



POSTER SESSION 8 – TRIPLE I SECTION
SEPTEMBER 16, 2021 – 13:30 – 14:30 CEST

ID 116 - NEONATAL ANTIBIOTICS IMPACT BLOOD IMMUNE AND PROTEOME DEVELOPMENT IN PRETERM NEONATES

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Background:

Preterm infants are at high risk of neonatal infectious diseases and a majority of them receive antibiotics (AB) immediately after birth to prevent serious infections. Prolonged AB treatment predisposes to gut dysbiosis, impaired immunity, late-onset sepsis and necrotizing enterocolitis. Using preterm pigs as a model, we hypothesized that AB during the first days of life negatively affects systemic immune development and the associated plasma proteome profiling, even after termination of AB treatment.

Methods:

Caesarean-delivered preterm pigs (90% gestation) were fed increasing amounts of formula for 9 days and treated with saline (CON) or enteral AB (amoxicillin/clavulanic acid, neomycin) from day 1 to 5. On days 5 and 9, blood was collected for haematology, in vitro stimulation with TLR4 agonist (LPS), and LC/MS-based plasma proteomics.

Results:

AB treatment induced changes in abundance of 21 and 47 plasma proteins on days 5 and 9, representing 6.6% and 14.8% of the total annotated plasma proteins, respectively. Most AB-regulated plasma DEPs have their functions related to the complement cascade, neutrophil degranulation, and acute phase responses. Four inflammatory reaction-related differential expressed proteins (DEPs) were overlapped between days 5 and 9. Among which Ceruloplasmin (CP), Leucine-rich alpha-2-glycoprotein 1 (LRG1), Serpin A3-8 were consistently lower in AB group, whereas Periostin, a Th2-cytokines induced protein, persistently maintained higher level in AB group. Neutrophil and lymphocyte counts were higher in AB-treated pigs on day 5, unchanged from day 5 to 9, contrasting the gradually increasing levels in CON pigs. Moreover, AB treatment suppressed TNF-alpha and IL-10 responses to in vitro LPS challenges on both days 5 and 9.

Conclusion:

In conclusion, few days of AB treatment following preterm birth is associated with marked changes in systemic immune development and plasma proteome, and the changes last several days after the termination of AB treatment. How this affects longer-term infection and sepsis risk remains unclear. However, empirical neonatal AB treatment of preterm infants should be carefully considered to avoid long-term risks of impaired immunity and infections.



ID 246 - IMPROVING LUMBAR PUNCTURE SUCCESS IN NEONATES: A MULTICENTRE RANDOMISED CONTROLLED TRIAL (NeoCLEAR)

Dr Andrew SJ Marshall¹, Dr Alexandra Scrivens¹, Ms Jennifer L Bell², Associate Professor Louise Linsell², Dr Jean Yong¹, Dr Eleri Adams¹, Dr Manish Sadarangani³, Professor Edmund Juszczak⁴, Dr Charles Roehr², on behalf of 'The NeoCLEAR Collaborative Group'

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BACKGROUND:

Lumbar puncture (LP) is a common procedure in neonates, and is essential for diagnosing or excluding meningitis. Published neonatal LP success rates are 50–60%; many procedures yield heavily blood-stained cerebrospinal fluid (CSF), or no sample at all. Evidence for optimal infant LP technique is limited. Sitting position has anatomical advantages, and is often used in adults. 'Early stylet removal' (removal after transecting the skin and subcutaneous tissues) has some observational evidence of benefit.

AIMS:

To determine the optimal neonatal LP technique by evaluating the success rate, as well as short-term clinical, resource and safety outcomes, when comparing sitting vs lying position, and early vs late stylet removal.

METHODS:

NeoCLEAR ('Neonatal Champagne Lumbar punctures Every time – An RCT') was a 2x2 factorial pragmatic trial, conducted in UK neonatal and maternity units. Infants who required LP, with corrected gestational age 27+0 to 44+0 weeks and >1,000g, following written parental consent, were randomly allocated to sitting or lying position, and to early or late stylet removal. The trial was powered to detect a 10% absolute difference in the primary outcome: the percentage of infants with successful LP (CSF <10,000 red cells/mm³), analysed by modified intention to treat. Trial registration: ISRCTN14040914.

RESULTS:

Of 1,082 infants randomised, 1,076 were followed-up until discharge. 950 (88.3%) were term babies; 936 (87.0%) were recruited <3 days old. Baseline characteristics were balanced across groups. Sitting position was significantly more successful than lying (346/543 (63.7%) vs 307/533 (57.6%), adjusted risk ratio (aRR) 1.11 (95% confidence interval (CI) 1.01 to 1.21, p=0.027; number needed to treat = 16 (95% CI 9 to 34)). There was no evidence of a significant difference between early and late stylet removal (338/545 (62.0%) vs 315/531 (59.3%), aRR 1.04 (95% CI 0.95 to 1.15, p=0.391)). Resource outcomes were virtually identical, irrespective of allocation. All techniques were generally well tolerated and safe.

