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ABS 1

EARLY PAIN EXPERIENCES AND NEONATAL CEREBRAL CONNECTIVITY EVALUATED WITH rs-fMRI AT TERM CORRECTED AGE

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INTRODUCTION

Neonates admitted to NICUs are exposed to numerous painful procedures. Our hypothesis is that the nociceptive experiences could change brain functional organization. The study's aim is to establish how early pain exposure can alter neonatal brain functional connectivity evaluated with resting state functional-MRI (rs-fMRI).

METHODS

We enrolled 46 newborns admitted to Giannina Gaslini Children's Hospital's NICU between January 2015 and January 2017 who underwent rs-fMRI at term or term-equivalent age. Clinical data of the infants were collected from hospital charts. Infants were divided into 4 categories based on exposure to the severity of the invasive procedures (> 5 heel lances, endotracheal intubation, surgery). Brain functional connectivity was evaluated with two different approaches. The first, termed seed-to-voxel component analysis (SCA), is based on the analysis of 43 seeds selected "a-priori" and known to be involved in adult pain processing. The second, called multi voxel pattern analysis (MVPA), by whole-brain mapping identifies the areas potentially involved in neonatal pain processing without the "a-priori" selection bias. Significant voxel clusters of this latter analysis were used to perform a post-hoc seed-to-voxel analysis (SCA) to quantify brain connectivity of these seeds with the remaining brain areas. Functional data analysis was performed by using a generalized linear model (GLM), taking into consideration the possible effect of other 15 clinical factors.

RESULTS

46 patients born at a mean gestational age of 31.6 ± 4.9 weeks were included. SCA results showed highly significant alterations ($p < 0.001$) connected with pain exposure in 7 (the posterior cingulate [Fig. 1], the right pre-central gyrus, the left supplementary motor area, the left insular cortex, the right insular cortex, the right inferior frontal gyrus or opercular area and the right middle frontal gyrus) of the 43 areas explored. Dissimilar from adults, we did not observe any brain connectivity alterations in the amygdala and orbitofrontal cortex. MPVA results showed highly significant brain connectivity alterations ($p < 0.001$) in 5 areas: right insular cortex, opercular portion of right inferior frontal gyrus, right middle frontal gyrus, cerebellum, left occipital pole.

CONCLUSIONS

We have demonstrated for the first time how nociceptive experiences can modify brain functional connectivity in neonates even at a distance of time from stimulation. Somatosensory areas, the insulae and the cerebellum known for stress and pain response, seem to be involved also in neonates similarly to adults; a potential role for the posterior cingulate and the lateral occipital cortex influence seems to characterize neonatal network after painful experiences. Delayed maturation of the frontal region (myelination and cortical folding) of the frontal region could explain the lack of brain connectivity alterations in the amygdala and orbitofrontal cortex.

ABS 2

PLACENTAL HISTOLOGY FINDINGS AS POSSIBLE RISK FACTORS FOR MRI-DETECTED BRAIN LESIONS IN VLBW INFANTS

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INTRODUCTION

Various perinatal factors can influence development of prematurity-related brain lesions, but their

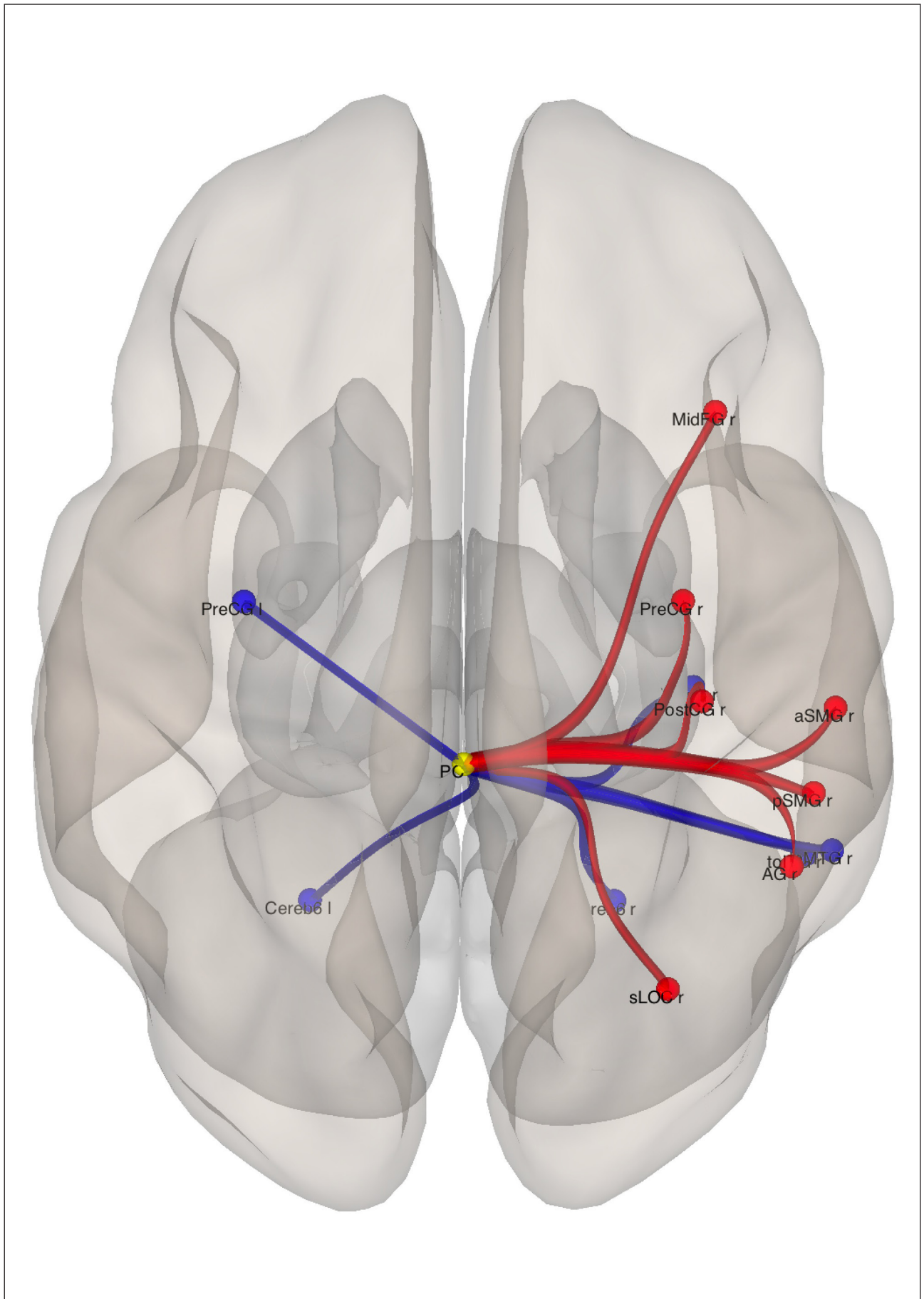


Figure 1 (ABS 1). Regions with increased (red) and decreased (blue) connectivity starting from posterior cingulate gyrus (PC).

precise individual roles are yet to be defined. In particular, the role of placental inflammation in the development of ultrasound-detected white matter lesions and intraventricular haemorrhage is still matter of debate. The goal of our study was to identify perinatal risk factors, with particular attention to placental histopathology, for MRI-diagnosed brain lesions in a cohort of VLBW infants.

