured using the glucose oxidase–peroxidase method using a UB A1 Analyzer (Arrows Co, Osaka, Japan). Serum bilirubin and albumin concentrations were measured spectrophotometrically. Following our treatment criteria, infants received phototherapy based on threshold levels of TB or UB stratified by post-conceptional age (see Table 1). We excluded the data obtained from the samples received phototherapy. B/A ratios were calculated and correlates with serum UB levels. The subjects were then stratified by gestational age: A (22-27), B (28-29), C (30-31), and D (32-34 wks), and B/A ratios correlated with UB concentrations. Then, the cutoff value of the B/A ratio to serum UB levels that needs treatment of each group were determined by ROC curve analysis.

1221 serum samples were obtained from 381 newborns <35 wks’ gestation [30.8±3.2 (median 32, range 22-34) weeks, birthweight 1,558±589 (median 1604, range 284-2,962) g, Male 205 (53%)], who were admitted to Kobe University Hospital from 2014 to 2018. B/A ratio significantly correlated with serum UB levels in infants <35 wks’ gestation (y = 1.80 x-0.14, R2 = 0.88, n=1221). When stratified by gestational age, the correlation remained (Table. 2). The cutoff value of the B/A ratio to serum UB levels that needs treatment of each group is 0.257 (sensitivity 100%, specificity 91%) for UB levels of 0.4 in group A, 0.323 (93%, 93%) for UB levels of 0.5 in group B, 0.359 (92%, 90%) for UB levels of 0.6 in group C, and 0.414 (90%, 85%) for UB levels of 0.7 in group D (Table. 3).

Even in preterm infants <35 wks’ gestation, the B/A ratio showed a strong positive correlation with serum UB concentrations. Therefore, we conclude that B/A ratios can be used as an index of UB values with a high sensitivity and specificity, even in preterm infants <28 wks’ gestation.

IMAGES: https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=444fe2a3c215fdf2e41c72af170c31bd-MjAxOS0wNSM1Y2UyNyM2YzZl

COI: None declared
ID: 155

TITLE: THE EFFICIENCY OF EARLY AND LATE ADMINISTRATION OF VARIOUS DOSES OF RECOMBINANT HUMAN ERYTHROPOIETIN IN EXTREMELY AND VERY LOW BIRTH WEIGHT INFANTS

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CONTENT:

Anemia of prematurity is a common disorder of premature infants. The prevalence of anemia of prematurity is inversely proportional to the gestational age and body weight at birth. The pathogenetic importance of impaired erythropoietin (EPO) production in anemia of prematurity provides the rationale for therapy with erythropoiesis stimulating agents (ESAs) including recombinant EPO. The aim of the study was to assess the effectiveness and safety of different applying schemes of human recombinant erythropoietin in extremely and very low birth weight infants (ELBW and VLBW).

A randomized, placebo-controlled study of 133 VLBW and ELBW infants was conducted. Gestational age (GA) of newborns ranged from 26 to 33 weeks, more than half of them – 30 weeks or less (56%). All newborns were divided into 5 groups according to anemia prevention and treatment schemes: group 1 (n=26) – were administered ESAs 200 IU/kg 3 times per week from 3 day after birth; group 2 (n=21) – were administered ESAs 400 IU/kg 3 times per week from 3 day after birth; group 3 (n=37) – were administered ESAs 200 IU/kg 3 times per week from 8 day after birth; group 4 (n=18) – were administered ESAs 400 IU/kg 3 times per week from 8 day after birth; group 5 (n=31) – did not receive treatment with ESAs (control group). Subgroups of newborns ≤ 30 gestational weeks were identified in each group.

There were no statistically significant differences in the age of the 1st transfusion, the frequency and total volume of transfusions, the duration of respiratory therapy, the duration of hospitalization, including treatment in NICU, body weight and postnatal age at discharge, the frequency of retinopathy of prematurity stage ≥ 3, periventricular leukomalacia, bronchopulmonary dysplasia, intraventricular hemorrhages, necrotizing enterocolitis. The concentration of peripheral blood hemoglobin of premature infants at discharge was significantly different: lower level in the control group (94 g/l) compared with the groups of early ESAs administration (109 g/l and 107 g/l in groups 1 and 2, respectively; P0-1=0.048 and P0-2=0.047) due to newborn GA ≤30 weeks.