CONCLUSIONS:

Sitting position resulted in an increased chance of a successful LP compared with lying position. Sitting technique is free, safe, well tolerated, and can be easily learned and applied. This result is globally relevant, and strongly supports the implementation of sitting technique for neonatal LP.

MS is supported via salary awards from the BC Children's Hospital Foundation, the Canadian Child Health Clinician Scientist Program and the Michael Smith Foundation for Health Research. MS has been an investigator on projects funded by Pfizer, Merck, VBI Vaccines, Seqirus, Sanofi-Pasteur and GlaxoSmithKline. All funds have been paid to his institute, and he has not received any personal payments. EJ was a member of the NIHR HTA General Board from 2016 to 2017 and the HTA funding committee (commissioning) from 2013 to 2016, but was not involved in reviewing the NeoCLEAR funding application. EJ and LL report receipt of funding from NIHR, outside the submitted work. There are no further conflicts of interest to declare

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ID 442 - VACCINATION GUIDELINES AFTER NEONATAL EXCHANGE TRANSFUSION REEVALUATED

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BACKGROUND

The current vaccination guidelines suggest postponing administration of live vaccines for six months after exchange transfusion (ET) and administration of dead vaccines without delay. The objective of the study is to investigate the impact of neonatal ET on cellular and humoral immune response and reevaluate vaccination guidelines after neonatal ET.

METHODS

Determination of blood lymphocyte populations in 86 healthy children at birth, six weeks and 13 months of age; 30 of them received ET due to neonatal haemolytic disease (NHD) and no other blood product afterwards, while 56 did not receive any blood products. Determination of serum diphtheria and tetanus antibodies in 74 healthy children after four doses of diphtheria and tetanus toxoid vaccine; 41 of them received ET due to NHD and no other blood product afterwards, while 33 did not receive any blood products.

RESULTS

At the age of six weeks ET recipients had significantly lower concentrations of activated monocytes (14718.34 ± 5798.39 vs. 20471.7 ± 8975.02 HLA-DR fluorescence intensity, $p=0.025$), activated helper T cells (0.239 ± 0.153 vs. $0.378 \pm 0.024 \times 10^9$ cells/L, $p=0.0074$), regulatory helper T cells (0.115 ± 0.097 vs. $0.221 \pm 0.051 \times 10^9$ cells/L, $p<0.001$), naïve B lymphocytes (0.487 ± 0.329 vs. $0.864 \pm 0.317 \times 10^9$ cells/L, $p<0.001$) and transitional B lymphocytes (0.264 ± 0.207 vs. $0.515 \pm 0.273 \times 10^9$ cells/L, $p=0.0057$) compared to healthy controls. Thirteen months after ET the difference of these cells was no longer present. After four doses of diphtheria and tetanus toxoid vaccine ET recipients had significantly higher serum concentration of diphtheria toxoid antibodies (1.016 ± 0.963 vs. 0.515 ± 0.351 IU/mL, $p=0.011$) and equal serum concentration of tetanus toxoid antibodies (1.798 ± 1.686 , vs. 1.036 ± 1.474 IU/mL, $p=0.09$) compared to healthy controls.

CONCLUSION

Neonatal ET affects specific cellular and humoral immune response. It causes short-term immune exhaustion at six weeks of life that resolves by 13 months of age. Moreover, it improves long-term humoral immune response to diphtheria toxoid vaccine. The humoral immune response to diphtheria and tetanus toxoid vaccine in ET recipients is at least comparable to the efficacy of the vaccine in healthy children, so ET recipients should be vaccinated with these two vaccines according to the official vaccination schedule for healthy children.

None declared



ID 488 - EFFECT OF DIETARY MILK FAT AND FETAL GROWTH RESTRICTION ON IMMUNE DEVELOPMENT IN NEONATAL PIGLETS

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Background

Infant formulas offer an alternative to breast milk for both normal birth weight (NBW) and immunocompromised intrauterine growth restricted (IUGR) infants. The lipid fraction in formulas is commonly of vegetable origin, due to its higher LC-PUFA content. However it is unclear if this improves immunological outcomes, relative to more saturated lipids with intact milk fat globule membranes from bovine milk, and whether effects differ between IUGR and NBW infants. Using newborn pigs as models for infants, we hypothesized that replacing vegetable oil with bovine milk fat in formula would affect immune development in IUGR and NBW neonates.