METHODS

All VLBW infants born in our hospital between January 2012 and October 2016 who had received a term equivalent age brain MRI scan as a part of follow-up program were retrospectively identified. Scans were performed at 1.5 T system and included T1, T2, diffusion and susceptibility weighted sequences. Among the identified patients, only newborns with an available placental histology were included in the study. Perinatal data including placental histology were collected from NICU electronic database and clinical charts. Univariate and multivariate analyses of potential risk factors were performed for germinal matrix-intraventricular haemorrhage (GMH-IVH), cerebellar haemorrhage (CBH), cystic periventricular leukomalacia (c-PVL) and punctate white matter lesions (PWML).

RESULTS

The study group consisted of 286 patients. Independent risk factors for GMH-IVH (prevalence: 23.8%) identified by multivariate analysis are shown in **Tab. 1**. As for CBH (prevalence: 16.8%), multivariate analysis identified the use of inotropic support within 72 h after birth (OR 5.24) and contemporary presence of GMH-IVH (OR 6.38) as independent risk factors. In our study, placental characteristics, including chorioamnionitis, were not identified as independent risk factors for white matter lesions, including both c-PVL (prevalence: 2.4%) and PWML (prevalence: 19.9%).

CONCLUSIONS

Our study shows that placental inflammation or infarction are risk factors for the development of GMH-IVH, a disease occurring in the first days of life. Moreover, Apgar score and incomplete or absent antenatal steroid prophylaxis are confirmed risk factors for GMH-IVH. Interestingly, chorioamnionitis is not associated to MRI-diagnosed white matter lesions, in contrast with previous studies based mainly on ultrasound findings.

ABS 3

PATTERN OF NEURODEVELOPMENTAL OUTCOME AT 2 YEARS OF CORRECTED AGE (CA) IN ISOLATED LOW-GRADE INTRAVENTRICULAR HEMORRHAGES VS LOW-GRADE CEREBELLAR HEMORRHAGES

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INTRODUCTION

How minimal bleeding of germinal matrix could affect neurodevelopmental outcome of VLBW is still debated. Aim of our study is to find out neurodevelopmental features of isolated low grade intraventricular haemorrhage (LG-IVH) compared with isolated low grade cerebellar haemorrhage (LG-CBH) in order to establish their possible independent involvement in neuropsychiatric outcome at 2 years of corrected age (CA) in a cohort of VLBW.

MATERIALS AND METHODS

VLBW admitted to our NICU who underwent brain MRI at TEA and completed Griffiths Mental

Table 1 (ABS 2). Independent risk factors for germinal matrix-intraventricular haemorrhage (GMH-IVH).

Perinatal risk factors	GMH-IVH (n = 68)	Controls (n = 218)	OR (95% CI)	p-value
Apgar score at 5 th min ≤ 5	10.3%	1.8%	6.62 (1.48-29.6)	0.01
Incomplete or no antenatal steroids	24.4%	19.2%	2.45 (1.17-5.16)	0.02
Maternal hypertension/preeclampsia	11.8%	21.6%	0.26 (0.09-0.72)	0.009
Mechanical ventilation in the first 72 hours of life	72.1%	45.9%	2.14 (1.09-4.20)	0.03
Surgical ligation of ductus arteriosus	23.5%	6.9%	3.45 (1.45-8.18)	0.005
Umbilical vein vasculitis	22.1%	9.2%	3.80 (1.59-9.06)	0.003
Villous infarction	25%	10.5%	5.94 (2.49-14.2)	0.0001

Developmental Scale (GMDS) at 2 years were retrospectively identified and included in the study. MRI scans were performed at 1.5 T system and included T1, T2, diffusion and susceptibility weighted (SWI) sequences. LG-IVH was defined as presence of hemosiderin deposits inside germinal matrix and/or along the ependyma of the ventricles (as seen on SWI), in absence of ventricular dilatation or periventricular infarction. LG-CBH was defined as presence of punctate haemorrhagic lesions within cerebellum. Patients completed neurological examination according to Hempel model, to assess any minor neurologic dysfunction (MND) and Griffiths Mental Development Scale-Extended Revised (GMDS-ER) performed by a single operator blinded to MRI results. Mean values were reported for continuous variables. T-Student test was performed.

RESULTS

The study group consisted of 173 patients (mean GA 28 weeks). When all grades of lesions were considered, prevalence of IVH (57 patients, 32.9%) was higher than prevalence of CBH (35 patients, 20.2%). Isolated LG-IVH was found only in 8 patients (prevalence 4.6%), and isolated LG-CBH in 10 (prevalence 5.8%). Mean gestational age was 28 and 27.5 in LG-IVH and LG-CBH groups, respectively (non-significant difference, $p = 0.7$). A Griffiths score of 85 was used as cut off for normal outcome. LG-IVH group showed higher scores in all subscales. Statistical significance between the two groups was achieved for total developmental score ($p = 0.041$), motor ($p = 0.044$), social ($p = 0.040$) and coordination ($p = 0.027$) subscales (**Tab. 1**). In the LG-IVH group 4/8 cases had MND; in the LG-CBH group 4/10 cases had MND.

CONCLUSIONS

In our cohorts, even if MND are more frequent in LG-IVH, LG-CBH babies showed a trend of worst impairment on developmental outcome. LG-CBH group showed lower score in all domains and statistic significance was present for the total DQ

and for the subscales A (gross-motor), B (social and adaptive) and D (visual-spatial). This could be explained by involvement of cerebellar-thalamic-cortical bundles and cognitive role played by cerebellum. This finding seems not to be related to GA. Longer follow-up on this population is recommended in order to confirm higher risks for neurological impairments due to LG-CBH.

ABS 4

TWIN PREGNANCY AND PRETERM BIRTH: FOCUS ON “AUTOPHAGY BIOMARKERS” AS REGULATORS OF THE IMMUNE RESPONSE

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INTRODUCTION

Preterm birth (PTB) occurs in 5-18% of all pregnancies and remains the most common cause of death under the age of 5 years. The incidence of PTB is higher in twin pregnancies than in single ones (56.6% vs 9.7%). The pathogenesis of PTB is multifactorial but it is known that an excessive inflammatory response of the placental-fetus unit and an alteration of the immune defense mechanism play an important role. Specific proteins within peripheral blood mononuclear cells (PBMCs) are involved in immune tolerance promoting autophagy to maintain intracellular homeostasis. Alterations in their biological activity are associated with a wide spectrum of human diseases. We sought to examine the relationship between maternal autophagy biomarkers and PTB in women with twin pregnancy.

Table 1 (ABS 3). Griffiths Mental Development Scale-Extended Revised (GMDS-ER) scores at 2 years of age.

GMDS-ER scores	GMH-IVH (s.e.)	CBH (s.e.)	p
Total DQ	93.75 ± 5.09	81.90 ± 4.05	0.041
A DQ Locomotor	95.75 ± 5.27	82.5 ± 4.99	0.044
B DQ Personal-social	90.62 ± 4.75	78.70 ± 4.30	0.040
C DQ Hearing and Language	84.5 ± 7.4	74.0 ± 3.68	0.117
D DQ Eye and Hand Coordination	100.62 ± 5.65	85.60 ± 4.62	0.027
E DQ Performance	93.50 ± 4.48	85.40 ± 3.56	0.085

Results are presented as mean ± standard error.