The administration of early or late EPO in VLBW and ELBW infants did not significantly reduce the use of one or more RBC transfusions, the number of transfusions per infant, so the routine use of EPO is not recommended. Among newborn with GA ≤30 weeks the early administration of EPO leads to increase the level of hemoglobin at discharge. The effectiveness of erythropoietin therapy remain controversial, therefore further researches are necessary.

COI: None declared
ID: 250
TITLE: PLATELET COUNT WITHIN THE FIRST WEEK OF NICU ADMISSION MAY PREDICT IVH SEVERITY IN VERY PRETERM INFANTS
AUTHORS: Fatma Nur Sari 1; Mehmet Buyuktiryaki 2; Evrim Alyamac Dizdar 3; Cuneyt Tayman 4; Serife Suna Oguz 5
AFFILIATIONS: University of Health Sciences, Ankara Dr Zekai Tahir Burak Women's Health, Health Application and Research Center, Ankara, Turkey

CONTENT:
Despite recent advances in neonatal care, the absolute numbers of infants with intraventricular hemorrhage (IVH) still remain significant which is due to the increased survival rate of very preterm infants. In this study we aim to determine whether there is an association between platelet indices and severity of IVH in very preterms.

Preterm infants born before 32 weeks of gestation and hospitalized in the NICU were retrospectively evaluated. Platelet counts, mean platelet volume, platelet distribution width and platelet mass of the infants on the first day of life (DOL) and on DOL 2-7 were recorded. IVH was evaluated by cranial ultrasonography according to standard NICU protocol. The infants further categorized according to findings of cranial ultrasonography as; no IVH, mild IVH or severe IVH.

Totally, 1051 infants were evaluated. Mean gestational age and birthweight of the whole cohort were 27.9±1.6 weeks and 1058±247 g, respectively. Of the infants, 93 (9%) were diagnosed with severe IVH. Severe IVH group had a lower gestational age (p<0.001) and birthweight (p<0.001) compared to no or mild IVH groups. Male gender and mechanical ventilation were more common in severe IVH group. There were significant differences with regard to platelet count and platelet mass between groups on the first DOL and on DOL 2-7. Moreover, trombocytopenia on the first and 2-7 DOL was significantly higher in infants with severe IVH. Logistic regression analysis revealed that gestational age, male gender, mechanical ventilation and thrombocytopenia on 2-7 DOL were independently associated with the severity of IVH.

Consideration of gestational age along with gender and platelet count may be a predictor of severe IVH in very preterms.

COI: None declared
ID: 258  
**TITLE:** FACTORS ASSOCIATED WITH PORTAL VEIN THROMBOSIS AFTER UMBILICAL VEIN CATHETERIZATION: IMPLICATION OF THERAPEUTIC HYPOTHERMIA  
**AUTHORS:** Marina Colella 1,2; Anna Zanin 1,3; Paul Picq 4; Marianne Alison 2,5; Sophea Khat 1; Sophie Guilmin-Crepon 4; Olivier Baud 2,6; Valerie Biran 1,2  
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**CONTENT:**  
Neonatal portal vein thrombosis (PVT) is generally related to umbilical venous catheterisation (UVC). Nevertheless, sepsis, hemodynamic instability and perinatal asphyxia are recognised risk factors for venous thrombosis but their contribution to neonatal PVT is not clear. Nowadays, therapeutic hypothermia (TH) is the only treatment in case of hypoxic ischemic encephalopathy. Infants undergoing TH have an increased risk for cerebral thrombosis, but the incidence of PVT in this population is currently unknown.  
The aim of our study was to analyse the factors associated to neonatal PVT after UVC and to determine if TH can independently increase PVT incidence in newborns.  