Methods

Two-day old piglets were selected for signs of IUGR by of birthweight and head morphology (NBW, n=18 and IUGR, n=18). Each group of animals were fed a diet based on either vegetable oil (VEG, n=9+9) or bovine milk fat (MILK, n=9+9) in a 2x2 factorial design. Animals were reared until day 23 or 24 and systemic immune parameters were evaluated during the study.

Results

Milk fat feeding led to lower blood neutrophil counts and better neutrophil function by the end of the experiment and transiently reduced the expression of several genes related to adaptive (TNFA, IL2, IL17, GATA3), and innate immunity (CXCL10, TLR2, TLR4) as well as energy metabolism (PPARG, PDHA1, PKM) in stimulated whole blood on day 10, but not day 23/24. Regardless of diet, IUGR pigs showed lower blood leucocyte counts with lower fractions of helper and cytotoxic T cells with limited effects on leucocyte gene expression (lower expression of PPARG and, TGFB1). Finally, there were few interactions between milk fat and birthweight status (higher blood regulatory T cell fractions in IUGR animals fed vegetable fats and higher CRP in IUGR fed milk fat).

Conclusions

Milk fat feeding improved neutrophil maturation and led to a transient drop in systemic pro-inflammatory capacity in the neonatal period with leucocytes seemingly showing less energy consumption for inflammatory responses, compared to animals fed vegetable fat. IUGR had a minor impact on the developing immune system with no substantial interactions with the diet.

None declared



ID 524 - CHARACTERISATION OF INNATE IMMUNITY ACROSS AGES: NEWBORN TO OLD AGE

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Background:

Neonates are usually susceptible to viral illness but are not commonly infected or symptomatic with acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in contrast to the elderly. We hypothesised that alterations in immune function may be protective in neonates.

Methods:

Healthy subjects were recruited across all age groups from neonates (< 1 week old), school age children (age 1,5-15 years), adults (25-38 years) and elderly (age: 71-92 years). Innate immune cells were analysed by flow cytometry and CD11b (cell activation and migration) and Toll-like receptor (TLR)-4 (recognition of endotoxin/lipopolysaccharide/LPS) in neutrophils (CD66b+) and subpopulations of monocytes (CD14/CD16+) stimulated without/with LPS.

Results:

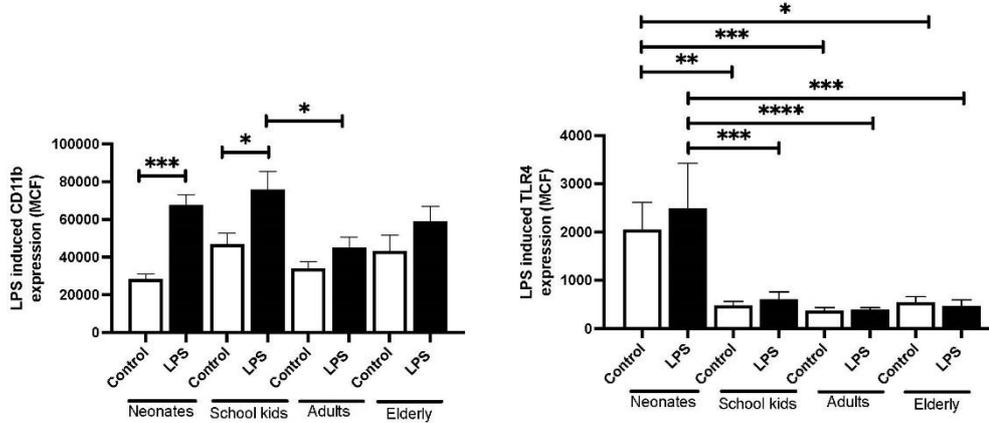
Eighty-seven patients were recruited (neonates n=28; School-age children n=28); Young adults n=21 older adults n=10). CD66b+ neonatal neutrophils had significantly increased CD11b expression with LPS not seen in other age groups. CD11b expression in monocytes showed no differences between neonates and other age groups although neonatal neutrophil TLR4 expression was significantly increased in neonates compared with the other age groups (Figure 1A, Figure 1B). Nevertheless, when evaluated based on subpopulations of monocytes determined by CD14 and CD16 expression, neonates had significantly lower basal expression of CD11b for classical, intermediate and non-classical monocytes compared to school children, but not any adult group. Similar low expression of CD11b was seen in classical and intermediate populations stimulated with LPS when compared neonates to schoolchildren, and for intermediate type versus neonates and older adults.