GMDS-ER: Griffiths Mental Development Scale-Extended Revised; IVH: intraventricular haemorrhage; CBH: cerebellar haemorrhage.

METHODS

This is an observational study on women with twin pregnancy recruited from 12th to 29th week of gestation between 2015 and 2017. Women were divided into two groups, term-birth group and PTB group, according to gestational age at delivery (\geq or $<$ 37 weeks, respectively). The PTB group was further divided according to type of birth: with spontaneous onset of labor or medically indicated. PBMCs were isolated by a blood sample the day of the recruitment at Careggi University Hospital in Florence. Intracellular levels of a2V isoform of vacuolar ATPase (a2V), heat shock protein 70 (HSP70), p62 protein and extracellular levels of brain derived neurotrophic factor (BDNF) and HSP70 were assayed by ELISA test at Well Cornell Medicine in New York. Associations were analyzed by the Spearman rank correlation, Mann-Whitney and Kruskal-Wallis tests as appropriated. A p-value $<$ 0.05 was recorded and considered statistically significant.

RESULTS

Overall, 58 women were recruited in this preliminary study. The a2V concentration in PBMCs was higher in the 16 women who had a spontaneous PTB compared to the 22 women who had a delivery at term and to the 20 women with a medically indicated PTB (median 3.1 ng/ml vs 1.6 ng/ml, vs 1.4 ng/ml, $p = 0.01$) (**Tab. 1**). The a2V concentration in PBMCs was negatively correlated with interval from sample collection to delivery in the group 1 ($r = -0.555$, $p = 0.0258$). The intracellular levels of a2V and HSP70 were negatively correlated in group 1 ($r = -0.784$, $p = 0.000321$). No difference for the other biomarkers levels were found among the three groups.

CONCLUSION

Expression of the a2V in PBMCs is associated with altered immunity increasing susceptibility to labor

induction. Measurement of a2V in PBMCs prior to 30 weeks of gestation is a sensitive predictor of PTB in twin pregnancy.

ABS 5

THE ROLE OF ELASTOGRAPHY IN PREDICTING PRETERM BIRTH

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INTRODUCTION

Elastography is an ultrasound-based imaging technique calculating the stiffness of examined region. The aim of the study was to estimate the potential value of elastographic evaluation of cervix at 22-34 weeks of pregnancy in patients with short cervical length for prediction of preterm delivery (PTD).

METHODS

We conducted a prospective observational study by March to December 2017. We enrolled 60 symptomatic patients between 22-34 week of gestation with singleton pregnancy, irregular uterine activity and/or lower abdominal pain and pelvic pressure, intact membranes and cervical length $<$ 20 mm and funneling. Patients were initially managed according to the internal protocol: prophylactic corticosteroid betamethasone i.m. 12 mg/day for 2 days and primary tocolysis for 48 hours. Ultrasound examinations of the cervix were performed transvaginally with a Samsung Medison WS80 Elite equipped with a transvaginal (4-9 MHz) convex probe and

Table 1 (ABS 4). Biomarkers distribution in the three groups.

Markers	Term birth	Spontaneous PTB	Medically indicated PTB	p-value ^a
n	22	16	20	
a2V intra	1,612.00 [507.00; 4,798.96]	3,112.88 [988.00; 5,694.25]	1,449.50 [325.00; 4,606.31]	0.011
HSP70 intra	38,980.32 [0.00; 98,569.68]	23,729.30 [0.00; 123,393.88]	37,116.46 [5,710.22; 112,702.43]	0.421
p62 intra	2.04 [1.36; 6.64]	2.56 [1.17; 13.60]	3.40 [1.31; 8.64]	0.204
BDNF extra	4,758.36 [1,622.31; 20,498.52]	3,016.97 [1,114.69; 19,517.70]	4,192.19 [1,702.88; 16,021.87]	0.109
HSP70 extra	2,767.83 [1,467.66; 4,857.52]	2,702.95 [1,951.61; 5,719.32]	2,767.83 [1,333.67; 4,446.43]	0.991

^aKruskal-Wallis test.

Intra: intracellular; extra: extracellular; a2V: a2V isoform of vacuolar ATPase; HSP70: heat shock protein 70; BDNF: brain derived neurotrophic factor.

ElastoScan™ option. Stiffness of the internal cervical os was assessed by elastography calculating the hardness ratio. The hardness ratio was calculated and compared between two groups according the time of delivery: preterm (A group) and term deliveries (B group).

RESULTS

In A group (30 patients) the mean of hardness ratio was 24.75 ± 4.39 ; in B group (30 patients) it was 57.38 ± 2.05 . Data were compared with paired t test. When stratified by hardness ratio, there was a statistically significant difference between two groups ($p < 0.0001$).

CONCLUSIONS

Elastographic evaluation of the cervix at 22-34 weeks of pregnancy in patients with short cervical length may be useful in predicting PTD. However, our conclusions are based on a small sample, so further studies are needed. If our results will be confirmed, the device could be considered an excellent test to rapidly assess the risk of preterm delivery.

ABS 6

MRI-DIAGNOSED WHITE MATTER LESIONS IN THE BRAIN OF VLBW BABIES: RISK FACTOR ANALYSIS

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INTRODUCTION

In the last decades, perinatal care and the survival rates of very low birth weight infants (VLBW) have improved significantly. Following this trend, the incidence of major brain lesions, like cystic periventricular leukomalacia (c-PVL), have been constantly decreasing. On the other hand, milder forms of white matter damage, like punctate white matter lesions (PWML), are frequently seen in preterm infants undergoing MRI at term-equivalent age. The aim of this study was to analyze prevalence of different types of the white matter injury (WMI) as seen on term-equivalent age MRI, and investigate related clinical risk factors.

PATIENTS AND METHODS

All VLBW infants admitted at birth to our NICU between January 2012 and October 2016 and consecutively scanned at term-equivalent age as a part of follow-up program were retrospectively identified and included in the study. Prenatal, perinatal and post-natal clinical data were collected from NICU electronic database and clinical records. MRI scans were performed at 1.5 T system and included T1, T2, diffusion and susceptibility weighted (SWI) sequences. Images were reviewed in order to evaluate prevalence of c-PVL and prevalence, number (less or more than six) and type of PWML (hemorrhagic or non-hemorrhagic according to SWI appearance). Univariate and multivariate analysis of risk factors for all types of WMI was performed.

RESULTS

Study population included 321 newborn. Nine of them (3%) presented c-PVL and 61(19%) presented PWML. Inside the last group, in 26 cases (43%) 6 or more PWML were present, while in 15 cases (25%) PWML were seen on SWI indicating haemorrhagic nature of the lesions. Placental abruption (OR = 4.67) and presence of GMH-IVH (OR = 3.94) emerged among the risk factors for cPVL, while incomplete antenatal steroid treatment (OR 2.71) and intubation (OR = 10.1) resulted significant for PWML ≥ 6 . Oxygen treatment for more than 7 days (OR = 0.19) and cesarean section (OR = 0.22) presented OR < 1 . The only risk factor associated with SWI + PWML was the presence of GMH-IVH (OR = 8.67).