We performed a monocentric observational prospective analysis of collected data from January 2012 to December 2017 at Robert Debré University Children’s Hospital, Paris, France.  
All infants with a gestational age (GA) ≥ 36 weeks and a neonatal weight ≥ 1500 g admitted in NICU were considered eligible for this study if a UVC was placed and if they underwent an abdominal radiography and at least one abdominal ultrasound in the first 10 days of life. Clinical data referred to the pregnancy, birth and the clinical evolution within the first 10 days were recorded. Hypothermia protocol was applied according to the established recommendations. Grade and localisation of PVT were also evaluated.  
PVT was diagnosed in 57 (27%) of 213 patients included in the study. 87 infants (41%) were cooled for hypoxic ischemic encephalopathy. TH was significantly associated with PVT (P=.01). PVT was nearly 2 times more frequent in cooled infants than in control group (OR 1.94; P=.04). Nearly all PVT (54) were localized in the left portal vein branch; 28 (49%) were of grade 1, 22 (39%) of grade 2 and 7 (12%) of grade 3. There were no significant differences in gender, birth weight, intrauterine growth, preeclampsia, maternal diabetes or antenatal steroid therapy. Apgar score, cord pH, lactates, haemoglobin and platelets did not differ between the groups. Clinical complications as sepsis were similar in the 2 groups. The inappropriate location of UVC was not more frequent in PVT group; in contrast, the duration of UVC was related to an increased risk of PVT (OR 1,36; P=.008).  
Left portal venous thrombosis is often observed in nearly term neonates who need an UVC placement. Asphyxiated cooled infants are particularly at risk to develop PVT. We could suggest to limit the duration of UVC and to control the presence and evolution of PVT with routine ultrasound. However, further studies with larger sample sizes are needed to determine the effect of the detection and treatment of PVT, especially in infants undergoing TH.
Figure 1. Portal vein thrombosis (PVT) prevalence in therapeutic hypothermia (TH) group and no TH group (P=.01).

COI: non declared
**ID:** 314  
**TITLE:** DETERMINANTS OF LARGE DIFFERENCES BETWEEN SKIN AND SERUM BILIRUBIN AND THEIR POSSIBLE IMPACT ON PHOTOTHERAPY IN LATE PRETERM AND TERM NEONATES  
**AUTHORS:** Emmanuelle Letamendia-Richard MD, Silvia Foligno MD, Giulia Vigo MD, and Daniele De Luca MD, PhD  
**AFFILIATIONS:** Division of Pediatrics and Neonatal Critical Care, “A.Beclere” Medical Center, South Paris University Hospital, APHP  
South Paris-Saclay University, Paris, France  

**CONTENT:**

Background. AAP recommends predischarge measurement of either transcutaneous (TcB) or total serum bilirubin (TSB) while decisions about treatment should be based on TSB levels.[1] Modern second generation transcutaneous devices are supposed to be more accurate than the older ones.[2] however, large discrepancies between TSB and TcB are rarely observed. It is not clear what are the factors causing these discrepancies and their possible consequences, when TcB is used as pre-discharge screening, in terms of therapeutic decisions. We embarked in a large, prospective cohort study to determine: 1) the factors affecting a large difference TSB-TcB (defined as absolute values >50 µmol/L); 2) if this difference would have had clinical consequences in terms of jaundice treatment, when TcB is used as predischarge screening.

We enrolled term and late preterm neonates who had the TcB measurement (Bilicheck®, Philips inc), as predischarge screening and whose value exceeded the 75th percentile of the European TcB nomogram.[3] In these babies a TSB was obtained within 30’ from the TcB, as per our internal protocol. Phototherapy was instigated if TSB fulfilled criteria as per AAP guidelines.[4] Jaundice risk factors (as per AAP guidelines [1]) were also recorded. Patients were divided between those with underestimation or overestimation if the TSB-TcB difference was >50 or >-50 mmol/L, respectively and univariate analyses for all jaundice risk factors were performed. Multivariate logistic regression having as outcome the large TSB-TcB error (as absolute value) was performed, including covariates with an univariate p>0.10.

Results: We enrolled 837 babies, (59% males; GA 40 (1.8) weeks; BW 3458 (537)g; postnatal age 63.5 (29)h). Under- and overestimation were 36 and 110, respectively. Tab. 1 shows univariate analyses results. Multivariate analysis (Tab. 2) shows the non-Caucasian ethnicity to be the main variable increasing the risk for large TSB-TcB error, while the presence of cephalohematoma seems to reduce it; postnatal age seems to have a milder effect. When TcB largely underestimated TSB, fifteen (1.8%) neonates needed phototherapy, while, when TcB largely overestimated TSB, eight (0.9%) babies did not finally need any treatment.