Conclusion:

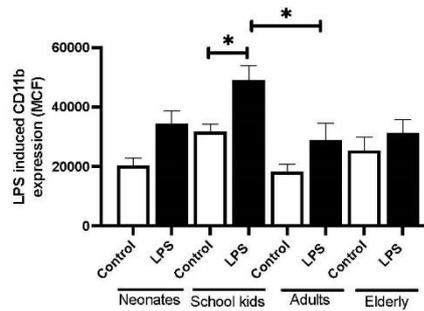
Neonatal neutrophil TLR4 was increased compared with other age groups with a lower response of different monocytes subpopulations. These responses could contribute to the decreased susceptibility of neonates to SARS-CoV-2 infection. Further studies at cellular and molecular level could characterise changes in immunophenotype across age groups to identify potential immunomodulatory therapies.



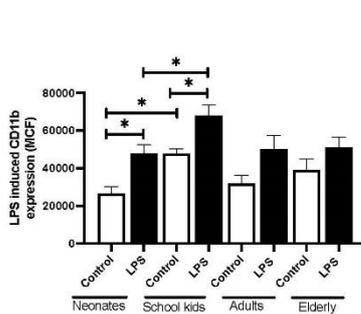
A Neutrophils



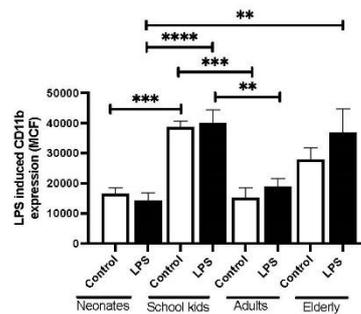
B Monocytes



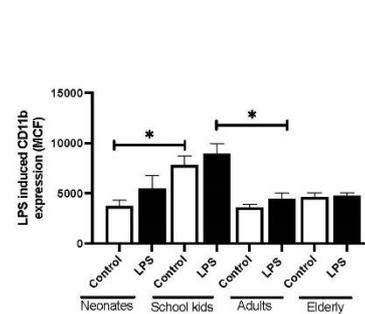
Classical



Intermediate



Non-Classical



Innate immune populations determined in neonates, school age kids, adults and elderly. CD11b and TLR4 were evaluated in neutrophils, and monocytes with/without LPS. Results represented as MCF with SEM. None declared



ID 560 - DECLINE IN CENTRAL LINE ASSOCIATED SEPSIS IN VERY LOW BIRTHWEIGHT NEONATES: THE SPANISH NEOKISSES SURVEILLANCE SYSTEM

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Background:

Very low birthweight (VLBW) neonates ($\leq 1,500$ grams at birth) are at extreme risk of developing nosocomial infections (NI) during their neonatal intensive care units (NICUs) stay. Central-line-associated sepsis (CLAS) are strongly associated to increased mortality and short and long-term sequelae. Surveillance of NI is a mainstay for their reduction. We describe the five-year experience of the Spanish NeoKissEs surveillance system regarding CLAS.

Methods:

NeoKissEs (www.neokisses.es) is a voluntary surveillance system for VLBW infants, derived from the German Neo-Kiss system. It started collecting data in 2014 from 45 Spanish level 3 NICUs, furtherly classified into three sublevels (3A, 3B and 3C) according to complexity of healthcare services provided (currently more than 50 NICUs). Clinical data, including late-onset sepsis (clinically suspected or culture-confirmed), as well as data on the use of vascular lines and other devices are recorded. Before starting a bundle-based initiative to prevent CLAS, a survey was sent to participating units in 2019, asking about general resources available and infection prevention and control (IPC) measures in place. Data on CLAS incidence rate (per 1,000 days of CL in use) were annually recorded for 40 NICUs that provided data for the whole 2014-2018 period and had the questionnaire filled in. Two-level mixed Poisson regression analysis was carried out with individual data for VLBW neonates which had a CL inserted and NICU-level data for self-reported active IPC strategies. Adjusted incidence rate ratios (IRR) were estimated (adjusted by gestational age, birthweight, type of delivery).

Results:

6,446 VLBW neonates were included (1,052 from 13 level 3A NICUs, 3,457 from 21 3B units and 1,937 from 6 3C NICUs). CLAS incidence rates declined over the five-year period in all levels of healthcare complexity (Table) (overall IRR 0.76 for 2018 CLAS rates as compared with 2014 rates [95% CI 0.66-0.89]). Among the reported IPC activities, only the existence of some type of hand hygiene observation strategy was associated with lower CLAS rates (overall IRR 0.69 [0.50-0.94]).

Conclusions:

A significant decline in NeoKissEs CLAS rates was observed in the 2014-2018 period. Having some hand hygiene observation program associates with significantly reduced CLAS incidence rates.