CONCLUSIONS

Our study confirms an important reduction in cPVL prevalence in modern NICUs. Respiratory distress emerges as an important risk factor in the development of PWML. Accordingly, incomplete antenatal steroid treatment for pulmonary maturation seems to influence the development of those lesions, while intubation increases the odds of having more than 6 PWML ten-fold. Further studies could help to corroborate our findings.

ABS 7

MATERNAL AND FETAL OUTCOMES IN TWIN OOCYTE DONATION PREGNANCIES: EXPERIENCE OF A TERTIARY REFERRAL OBSTETRIC ITALIAN CENTER

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INTRODUCTION

To evaluate the rate of pregnancy complications, maternal and neonatal post-partum outcomes in a cohort of twin pregnancies from oocyte donation, compared to a cohort of ICSI/FIVET patients.

METHODS

This is a retrospective study on a cohort of twin pregnancies from oocyte donation (OD), compared to twin pregnancies from ICSI/FIVET, delivered in a tertiary referral center. 157 OD and 443 ICSI/FIVET pregnancies were encountered, between 2014 and 2017: 42 and 91 twin pregnancies from OD (26.8%) and ICSI/FIVET (20.5%) were included.

RESULTS

OD patients were significantly older than ICSI/FIVET patients (44 ± 4 vs 36 ± 4 years), while no differences were noted for BMI (26.7 ± 3 vs 25.9 ± 6.6 kg/m²) and the rate of nulliparous women (76% vs 87%). The rate of twin pregnancies was not significantly different between OD and ICSI/FIVET. Among OD twins, 90% were dichorionic (BC/BA n = 38) and 7% were monochorionic (MC/BA); 1 case of a dichorionic triamniotic triplet (BC/TA) was also described. Among ICSI/FIVET twins, 85% were BC/BA (n = 78) and 7.7% were MC/MA; 3 cases of BC/TA triplets and 3 cases of trichorionic triamniotic triplets were registered. No differences were noted considering the chorionicity. OD pregnancies were more often complicated by hypertensive disorders (chronic hypertension, gestational hypertension and preeclampsia), in 29% of cases towards the 5.5% of ICSI/FIVET. No differences were noted for gestational diabetes (11% vs 7%), cholestasis (16% vs 8%) or disorders of placentation (7% vs 2%). Considering only BC/BA twins, the rate of pregnancies complicated by IUGR of at least one fetus was not significantly different in OD (16%) versus ICSI/FIVET (10%). According to local protocols, only BC/BA twins were admitted to labor. Among BC/BA pregnancies, almost all underwent a cesarean section (95% in OD vs 91% in ICSI/FIVET); only 2 OD patients and 7 ICSI/FIVET patients managed to have a vaginal delivery. Considering maternal post-partum outcomes, almost half of both OD and ICSI/FIVET patients experienced a hemorrhage > 500 ml (55% vs 54%), without any difference even when stratifying for the severity of blood loss. Neonatal adverse outcomes, defined as pH < -12 and Apgar score < 7 at 1', occurred on 7% and 13% in OD and ICSI/FIVET,

respectively (p = 0.30). Neonatal weight was similar in both groups: $2,227 \pm 636$ g in OD vs $2,271 \pm 631$ g in ICSI/FIVET pregnancies. Mean gestational age at delivery was 34.9 ± 2.6 weeks in OD and 35.3 ± 2.9 weeks in ICSI/FIVET. 74% of twins from OD were born before 37 gestational weeks, compared to 45% of twins from ICSI/FIVET (p < 0.05).

CONCLUSIONS

In our population, OD patients more often developed hypertensive disorders of pregnancy. At delivery, both groups experienced the same rate of cesarean section and post-partum maternal and neonatal outcomes. The prematurity rate was higher for OD twins, even if the majority of premature babies experienced a mild prematurity.

ABS 8

MATERNAL AND FETAL OUTCOMES IN SINGLETON OOCYTE DONATION PREGNANCIES: EXPERIENCE OF A TERTIARY REFERRAL OBSTETRIC ITALIAN CENTER

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INTRODUCTION

To evaluate the rate of pregnancy complications, mode of delivery, maternal and neonatal post-partum outcomes and the rate of prematurity in a cohort of singleton pregnancies from oocyte donated patients, compared to a cohort of ICSI/FIVET patients.

METHODS

This is a retrospective study on a cohort of singleton pregnancies from oocyte donation (OD), compared to a cohort of single pregnancies from ICSI/FIVET, delivered in a tertiary referral obstetric Italian center. 157 OD pregnancies and 443 ICSI/FIVET pregnancies were encountered between 2014 and 2017: we included 115 and 352 singleton pregnancies from OD and ICSI/FIVET, respectively.

RESULTS

OD patients were significantly older than ICSI/FIVET patients (44 ± 4 vs 37 ± 4 years), while no differences were noted for BMI (26 ± 4.5 vs 25.8 ± 4.3 kg/m²) and the rate of nulliparous women (87% vs 80.7%).

OD pregnancies were more often complicated by hypertensive disorders of pregnancy (chronic hypertension, gestational hypertension and

preeclampsia), in 8.7% of cases towards the 3.7% of ICSI/FIVET ($p < 0.05$). No differences were noted for gestational diabetes (5.2% vs 16%), cholestasis of pregnancy (3.5% vs 2.6%), disorders of placentation (2.6% vs 1.4%) and for the rate of intrauterine growth restriction (1.7% vs 4%). The rate of cesarean section was 73% and 38.4% for OD and ICSI/FIVET pregnancies, respectively: in particular, among OD patients the rate of maternal-choice cesarean section was 50%, significantly higher than ICSI/FIVET patients (13%). 217 (61.6%) ICSI/FIVET patients managed to have a vaginal delivery, while only 31 (26%) OD delivered vaginally (25.2% vs 24.4%, respectively), even when stratifying for the severity of blood loss. Neonatal adverse outcomes, defined as pH < -12 and Apgar score < 7 at 1', occurred on 11.3% and 9.4% in OD and ICSI/FIVET, respectively ($p = 0.25$). Neonatal weight was similar in both groups: $3,179 \pm 663$ g in OD vs $3,180 \pm 652$ g in ICSI/FIVET pregnancies; the rate of low birth weight ($< 2,500$ g) was 12% in OD vs 9% in ICSI/FIVET ($p = 0.38$). Mean gestational age at delivery was 38.2 ± 2.3 weeks in OD and 38.6 ± 2.3 weeks in ICSI/FIVET. In OD group, 12.2% of neonates were born prematurely before 37 gestational weeks; in ICSI/FIVET group, the 8.2% of babies were premature ($p = 0.28$). In both groups, the majority of premature neonates were delivered after 32 gestational weeks (9.5% and 7% in OD and ICSI/FIVET patients, respectively).

CONCLUSIONS

OD patients more often developed hypertensive disorders of pregnancy. The rate of cesarean section was higher than in ICSI/FIVET group, because of a greater rate of maternal-choice cesarean sections. Post-partum maternal and neonatal outcomes and the rate of prematurity were similar in both groups.