In a large population of term and late-preterm babies, only non-Caucasian ethnicity seems to increase the occurrence of large discrepancies between TSB and TcB. The vast majority of large errors is represented by overestimation and their impact on therapeutic decisions seems minimal.

References
[2] De Luca, Jackson, Engle. Transcutaneous bilirubinometry, NOVA Publisher 2013

**IMAGES:**
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=742faddedab5b7ccb645c7e3c2ad81a2-MjAxOS0wNSM1Y2UyNjY2YzJhMDRj

Univariate and Multivariate analysis
COI: D. De Luca in the past has received travel grants and research technical assistance from PHILIPS inc, outside of the present work.
ID: 494

TITLE: INTEGRATION OF MOLECULAR PROFILES OF PRETERM BABIES

AUTHORS: Hanna Danielsson 1; Linn Fagerberg 2; Gunnel Hellgren 3; Nele Brusselaers 4; Mathias Uhlén 5 and Ann Hellström 6.

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CONTENT:

The dawn of new omics tools for analyzing clinical samples such as genomics, proteomics and metabolomics has opened up new possibilities to study both health and disease with significant clinical accuracy. Here, we have used this approach to analyze the molecular profiles of extremely preterm babies with a focus on protein profiles in blood. The results of the longitudinal sampling have been analyzed and integrated with perinatal variables and clinical outcomes.

We conducted in-depth analyses of molecular profiles during the first weeks after birth of preterm babies born in week 22 to 28. The Longitudinal Integrative Program of Preterm Children (LIPPC) described here combines classical clinical chemistry with extensive omics profiling, including the analysis of the plasma proteome, the plasma metabolome and gut microbiota composition. In total, 450 protein targets have been studied from 14 extremely preterm babies and the protein profiles that have changed during the first weeks after delivery has been identified and correlated with clinical metadata.

The results show dramatic changes in molecular profiles during the early weeks of life. The analysis confirms patterns of well-known proteins known to be involved in for example weight gain, but more interestingly many protein targets, not described in this context previously, were identified with significant changes in protein levels. Some different patterns (clusters) of protein profiles have been identified, involving more than 200 proteins with strong correlation in longitudinal protein profiles across the analysed preterm babies. Examples of proteins with increasing protein levels (MYOC) and decreasing protein levels (COLECT12) are shown in figure 1. MYOC (myocilin) is believed to have a role in cytoskeletal function. COLEC12 (Collectin subfamily member 12) is a scavenger receptor, a cell surface glycoprotein that displays several functions associated with host defence.

This longitudinal study shows dramatic changes across many protein targets in peripheral blood of preterm babies. These changes were most profound during the first days of life after preterm birth. Time after birth seems more significant than...
postmenstrual age with regard to the patterns of protein levels. The study has allowed us to study the prediction of clinical outcome of the babies based on the integration of the omics profiles.

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Fig 1. Two examples of correlation in longitudinal protein profiles among the analysed pre-term babies.

COI: None declared
ID: 841

**TITLE:** DO PROPHYLACTIC PLATELET TRANSFUSIONS REDUCE BLEEDING RISK IN PRETERM NEONATES WITH SEVERE THROMBOCYTOPENIA? A TIME-DEPENDENT PROPENSITY SCORE MATCHED COHORT ANALYSIS.

**AUTHORS:** Susanna F Fustolo-Gunnink 1-2, Karin Fijnvandraat 2-3, Hein Putter 4, Isabelle M Ree 5, Camila Caram-Deelder 1, Peter Andriessen 6, Esther J d’Haens 7, Christian V Hulzebos 8, Wes Onland 9, André A Kroon 10, Daniel C. Vijlbrief 11, Enrico Lopriore 5, Johanna G van der Bom 1-12.

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**CONTENT:**

In a recent randomized trial in preterm neonates, platelet transfusions given at a platelet count threshold of 50x10^9/L were associated with increased risk of major bleeding and/or mortality when compared to a threshold of 25x10^9/L. Adult studies have suggested that lower thresholds or even no prophylaxis policies are safe in some patient groups. We aimed to assess in preterm neonates with severe thrombocytopenia whether prophylactic platelet transfusions reduce risk of bleeding and/or mortality when compared to therapeutic transfusions.