Healthcare complexity Level	Year	CLAS sepsis rate (x1000 days of CL) (all NICUs)	N	CLAS sepsis rate (x1000 days of CL) (NICUs with HHO)	N	CLAS sepsis rate (x1000 days of CL) (NICUs without HHO)	N
IIIA	2014	21.2	179	17.1	116	28.8	63
	2015	11.6	213	8.8	159	19.8	54
	2016	16.2	238	11.5	149	24.0	89
	2017	10.8	223	7.6	144	16.7	79
	2018	10.1	199	9.9	140	10.6	59
IIIB	2014	15.3	612	8.6	192	18.3	420
	2015	12.3	810	7.2	218	14.2	592
	2016	11.9	708	7.4	205	13.7	503
	2017	9.8	687	6.1	196	11.2	491
	2018	12.1	640	9.0	203	13.5	437
IIIC	2014	23.1	395	22.2	311	26.4	84
	2015	20.7	392	22.0	286	17.2	106
	2016	19.5	393	20.5	300	16.5	93
	2017	19.9	393	16.1	300	32.0	93
	2018	14.4	364	13.2	284	18.9	80

CLAS incidence rates, by surveillance year, NICU level of healthcare and existence of hand hygiene observation program (HHO); CLAS: Central-Line-Associated-Sepsis; NICUs: Neonatal Intensive Care Units; N: number of VLBW neonates
None declared



ID 580 - DOES THE CURRENT PRACTICE OF 36 HOUR BLOOD CULTURE REPORTING FOR PRESUMED EARLY ONSET SEPSIS FACILITATE TIMELY DISCHARGE?

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Introduction

Due to non-specific presentation, newborn infants receive antibiotics if they are deemed to be at high risk for infection. Following the evidence from the recent studies on the time to positivity (TTP) of neonatal blood cultures, NICE (national institute of health and clinical excellence), UK in their guidance (CG149) suggests discontinuing antibiotics at 36 hours, in asymptomatic infants whose inflammatory markers are normal and blood culture is negative at 36 hours. We carried out a prospective study to review the practical application of this guidance in a tertiary neonatal setup, to understand the impact on our patient throughput and facilitate timely discharge.

Methods

This prospective study was performed at a large maternity and newborn services with an annual birth rate of over 10000 deliveries. We included well, asymptomatic infants, born > 37 weeks gestation, who received prophylactic IV antibiotics in the postnatal ward. We analysed various time points including time of collection, reporting, and discharge from the postnatal ward.

In cases of the delay in discharge, a plausible reason for the delay was searched to identify an alternate explanation. All data were collected on dedicated study proforma and analysed using statistical package spss (20.0).

Results

134 infants met the inclusion criteria during the study period of June to August 2020. 25 of them had a valid reason for the delay in discharge (Group B, Table 1). Data on 109 infants without a plausible reason (Group A, Table 1) was then analysed to study the patterns for the delay in discharges.

The exercise showed that there was a mean delay of 26 hours from the stipulated 36 hours of collection of blood culture. Despite consideration of 4 hours for the time taken from collection to incubation, a delay of further 22 hours was noted much to the inconvenience of the families. The time periods are explained in more details in table 1.

Summary and Conclusions

The study highlighted that the current system of managing babies with suspected infection is inefficient in causing delayed discharges. This has both costs as well as patient flow implications and therefore needs further investigations into modifiable factors.



Time interval (in hours)	Group without obvious explanation for the delay (Group A)	Group with explanation for the delay (Group B)	p-value
Time of birth - Time of collection of blood culture, Mean (SD)	7.9 (8.1)	10.8 (13.0)	.301
Time of collection of blood culture - Time of blood culture incubation, Mean (SD)	4.0 (3.6)	4.1 (2.9)	.850
Time of blood culture collection - Time of blood culture reported, Mean (SD)	43.2 (6.7)	43.3 (4.5)	.957
Time of incubation - Time of blood culture reported check, Mean (SD)	39.3 (5.2)	39.0 (3.4)	.824
Time of collection - Time of Discharge, Mean (SD)	61.9 (25.5)	96.7 (42.5)	<.001
Time of Birth - Time of Discharge, Mean (SD)	69.9 (25.7)	107.5 (37.7)	<.001

Table 1: Timeline of the blood culture reporting and patient stay
None declared



ID 353 - NEONATAL OUTCOMES OF PRETERM INFANTS BORN DURING THE COVID-19 LOCKDOWN IN MELBOURNE, AUSTRALIA

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Background:

Studies have suggested a reduction in preterm birth rates during community lockdowns during the COVID-19 pandemic. In this study, we investigated the impact of COVID-19 community lockdown on neonatal outcomes of preterm infants.

Methods:

We conducted a comparative cohort study in the largest hospital network in Melbourne, Australia. We compared outcomes of preterm infants (<34 weeks' gestation) born to women exposed to mitigation measures from 12-24 weeks' gestation until delivery during the 2020 lockdown (exposed group) to infants born to a similar cohort of women pregnant a year earlier in 2019 (control group). The main outcome was a composite of poor neonatal outcomes, including chronic lung disease, severe intraventricular haemorrhage, necrotising enterocolitis, retinopathy of prematurity requiring treatment, culture positive sepsis, or neonatal death. Secondary outcomes included neonatal outcomes assessed individually, and inflammatory markers of infants within seven days post birth and their mothers pre-delivery to assess for differences in inflammatory states around time of birth.