ABS 9

PREECLAMPSIA OR CHRONIC KIDNEY DISEASE? A CORRECT DIAGNOSIS CAN PREVENT PRETERM BIRTH. A CASE REPORT

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INTRODUCTION

Preterm birth and low birth weight might affect nephrogenesis and they are associated with a risk of chronic kidney disease (CKD) and high blood pressure in later-life. The differential diagnosis between preeclampsia (PE) and CKD is not yet systematically posed in women who present hypertension and proteinuria in pregnancy. Since PE is associated with defective placentation, foetal growth is often impaired. Hence, the finding of a normal fetal growth may offer a first insight suggesting to consider the differential diagnosis of a glomerular disease, thus substantially modifying follow-up and treatment and reducing the risk of subsequent preterm birth.

METHODS

The case of a pregnant woman followed at Sant'Anna Hospital, Turin, is reported in this paper.

RESULTS

A 22-year-old woman with a silent clinical history was referred at the 25th gestational weeks of her first pregnancy for hypertension (140/95 mmHg), nephritic proteinuria (3.72 g/day) and visual troubles; she had a normal body mass index pre-pregnancy (BMI: 23), but had gained 10 kg in the last month, and reported, in the last days, a reduction of the diuresis. She was hospitalized with a diagnosis of PE. The tests performed to assess fetal well-being (biometry and Doppler flows) were however fully normal. She underwent betamethasone treatment to enhance foetal lung maturation, in the case of need for delivery. In the following days, blood pressure normalized without treatment; proteinuria reached 4.5 g/day, but then rapidly decreased to 1.01 g/day. On the account of the normal foetal growth, of the partial response to pulse steroids and of the clinical well being, a minimal change nephropathy was hypothesized. The patient was empirically treated by oral steroids (prednisone 37.5 mg), with full remission of the nephritic syndrome, of blood pressure. The patient was discharged with normal blood pressure; proteinuria was 1.35 g/day. Pregnancy was uneventful until spontaneous labour occurred at 37 weeks and 5 days. A healthy female baby, adequate for gestational age (3,120 g, 69th centile of the Italian growth curves) was delivered. The patient was discharged normotensive and without significant proteinuria (0.26 g/day). The ratio between the antiangiogenic markers s-flt-1 (soluble fms like tyrosine kinase 1) and the angiogenic placental growth factor (PlGF) usually increased in case of PE, was not available in routine at that

time in our Unit; however, blood samples were stored and later analysed; the low ratio (28 weeks: 7.22; 32 weeks: 13.46; 34 weeks: 6.29; 36 weeks: 4.24) was indeed in keeping with a kidney disorder different from PE.

CONCLUSIONS

The present case may highlight the importance of considering acute and chronic kidney disease in the differential diagnosis of PE. While the availability of s-flt-1/PIGF ratio may support the differential diagnosis between PE and glomerulonephritis, the simple considerations of foetal growth and Doppler flows may guide the clinical diagnosis and management.

ABS 10

THE CERVICAL SLIDING SIGN: A NEW ULTRASOUND TOOL IN THE ASSESSMENT OF THREATENED PRETERM LABOR

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OBJECTIVES

To assess the impact of the cervical sliding sign (CSS) in case of threatened preterm labor (TPL).

METHODS

Single centre prospective study. A non-consecutive series of pregnant women between 24⁺⁰ and 36⁺⁶ weeks presenting with TPL were assessed by transvaginal ultrasound (TVU) to obtain cervical length (CL) measurement. TPL was defined as evidence of > 6 contractions/hour + CL modifications at the digital examination. The CSS was defined as the sliding of the anterior cervical lip on the posterior one under gentle pressure of the TV probe (**Fig. 1**). After the initial evaluation, the time-to-delivery (TtD – days) was recorded in each case. In case of CL > 30 mm the patient was discharged, whilst when CL was < 20 mm

the patient was admitted and treated (tocolysis + steroid prophylaxis). If the CL was 20-30 mm, the management depended on the fibronectin test result. The main outcomes were: delivery before 34 weeks, within 7 days and 14 days.

RESULTS

We recruited 58 patients for the study purpose. Of these, 15 delivered < 34 weeks (26%) and the average TtD was 33.8 ± 30.2 days. Among the patients with CL > 20 mm, compared with cases with shorter cervix, delivery < 34 weeks occurred less frequently (3/14 or 21% vs 12/44 or 27%) and TtD was longer (45.7 ± 32.9 vs 30.0 ± 28.6, p = 0.09). The CSS was negative in all 14 cases with CL > 20 mm and was positive in all 4 cases with CL < 10 mm. In the subgroup of remaining 40 patients with CL between 10 and 20 mm the CSS was found in half, and was associated with a shorter TtD (21.1 ± 20.2 vs 43.3 ± 33.1 days, p < 0.05) and with a higher risk of delivery < 34 weeks (8/20 or 40% CSS positive vs 2/20 or 10% CSS negative, p < 0.05), < 7 days (10/20 or 50% vs 3/20 or 15%, p < 0.05) and < 14 days (13/20 or 65% vs 4/20 or 20%, p < 0.05).

CONCLUSIONS

In case of threatened preterm labor, the CSS seems associated with a higher risk of preterm delivery in the subgroup of patients with CL 10-20 mm.

ABS 11

IS MATERNAL SERUM PREGNANCY ASSOCIATED PLASMA PROTEIN-A (PAPP-A) A PREDICTIVE MARKER OF SPONTANEOUS PRETERM BIRTH?

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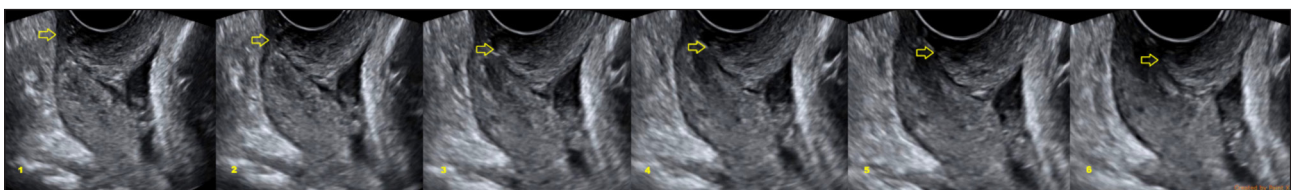


Figure 1 (ABS 10). From frame 1 to 6: progressive sliding of the anterior cervical lip (arrow) on the posterior one, as the pressure of the transvaginal probe increases.

INTRODUCTION

Preterm birth (PTB) is the most common cause of neonatal morbidity and mortality occurring in 6.8% of pregnancies in Italy. Two-thirds of PTB occur after spontaneous onset of labor (sPTB), whereas one third is medically indicated because of maternal or fetal complications, such as preeclampsia (PE) or fetal growth restriction (FGR). sPTB is often considered as if it were a single condition, however PTB is a syndrome attributable to multiple pathologic processes. In fact, some cases of sPTB appear to be caused by placental insufficiency. Pregnancy associated plasma protein-A (PAPP-A) is a glycoprotein produced by syncytiotrophoblast with a key role for normal placentation. Low maternal blood levels of PAPP-A in the first trimester have been associated with FGR and PE. However, a potential role of PAPP-A in the pathogenesis of PTB can be hypothesized. Thus, the aim of the study is to determine the relationship between PAPP-A and sPTB.