We included neonates with a gestational age <34 weeks and a platelet count <50x10^9/L in seven Dutch neonatal intensive care units. We developed a dynamic propensity score to estimate the probability for a neonate to receive a platelet transfusion at two hour time-intervals. Neonates who received a transfusion were matched to neonates who did not, but had a similar probability of receiving a transfusion. We assessed a composite of major bleeding and/or mortality within three and ten days from each transfusion, using conditional weighted logistic regression.

We included 640 neonates. The odds ratios for major bleeding and/or mortality within three and ten days for the transfusion versus the no-transfusion groups were 1.27 (95% confidence interval (CI) 0.77 – 2.08) and 1.16 (95% CI 0.74 – 1.80), respectively.

In preterm neonates with severe thrombocytopenia, prophylactic platelet transfusion events were not associated with reduced risk of bleeding and/or mortality when compared to similar clinical situations where platelet transfusions were withheld. These findings suggest that the clinical benefit of prophylactic transfusion in neonates may be limited.
Outcomes for platelet transfusion events versus no platelet transfusion events within the time-dependent propensity score matched cohort.

COI: None declared
**ID:** 851  
**TITLE:** THE HEMOSTATIC PROFILE OF VERY LOW BIRTH WEIGHT MULTIPLES AT BIRTH: A THROMBOELASTOGRAPHIC-BASED OBSERVATIONAL STUDY  
**AUTHORS:** Genny Raffaeli 1; Giacomo Cavallaro 1; Valeria Cortesi 1,2; Ilaria Amodeo 1,2; Nicola Pesenti 3; Erica Scalambro 4; Nicola Persico 5; Armando Tripodi 4; Fabio Mosca 1,2; Stefano Ghirardello 1.  
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1. Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, NICU, Milan, Italy.  
2. University of Milan. Department of Clinical Sciences and Community Health.  
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4. Angelo Bianchi Bonomi Hemophilia and Thrombosis Center, IRCCS Ca’ Granda Maggiore Hospital Foundation, Milan, Italy.  
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**CONTENT:**

Twinning rate is increasing worldwide, ranging between 1.3 and 1.6% in high-income countries. Preterm twins are at higher risk of mortality and morbidity than singletons. Compared to dichorionic (DC) twin pregnancy, monochorionicity (MC) has a negative impact on gestational age-specific mortality, especially in case of twin-to-twin transfusion syndrome (TTTS), which complicates 10% to 15% of MC pregnancies. The hemostatic profile in multiples is largely unexplored. The aim of this study was to investigate the effect of a) birth order and b) monochorionicity complicated by TTTS on the thromboelastographic (TEG) profile of very low birth weight (VLBW) multiples at birth.

This is an ancillary study of a larger prospective observational study aimed at defining TEG in healthy VLBW infants at birth. For the purpose of this study, we enrolled (July 2015-June 2018) consecutive VLBW (birth weight ≤1500 grams) multiples. We collected a venous blood sample in the first day of life to perform blood count, PT, aPTT, fibrinogen and recalcified native blood TEG assay (TEG® 5000 Haemoscope): reaction time (R, minute) and maximum amplitude (MA, millimeter). We compared the TEG profile between: a. first-born vs second/third-born twin in mono/bi/tri-chorionic multiples; b. donor vs recipient in monochorionic pairs complicated by TTTS, whose diagnosis was made based on ultrasound criteria. Delayed cord clamping (30 seconds) was implemented in 2017 in our level-III NICU.

We analyzed 33 sets of multiples (n=68), consisting of 14 DC-diamniotic and 17 MC-diamniotic twin pairs, 1 trichorionic-triamniotic and 1 MC-triamniotic triplet. Table 1 shows demographic and hemostatic variables of the study population. At birth the median (min-max) TEG values were: R 5.8 min (2–19), MA 65 mm (34-81) in the first-born and R 5.7 min (1.5-23), MA 64 mm (31–80) in the second (third)-born, respectively. In MC twin pairs with TTTS, the median (min-max) TEG values were: R 6.6 min (2-15), MA 59 mm (31-64) in the donor and R 7.4 min (2-19), MA 57 mm (34-61) in the recipient. TEG parameters for both DC and MC multiples were in the normal range, compared to institutional reference intervals for healthy VLBW singletons. No infants had polycythemia or anemia. Delayed cord clamping (DCC) was applied in a restricted cohort of patients, based on institutional practice (table 1).