Results:

We studied 3187 live neonates born to mothers who experienced mitigation measures and 3229 live neonates born to women pre-pandemic. In the exposed group, there were 90 infants born before 34 weeks of gestation (2.8%), vs. 129 (4.0%) in the unexposed group (risk ratio [RR] 0.71, 95% CI 0.54 to 0.92; p=0.01). The composite outcome occurred in 30/90 (33.3%) infants in exposed group vs. 36/129 (27.9%), in control group (RR 1.19, 95% CI 0.80 to 1.79; p=0.3). There were significant lower rates of jaundice requiring phototherapy and hypoglycaemia in preterm neonates of the exposed group, but no other significant differences in neonatal outcomes. There were no significant differences in maternal white cell count, or C-reactive protein (CRP) or in neonatal CRP, but premature neonates in the exposed group had lower white cell counts than those of unexposed mothers (median 9.2 x 10⁹/L [IQR 6.2 to 12.0] vs. 10.7 x 10⁹/L [IQR 7.9 to 13.8]; p = 0.01).

Conclusion:

COVID-19 community lockdown measures reduced preterm birth rates < 34 weeks, but the spectrum of disease among neonates was largely unaltered. Maternal infection parameters for premature neonates born in lockdown were comparable, but neonates had lower white cell counts.

None declared



ID 382 - NEONATES BORN TO MOTHER WITH SARS – COV2 INFECTION: A TERTIARY CHILDREN'S HOSPITAL EXPERIENCE FROM ATHENS, GREECE.

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Background:

Limited data on vertical and perinatal transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and health outcomes of neonates born to mothers with symptomatic or asymptomatic coronavirus disease 2019 (COVID-19) are available. Studies are needed to inform evidence-based infection prevention and control policies.

Our objective was to describe the outcomes of neonates admitted to our hospital born to mothers with perinatal SARS-CoV-2 infection during the three pandemic waves in Greece (March 2020-August 2020, September 2020 – December 2020 and January 2021- May 2021).

Material and methods:

This retrospective analysis reviewed the medical records of 47 neonates born to 45 mothers positive for SARS-CoV-2 infection. Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) tests for SARS-CoV-2 were performed to all the patients at the end of the first and the third day of life.

Results:

There was an increase in cases born to infected mothers during the third wave following the severity of the pandemic in Greek population (33/47 neonates, 70% in the third wave). None of the neonates developed clinical, radiologic, hematologic, or biochemical evidence of COVID-19. No vertical transmission of SARS-CoV-2 was confirmed in our study. Twenty one neonates (45%) were born prematurely. Cases of stillbirth or neonatal death were not observed. Delivery with C-section was performed in 39 cases (79%). In 8 out of the 39 cases delivery with C-section was performed due to respiratory failure of the mother, 6 of them prematurely due to medical decision. All these cases were observed in the third wave.

Conclusion:

Although the risk of vertical transmission is suggested to be low, severe maternal infection can lead to pre-term birth and C-section delivery. Further large-scale studies are needed to clarify the risk factors associated with viral transmission and severe infection in the neonatal population.

None declared



ID 388 - INTERACTIVE MEDICAL EDUCATION IN THE COVID-19 ERA: NEONATAL JOURNAL CLUB

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Background:

The Covid-19 pandemic brought with it challenges not only in the management of patients but also in the education of medical professionals. This encouraged innovation by creating socially distanced ways of interacting during learning.

Methods:

A trainee led journal club was started in April 2020 utilising cloud based applications including junior doctors (ST1-ST8), nurses and nurse practitioners. The group met weekly and participation was voluntary. Participants were encouraged to actively engage by choosing topics of interest, and leading the ensuing discussions. Chosen articles were shared in advance. Consultants facilitated the sessions and the Critical Appraisal Skills Programme (CASP) tool was employed.

Prior to the meetings, a pre-intervention questionnaire was distributed which provided information varying from trainee experience and confidence to determining the teaching platform (virtual or physical) and timing of meetings. After every review and discussion, a post-article anonymous survey was conducted to assess knowledge gained, expectations in improvements in quality of patient care, professional practice and any further suggestions to enhance the learning experience. This was also sent to the presenter for their portfolio and peer review. Formal teaching was also given by the facilitator to help participants understand the different types of studies. After one year, a post-intervention feedback questionnaire was carried out.