METHODS

This was a 3-year observational retrospective study conducted in Careggi University Hospital (Florence) on women with a singleton pregnancy who underwent first trimester screening for aneuploidy. Plasma values of PAPP-A were recorded. Women with cervical length (CL) measurement during the second trimester were included. Those pregnancies whose delivery outcome was not available were excluded. The PTB rate overall, sPTB and indicated PTB rate were evaluated. The association between low PAPP-A (< 0.4 MoM) and pregnancy complications, including FRG, PE and PTB, were evaluated. The predictive value of CL for PTB was explored. Chi-square test was applied and a ROC curve analysis was performed. SPSS® version 20 was used for statistical analysis and a p-value of 0.05 was considered significant.

RESULTS

The study population included 2,101 women with a singleton pregnancy undergoing first trimester screening. After exclusion criteria, 448 cases were analysed. The overall PTB rate was 9.2% whereas the sPTB rate was 2.2%. A low PAPP-A at first trimester was found in 4% of women and it resulted significantly associated with PTB ≤ 32 weeks (p = 0.039), while the association with sPTB was not significant. A significant increase in FGR (p = 0.007) and PE (p = 0.025) prevalence was observed in women with low PAPP-A (**Tab. 1**). We confirmed the known statistically significant correlation between short CL and sPTB (p = 0.009). Using the ROC curve,

Table 1 (ABS 11). Low pregnancy associated plasma protein-A (PAPP-A) and obstetric outcomes.

	PAPP-A ≤ 0.4 MoM (n = 28)	PAPP-A > 0.4 MoM (n = 420)	p
Age (years)	35 (32-38)	35 (34-35)	0.659
Smoking	1 (3.6%)	27 (6.4%)	0.462
Nulliparity	15 (53.6%)	237 (56.4%)	0.643
Gestational diabetes	9 (32.1%)	82 (19.8%)	0.090
FGR	9 (32.1%)	51 (12.1%)	0.007
PE	4 (14.3%)	15 (3.6%)	0.025
Obstetric cholestasis	2 (7.1%)	15 (3.6%)	0.288
PTB	4 (14.2%)	37 (8.8%)	0.247
sPTB	0 (0%)	10 (2.3%)	0.556
PTB ≤ 28 weeks	2 (7.1%)	5 (1.1%)	0.128
PTB ≤ 32 weeks	3 (10.7%)	7 (1.6%)	0.039
PTB ≤ 34 weeks	3 (10.7%)	19 (4.5%)	0.361

PAPP-A: pregnancy associated plasma protein-A; FGR: fetal growth restriction; PE: preeclampsia; PTB: preterm birth; sPTB: spontaneous preterm birth.

a CL ≤ 37 mm was observed to be the most relevant value for prediction of sPTB in our population. The sensitivity and specificity of cervical length ≤ 37 mm to predict sPTB were 100% and 56.4%, respectively.

CONCLUSIONS

PAPP-A plasma value at first trimester is predictive of iatrogenic preterm delivery, IUGR e PE related, while it is not associated with sPTB. We confirmed that CL is the best predictive marker of sPTB. However, because of the low prevalence, it is not possible to extensively explore the role played by PAPP-A in sPTB according to the different pathogenetic phenotypes.

ABS 12

INSIGHTS ON THE USE OF EXTERNAL VENTRICULAR DEVICE IN THE TREATMENT OF POST-HAEMORRHAGIC VENTRICULAR DILATATION IN PRETERM INFANTS

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INTRODUCTION

Severe intraventricular haemorrhage (IVH) and subsequent post-haemorrhagic ventricular

dilatation (PHVD) are still among major causes of neurodevelopmental impairment in preterm infants. No consensus exists yet regarding the best treatment strategy for progressive PHVD and results from randomised trials are waited. In our centre, the external ventricular device (EVD) is placed as a first therapeutic option, substituted with permanent ventricular-peritoneal shunt (VPS) if the stabilization of the ventricular size is not achieved. The aim of our study was to analyse the relation between clinical and neuroradiological parameters and need for VPS in preterm infants with PHVD.

METHODS

Preterm infants admitted to our Neonatal Intensive Care Unit between January 2012 and February 2017 with post-natal IVH and consequent PHVD treated with EVD were retrospectively identified. Infants were then divided in two groups based on the need for VPS at discharge (shunt-free and shunt dependent). Clinical characteristics and brain MRI parameters (ventricular size and ADC value in 8 regions of interest) before and after EVD placement were analysed. Haemorrhage severity was estimated using IVH score (0 to 23 points), based on the volume of blood present in each ventricle and ventricular dilatation. Statistical analysis was performed using the Mann-Whitney and the X^2 test.

RESULTS

Study group consisted of 19 infants with mean gestational age of 28.3 ± 2.8 weeks and mean birth

weight of $1,230 \pm 529$ g. VPS was needed in 10/19 infants (52.6%). Infants in shunt-dependent group had significantly lower gestational age (26.70 ± 2.54 weeks vs 29.5 ± 2.55 weeks, $p = 0.038$) and birth weight ($1,022 \pm 518$ g vs $1,460 \pm 462$ g, $p = 0.041$). There was a trend for earlier EVD placement in shunt-free group, 15.7 ± 3.5 vs 26.1 ± 15.1 days after birth ($p = 0.065$). No difference was observed in CSF protein levels between two groups. Infection occurred in 2 cases (1 in each group). There was a trend to lower IVH score in shunt-free group at first MRI (17.5 vs 53.5 , $p = 0.074$), and a significantly bigger change in IVH score after EVD placement, adjusted for time (7 vs 43 , $p = 0.005$). We have observed significantly higher ADC values in the right and left frontal white matter on both MRI scans in the shunt-free group. No difference was observed in superficial and ventricular siderosis, synechiae and subarachnoid membranes distribution. Results are presented in **Tab. 1**.

CONCLUSIONS

Patients that became shunt-dependent had lower gestational age, lower weight at birth, higher IVH score and a lower capacity to remove the blood from the ventricles. A bigger delay in EVD placement seemed to be related to permanent shunt dependency. Increased white matter ADC values in infants with PHVD that became shunt-free may reflect an increase of the extracellular water. Further studies are needed in order to understand the meaning of this phenomenon.

Table 1 (ABS 12). Comparison of clinical data between shunt-free and shunt-dependent groups.