Multiple pregnancy does not influence the hemostatic profile of VLBW multiples. TEG trace was comparable between first and second (third) order multiples and between donor and recipient of monochorionic sets, complicated by TTTS. The role of DCC in the hemostatic balance should be determined. Further research is required to validate our findings.

**IMAGES:**  
[Link to image](https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=0a76faa111fa1022c4406acba03a5809-MjAxOS0wNSM1Y2UyNy2ZDBjZDZj)

Table 1. Baseline characteristics and hemostatic profile of the study population at birth.
COI: None declared
ID: 874

TITLE: BILIRUBIN BINDS TO LIPID RAFTS

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CONTENT:

The mechanism of bilirubin neurotoxicity is poorly understood. Bilirubin has previously been reported to bind to phospholipids. We hypothesize that bilirubin binds specifically to the phospholipids in lipid rafts, microdomains of the plasma membrane critical for signal transduction, and inhibits their function. To test this hypothesis, we measured the binding of bilirubin to lipid rafts.

Our objective was to determine the location of bilirubin in the fractions of sucrose density gradients that separate lipid rafts from non-lipid rafts in lysates of cerebellar granule neurons.

Cerebellar granule neurons were isolated from postnatal day 5 rat pups and cultured overnight in neurobasal media with B27 additive (K5). Media was replaced with 100 µM human serum albumin in K5 with or without 5 µM bilirubin and incubated for 1 hour. Cell lysates made using 1% Triton X100 were added to sucrose density gradients followed by ultracentrifugation to isolate lipid rafts (LR) from non-lipid rafts (N). Ten 1 ml fractions were taken from the gradients, and aliquots dot blotted for bilirubin (B) and for GM1 ganglioside, a marker for lipid rafts. In some case, methyl beta-cyclodextrin (MBCD) was added to cell lysates prior to addition to sucrose density gradients.

In the absence of bilirubin addition to cell culture (B-), there was no immunoreactivity in the dot blot for bilirubin. Addition of bilirubin to the cultures (B+) resulted in bilirubin reactivity only in fractions with co-reactivity for GM1 ganglioside (Fisher Exact test: B immunoreactivity present yes/no, LR vs N, p<0.03). In lysates treated with MBCD to chelate cholesterol and eradicat lipid rafts, bilirubin reactivity was found in all fractions of the sucrose density gradient.

Bilirubin binds preferentially, if not exclusively, to phospholipids in lipid rafts. The binding of bilirubin to lipid rafts may disrupt lipid raft function and be one possible mechanism for bilirubin neurotoxicity.

IMAGES:
https://www.eiseverywhere.com/eeselectv3/v3/events/351149/submission/files/download?fileID=3e08b9d6e16a7af0d5663e45bca09809-MjAxOS0wNSM1Y2UyNjY2ZDE0YWIy

Figure: Panel A. Dot blot showing presence of GM1 ganglioside (GM1) in fractions of sucrose gradients indicating the presence of lipid rafts. Addition of Bilirubin (B) had no effect on the distribution in the presence or absence of methyl beta cyclodex

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TITLE: TOWARDS THE END OF KERNICTERUS IN SUB-SAHARAN AFRICA?

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CONTENT:

The burden of neonatal jaundice is the highest in countries with low socio-demographic index. Acute Bilirubin Encephalopathy (ABE) and kernicterus but remains a serious problem in low-and middle-income countries (LMIC), in part due to a high prevalence of G6PD deficiency. Bhutani (2013) estimated that more than 100,000 term or late preterm death and above 60,000 kernicterus are due to severe jaundice annually, with predominance in Sub-Saharan Africa (SSA) and South Asia. We describe the evolution of ABE in Benin (SSA) after our Global Development Alliance increased the availability of phototherapy lamps and dispensed an education program to prevent neonatal jaundice complications.