Results:

The journal club, although founded in one neonatal department, spread to 3 hospitals by word of mouth, and trainees rotating in different hospitals were keen to continue actively participating. The pre-feedback questionnaire showed 72% of participants had attended a journal club previously and found it useful, however only 29% found it easy to attend a journal club and 21% felt somewhat confident to appraise an article. The preferred mode of learning by most was virtual and outside normal working hours averaging 9 participants per session. Post intervention feedback was extremely positive (Table 1). All participants were keen to continue with the virtual platform post-covid as it allowed flexibility and participation from different sites.

Conclusions:

Virtual teaching provided a platform to build, develop and engage a wider multidisciplinary community. Virtual journal club proved easy to attend, and improved neonatal knowledge and critical appraisal skills.

Feedback	Weighted Average
Enhanced knowledge on the subject	4.46
Relevant to practice	4.63
Format was effective	4.59
Was able to contribute/engage to the discussion	4.32
Increased confidence in understanding/appraising a journal paper	4.24

Table1: Post-intervention feedback (Likert Scale 1-5, 5=strongly agree)
None declared



ID 337 - EARLY-ONSET SEPSIS AS AN IMPORTANT CAUSE OF MORBIDITY AMONG REFUGEE NEONATES

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BACKGROUND:

Early-onset sepsis (EOS) remains a common and serious problem for neonates with increased risk of morbidity and mortality. However, the burden of EOS among neonatal refugee population has not been well studied. The aim of the study was to assess the incidence of EOS in the refugee-infant populations.

METHODS:

All records of refugee neonates admitted to B' Neonatal Intensive Care Unit (NICU) and Neonatal High Dependency Unit (NHDU) during a 4-year period, up to December 2020 were analyzed. Demographics and corresponding risk factors were compared between neonates with and without EOS which was defined as neonatal sepsis during the first 3 days of life.

RESULTS:

A total of 77 refugee neonates (60% males, 35±4.3 weeks of gestation) were recorded. Among them, 17 neonates (23.9%) were diagnosed with EOS and admitted almost all to the NICU. Culture-proven EOS occurred in 3 (17.6%), with gram negative bacteria being the commonest (66.7%) isolate. Males and females did not differ statistically significantly. Almost all neonates with EOS (93.3%) belonged to families with no health insurance. Access to antenatal care seemed to have no effect in EOS, while 41.2% of those with EOS were transferred from the islands, compared to 15.4% of those without EOS (p<0.05). Among refugee neonates with EOS, 52.9% stayed in camps. No neonate with EOS died. Meconium-stained amniotic fluid was detected in 40% of neonates with EOS, compared to 14.6% of neonates without EOS (p=0.04). Endotracheal intubation prior to transfer to our Hospital was more common for neonates with EOS 58.8%, contrary to 27.8% of the neonates without EOS (p<0.001). Among term refugee neonates with respiratory distress, 47.1% had concomitant EOS, while 22.2% term neonates appeared with respiratory disorder but without EOS (p<0.05). Moreover, hypotension, need for inotropes, pulmonary hypertension, cerebral brain injury and periventricular leukomalacia were also more common in EOS, compared to neonates without EOS (70.6% vs. 32.7%; p=0.006, 76.5% vs. 35.3%; p=0.03, 41.2% vs 5.8%; p< 0.05, 29.4% vs 1,9; p= 0.002 and 46.7% vs. 15.7%; p=0.012, respectively).

CONCLUSION:

A very high incidence of EOS was shown in refugee neonates, with high rates of in-hospital complications.

No conflict of interest



ID 153 - UMBILICAL CORD BLOOD DERIVED CELL THERAPY FOR NEWBORN INFANTS - SYSTEMATIC REVIEW OF CLINICAL STUDIES

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Background

Umbilical cord blood (UCB) cell therapies are an emerging area of research in regenerative medicine, with good evidence of efficacy in pre-clinical models of hypoxic ischaemic encephalopathy (HIE), preterm brain injury, and bronchopulmonary dysplasia (BPD). We aimed to systematically review UCB cell therapy use in published neonatal clinical trials, and provide an update on forthcoming studies.

Methods

We conducted a systematic search of published and registered, not completed studies using UCB cell therapies for neonatal morbidities. Databases searched were PubMed, Ovid Medline, Google Scholar, Clinical Trial Registries (USA, EU, China, ANZ), Embase, and online cell therapy registries. Studies were included if UCB cell therapy was given via any route for neonatal morbidities. UCB transplants for malignancy/metabolic disease, or disease diagnosed outside the neonatal period were excluded. Data were examined for trial phase and type, participant demographics, therapeutic target, and type of cells given.