Parameters	Shunt-free	Shunt-dependent	p-value
Number of patients (%)	9 (47.4%)	10 (52.6%)	nd
GA (weeks), mean \pm SD	29.5 ± 2.5	26.7 ± 2.5	0.038
Birth weight (g), mean \pm SD	$1,460 \pm 463$	$1,022 \pm 518$	0.041
Apgar score 1', mean \pm SD	4.3 ± 3.0	4.3 ± 2.7	1.000
Apgar score 5', mean \pm SD	7.5 ± 1.5	7.1 ± 1.7	0.835
Development of IVH (days), mean \pm SD	4.5 ± 1.3	2.7 ± 1.2	0.052
Development of PHVD (days), mean \pm SD	10 ± 4.3	11.8 ± 6.6	0.621
Right Levene Index (mm), mean \pm SD	18.2 ± 1.1	16.2 ± 3.6	0.665
Right Levene Index (mm), mean \pm SD	17.4 ± 0.6	22.8 ± 13.4	0.660
EVD placement (days), mean \pm SD	15.7 ± 3.5	26.10 ± 15.1	0.065
CSF protein T0 (mg/dl), mean \pm SD	179.7 ± 116.3	152.8 ± 51.4	0.935
CSF protein pre-EVD removal (mg/dl), mean \pm SD	103.6 ± 41.2	81.56 ± 19.9	0.268
Delta CSF protein T0-pre EVD removal, mean \pm SD	-89.6 ± 124.6	-78.8 ± 57.3	0.923
EVD placed, duration (days), mean \pm SD	36.8 ± 8.4	54.0 ± 13.9	0.005
Infection (n, %)	1 (5.2%)	1 (5.2%)	nd
Mortality (n, %)	-	-	nd

IVH: intraventricular haemorrhage; PHVD: post-haemorrhagic ventricular dilatation; EVD: external ventricular device; CSF: cerebrospinal fluid.

ABS 13

ARE THE 2 YEAR GRIFFITHS SCORES OF BABIES WITH CEREBELLAR HAEMORRHAGE (CBH) AND INTRAVENTRICULAR HAEMORRHAGE (IVH) SIGNIFICANTLY DIFFERENT COMPARED TO THOSE OF BABIES SUFFERING FROM ISOLATED IVH?

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INTRODUCTION

Intraventricular haemorrhage (IVH) and cerebellar haemorrhage (CBH) are known pathologies affecting the developing brain of very premature infants (VPI). MRI is known to be superior in detecting all grades of these lesions, but little is known about the influence on neurological outcome of IVH and CBH diagnosed exclusively with MRI. In addition, influence of both lesions occurring together (frequent phenomenon) on neurological outcome, when compared to influence of isolated IVH, is still a matter of debate. The aim of our study is to investigate the potential adding value of CBH coexisting with IVH as an aggravating factor of the outcome in a cohort of VPI (< 32 weeks of gestational age).

PATIENTS AND METHODS

We revised data of VPI who underwent brain MRI on a 1.5 T system at term equivalent age and a complete neurological examination and Griffiths Mental Developmental Scales-Extended Revised (GMDS-ER) at 2 years of corrected age. Two groups were selected: the first consisted of VPI

with only IVH (any grade); the second consisted of VPI presenting IVH together with CBH (any grade). GMDS-ER were administered by a 10-year experienced single operator blinded to MRI results. Total developmental quotient (DQ) relates to global development, scale A assess gross motor skills, B – adaptive behaviour and social development, C – receptive/expressive language, D – fine motor functions, E – precursors of reasoning and planning. DQ above 85 was considered normal. T-student test was performed to compare mean values in IVH vs IVH + CBH groups.

RESULTS

Data about 173 very preterm infants were revised: 35/173 (20.2%) presented with isolated IVH (first group) and 22/173 (12.7%) with IVH + CBH association (second group). In the first group mean gestational age was 28 ± 0.4 and total DQ was 90.91 ± 2.7 (results are presented as mean \pm standard error). Patients with IVH + CBH association had a mean gestational age of 26 ± 0.3 weeks and total DQ of 84.27 ± 3.8 . Detailed results for total and subscale scores in two groups can be found in **Tab. 1**. Difference between two groups was present only as a trend for total DQ ($p = 0.149$), but have reached statistical significance for subscale A ($p < 0.05$). Mean gestational age was lower for babies with IVH + CBH association (28 ± 0.4) compared to those with IVH only ($p < 0.001$).

CONCLUSIONS

Presence of CBH in addition to IVH has ambiguous effects at 2 years. We cannot exclude further detrimental influence on longer outcome, as a significant reduction on scale A can conceal additional deficits. In fact, locomotor skills can be reliably distinguished from cognitive abilities only in older children, while at this stage scale A relates to mental energy and concentration as well. Our findings seem not to be independent from gestational age at birth.

Table 1 (ABS 13). Griffiths Mental Developmental Scales-Extended Revised (GMDS-ER) scores at 2 years of age.

GMDS-ER scores	IVH	IVH + CBH	p
Total DQ	90.91 \pm 2.70	84.27 \pm 3.80	0.149
A DQ Locomotor	88.63 \pm 2.97	78.32 \pm 3.21	0.038
B DQ Personal-social	90.21 \pm 2.58	83.59 \pm 3.89	0.155
C DQ Hearing and Language	84.46 \pm 2.90	78.18 \pm 4.09	0.166
D DQ Eye and Hand Coordination	97.06 \pm 3.21	91.27 \pm 3.24	0.301
E DQ Performance	93.37 \pm 3.16	86.54 \pm 4.77	0.195

Results are presented as mean \pm standard error.

GMDS-ER: Griffiths Mental Developmental Scales-Extended Revised; IVH: intraventricular haemorrhage; CBH: cerebellar haemorrhage; DQ: developmental quotient.

ABS 14**ARE PACKED RED BLOOD CELL TRANSFUSIONS (PRBCT) IN PRETERM INFANTS ASSOCIATED WITH IMPROVED GROWTH AND/OR FLUID RETENTION?**

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INTRODUCTION

Preterm infants often receive multiple packed red blood cell transfusions (PRBCT). PRBCT have been associated with increased weight gain, fluid retention, infections, electrolyte imbalances and other side effects. Object: the aim of this study is to investigate if PRBCT at our Institution are associated with increased weight gain and/or fluid retention.

METHODS

Retrospective evaluation of prospectively collected data in preterm infants (24^{0/7}-31^{6/7}), who received one or more PRBCT (volume 15 ml/kg ≤ 4 hours), at Salesi Children's Hospital between 2004.01.01 and 2017.12.31. We analyzed weight gain (WG), energy and protein intake before and after PRBCT (7 days before vs 7 days after and the day before vs the day after PRBCT). In addition we compared these data to a control group matched for birth weight and gestational age.

RESULTS

1,358 infants below 32 weeks were considered, 556 received one or more PRBCT. 140 were transfused between 21 and 90 days of life. Seven days WG was 15.8 g/kg/day (Q1 11.2-Q3 20.2) before and 15.4 g/kg/day (Q1 11.1-Q3 20.4) after PRBCT ($p = 0.709$). Seven days WG of the control infants was 16.1 g/kg/day (Q1 12.5-Q3 21.1) and 17.4 g/kg/day (Q1 13.3-Q3 21.0) before and after a "simulated day" which was set at the same postnatal age as the "case counterparts" ($p = 0.429$). Non-protein energy and protein intakes were not different before and after PRBCT in the transfused group and in controls. We also compared the actual weight the day before and the day after transfusion, the mean increase of the actual weight was 16.5 g/kg/day in the PRBCT group and 16.6 g/kg/day in controls; $p = 0.305$. 45 and 16 of 140 PRBCT patients received a second and a third transfusion, respectively. There were no significant effects of the most common diseases of

prematurity such as bronchopulmonary dysplasia and/or patent ductus arteriosus, on the above measures.