BOL-Benin is a multifaceted program targeting the main causes of neonatal mortality and morbidity, including neonatal jaundice. It was developed and implemented by our Global Development Alliance and co-funded by USAID Benin (2015-2017). Interventions to reduce complications from neonatal jaundice, namely death and ABE, included the provision of high intensity phototherapy lamps and an education program regarding clinical presentation of jaundice, ABE, as well as therapeutic modalities, to physicians and nurses in charge of newborns in neonatal units. We report the effect of BOL on severe complications from neonatal jaundice in the 3 main neonatal units of the country.

Preliminary data analysis show that clinical ABE and neonatal death attributed solely to severe jaundice have virtually disappeared from the inborn neonates admitted to one of the 3 largest neonatal units of the country, totalling close to 7000 admissions with close to 5000 inborn per year (only 2 cases reported in the past 3 years). High intensity phototherapy was initiated immediately following clinical recognition of jaundice on the chest or upper abdomen of the newborn (Kramer’s scale), up to the availability of a serum bilirubin level below phototherapy threshold when parents could afford the test, or up to clinical resolution of the jaundice when test could not be performed. Unfortunately, ABE and death from jaundice remained frequent in the population of outborn newborns, due to late recognition of the jaundice in the community and late referral for treatment.

Our program offering technical support and education has massively reduced ABE and death from severe jaundice in the inborn portion of hospitalized newborns. Considering the low cost of phototherapy equipment, our program should be easily reproducible in other LMICs. Community interventions to increase awareness of neonatal jaundice complications need to be held in those countries to eradicate completely the sequelae of neonatal jaundice.

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TITLE: PREDICTION OF SIGNIFICANT HYPERBILIRUBINEMIA USING AN ARTIFICIAL INTELLIGENCE APPROACH

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CONTENT:

Prediction of significant neonatal hyperbilirubinemia is classically based on hour-specific nomograms of total serum or transcutaneous bilirubin (TcB). However, the clinical performance of such tools is limited, mainly due to their inability to adjust for the numerous confounding factors related to neonatal jaundice. Machine learning represents an ideal method for approaching tasks that involve multiple and interacting classifiers. The purpose of the present study was to explore whether artificial intelligence can be applied to predict significant hyperbilirubinemia during the first 120 hours of life in healthy term and late-preterm neonates.

A computer model was developed using a database of 6,869 healthy newborns (gestational age [GA] ≥35 weeks) with a total of 35,648 serial TcB measurements at 12 ± 2, 18 ± 2, 24 ± 4, 36 ± 4, 48 ± 4, 60 ± 4, 72 ± 4, 96 ± 4 and 120 ± 6 postnatal hours. The outcome of interest consisted of significant hyperbilirubinemia (i.e., need for phototherapy) according to the hour-specific nomograms of the American Academy of Pediatrics. Sex, birthweight, GA, mode of delivery, ABO and Rh incompatibility, feeding method and daily weight loss were included as confounders. A multi-class classification approach was applied; for each iteration, an initial pool of 6,180 randomly selected samples was used for training and the rest for a 10-fold validation. The model was developed in MatLab.

The overall predictive ability of the model (at least 2 serial TcB measurements) was excellent, with an AUC of 0.98 at 24 postnatal hours and > 0.99 after 36 postnatal hours. A single TcB measurement at 24 hours had an AUC of 0.97 for predicting significant hyperbilirubinemia up to 48 postnatal hours, and an AUC of 0.91 for predicting significant hyperbilirubinemia up to 72 postnatal hours (Figure 1). The addition of a second TcB measurement at 36 or 48 postnatal hours would increase the AUC of the latter to 0.950 and 0.98, respectively (Figure 1).

Artificial intelligence can be used for the accurate prediction of significant hyperbilirubinemia during the first 120 hours of life in healthy term and late-preterm neonates. Our results suggest that machine-learning models are able to reflect the dynamic characteristics of neonatal bilirubinemia and, thus, may assist health care professionals in implementing individualized follow-up strategies for jaundiced neonates.

IMAGES:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=bc6aa547be229de9d2ac5608b872234c-MjAxOS0wNSM1Y2UyNjY2ZDI2YVj

Figure 1. Predictive ability of the artificial intelligence model

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