Results

Our search yielded 11 completed study cohorts (Table 1). Study participants totalled 200 neonates worldwide, 117 (58.5%) were term, 83 (41.5%) preterm. Studies by morbidity included HIE (3), BPD (3), preterm morbidity (2), intra-ventricular haemorrhage (1), congenital heart disease (1) and congenital hydrocephalus (1). 6 studies were open label phase 1, 3 open label dose-escalation, one open label placebo-control, and one phase 2 RCT. 63.5% of participants received UCB cells intravenously, 27% intra tracheal, 5% intra cardiac, and 4.5% intra ventricular injection. There are a further 26 registered, not completed trials using UCB cell therapy in neonates, with 50% administering cord blood mononuclear cells (UCB-MNCs), 42% cord-derived mesenchymal stromal cells (UC-MSCs), and 8% whole UCB. 15 registered trials are listed as recruiting, with 3 of those being RCTs. No serious adverse effects related to UCB cell therapy occurred in the studies.

Conclusion

UCB cell therapies have been administered to neonates in 10 early phase safety and feasibility trials, and one phase 2 RCT. Safety and feasibility of intravenous UCB cell therapy has been demonstrated in term HIE, and intra-tracheal UC-MSCs for BPD. Data are limited for preterm infants. Further phase 2 studies and RCTs are required to establish UCB cell therapies as an effective intervention for neonatal morbidities.



Study	Location	Design	Population	Intervention	Primary outcome
<i>Anh et al 2021</i> doi.org/10.1002/sctm.20-0330	S. Korea	Phase 2 randomised controlled trial	Preterm infants 23-28 wks at risk of BPD n = 33	Intra tracheal allogeneic UC-MSCs 1x10 ⁷ /kg day 5-14	Death or moderate-severe BPD
<i>Cotten et al 2020</i> doi.org/10.1016/j.jcyt.2020.04.052	USA	Open label, phase 1	Term infants with HIE n = 6	Intravenous allogeneic UC-MSCs 2x10 ⁶ /kg at 48 hours and 2 months	Safety and feasibility within 2 weeks of administration
<i>Powell et al 2019</i> DOI: 10.1016/j.jpeds.2019.02.029	USA	Open label, phase 1 dose-escalation	Preterm infants <28 weeks risk of BPD n = 12	Intra tracheal allogeneic UC-MSCs 1-2x10 ⁷ /kg day 5-14	Safety within 84 days of administration
<i>Ren et al 2019</i> doi.org/10.1002/sctm.19-0106	China	Open label, phase 1 placebo-control	Preterm infants <35 weeks n = 15	Intravenous autologous UC-MNCs 5x10 ⁷ /kg day 1	Mortality before discharge, rate of preterm complications
<i>Burkhart et al 2019</i> doi.org/10.1016/j.jtcvs.2019.06.001	USA	Open label, phase 1	Term infants hypoplastic left heart syndrome n = 10	Intra cardiac autologous UC-MNCs 1-3x10 ⁶ /kg during surgery	Safety and feasibility during surgery, and until 6 months
<i>Anh et al 2018</i> doi: 10.1002/sctm.17-0219	S. Korea	Open label, phase 1 dose-escalation	Preterm infants with severe IVH n = 9	Intra ventricular injection of allogeneic UC-MSCs 1-5x10 ⁶ /kg day 7-15	Safety and feasibility until term-corrected age
<i>Kotowski et al 2017</i> PMID: 29550804	Poland	Open label, phase 1 with matched controls	Preterm infants <32 weeks n = 5	Intravenous whole UCB on day 5	Safety and feasibility within 14 days
<i>Sun et al 2015</i> doi.org/10.1038/pr.2015.161	USA	Open label, phase 1	Term infants with congenital hydrocephalus n = 76	Intravenous autologous UC-MNCs 1-5x10 ⁷ /kg at day 6 to 4.5 years (median 2mo)	Safety and feasibility until 12 months
<i>Cotten et al 2014</i> doi: 10.1016/j.jpeds.2013.11.036	USA	Open label, phase 1, matched controls	Term infants with HIE n = 23	Intravenous autologous UC-MNCs 1-5x10 ⁷ /kg 12, 24, 48, 72hr	Safety and feasibility until 12 months
<i>Chang et al 2014</i> doi.org/10.1016/j.jpeds.2013.12.011	S. Korea	Open label, phase 1 dose-escalation	Preterm infants 23-29 wks at risk of BPD n = 9	Intra tracheal allogeneic UC-MSCs 1-2x10 ⁷ /kg day 7-14	Safety until term corrected age
<i>Jiun et al 2013</i> doi: 10.22494/cot.v1i1.45	Singapore	Open label, phase 1	Term infants with HIE n = 2	Intravenous autologous UC-MNCs 6x10 ⁶ at <24, 24, 48, 72 hrs	Safety and feasibility until 12 months

Published UCB cell therapy trials in neonates
There are no conflicts of interest to declare