CONCLUSIONS

PRBCT in preterm infants were not associated with increased WG after the transfusion nor with fluid retention. WG of PRBCT infants was not different than controls. 15 ml/kg PRBCT was well tolerated, however a significant proportion of infants received a second transfusion. The strategy of a larger volume of PRBC transfusion should be explored in a RCT with the aim of reducing subsequent transfusions.

ABS 15**LOOKING FOR NEUROLOGICAL BIOMARKERS IN VLBW BABIES: BLOOD ADENOSINE LEVELS AND NEUROLOGICAL OUTCOME**

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INTRODUCTION

The increased oxygen availability soon after birth and the low antioxidant levels seem to favor inflammation and oxidative stress in premature infants. We previously showed high blood levels of adenosine in very low birth weight (VLBW) babies and even significantly higher levels in those developing MRI-diagnosed white matter lesions. The aim of this retrospective analysis was to further investigate the role of adenosine as a neurological biomarker, relating its blood levels in VLBW infants to neurological outcome at 12 and 24 months of corrected age.

METHODS

Thirty two VLBW babies admitted at birth to our department from February 2014 to January 2015 who performed metabolic screening at 15 ± 2 days of life were included in the study. Adenosine level was assessed by Mass Spectrometry using dried blood spots collected. As a part of clinical post-discharge follow-up, Griffiths Mental Developmental Scale

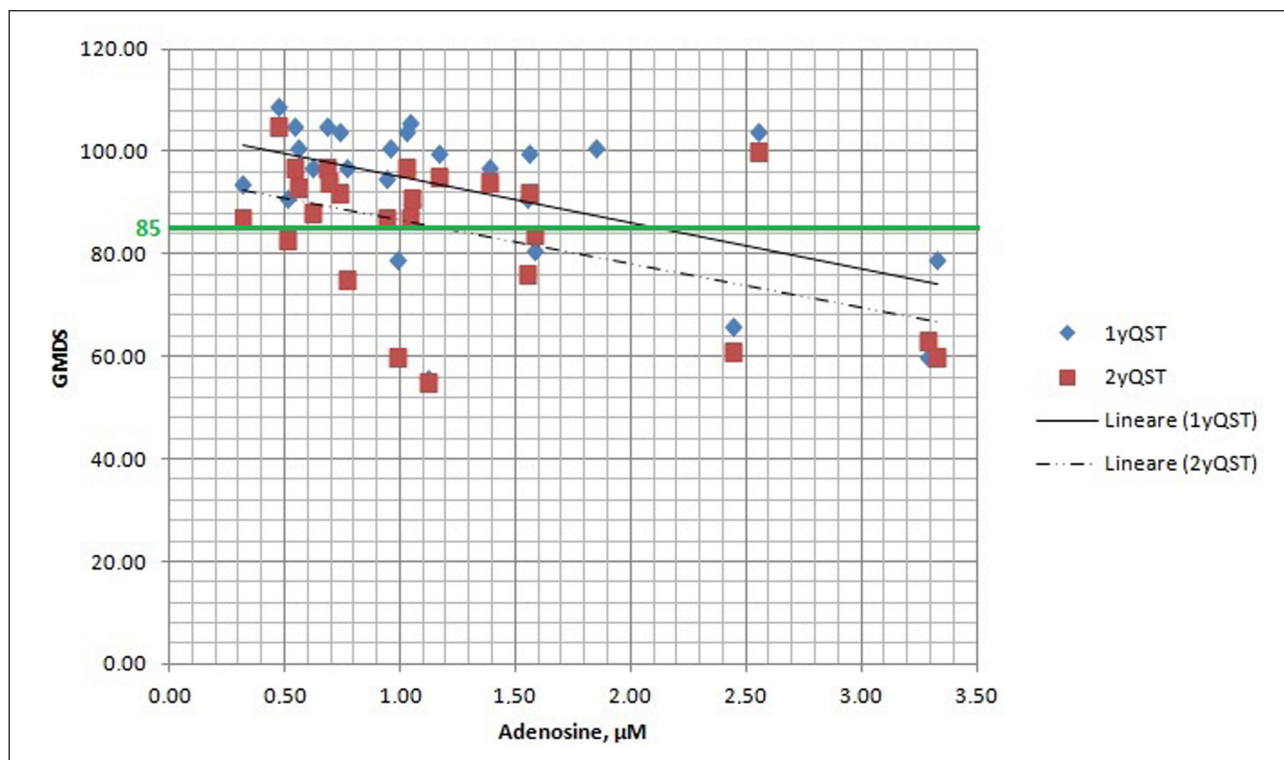


Figure 1 (ABS 15). Correlation between blood adenosine level at 15 days and Griffiths Mental Developmental Scale (GMDS) score at 12 and 24 months of corrected age.

(GMDS) was performed at 12 and 24 months of corrected age, and a linear relationship between adenosine values and Griffiths scores was evaluated.

RESULTS

Out of 32 enrolled patients, 27 completed GMDS at 12 months, and 25 at 24 months. The Pearson's correlation coefficient for adenosine/GMDS was of -0.52 at 12 months, and of -0.5 at 24 months. Taking in consideration infants with adenosine levels below 1 μM , only 1/13 patient presented abnormal GMDS score (< 85) at 12 months, and 3/12 patients at 24 months. Results are presented in **Fig. 1**.

CONCLUSIONS

The main finding of the present study is the medium strength linear association between higher adenosine levels at 15 days of life and a lower Griffiths score at 12 and 24 months of corrected age. Our results suggest that adenosine could be a promising early biomarker for neurological outcome in VLBW infants. Further prospective studies with higher number of babies and a longer duration of clinical follow-up are warranted.

ABS 16

PREDICTION OF PRETERM BIRTH IN MULTIPLE PREGNANCIES WITH SERIAL MEASUREMENTS OF CERVICAL LENGTH

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INTRODUCTION

The risk for preterm birth (PTB) in multiple pregnancies, defined as birth occurred before the 37th week of gestation, is dramatically higher than in singleton pregnancies (58% vs 11%). Preterm birth is strictly related with RDS, NEC, neonatal sepsis, cerebral palsy and neurological disorder in the newborn. The aim of our study is to identify women with multiple pregnancies at higher risk for PTB through serial measurements of cervical length (CL) in order to establish the right treatment and to improve neonatal outcome.

METHODS

The study was designed as a retrospective study in which 31 twin pregnancies were enrolled with following inclusion criteria: multiple gestation, two or more CL measurements and birth performed in our Department. The population enrolled in our study presented the following characteristics:

21 dichorionic and 10 monochorionic twin pregnancies; among these twin pregnancies, 30 were diamniotic and 1 monoamniotic; 16 spontaneous pregnancies and 15 obtained with assisted reproductive technologies. 8 women were primiparous (or more) and 23 were nulliparous. 17 of these patients had other risk factors related with pregnancy, 14 of them had no other risk factors. Every patient had serial CL measurements, and they were divided in four groups according to gestational age at ultrasound CL (20% and 25% CL had been considered in our study, and had been related with gestational age at delivery).

RESULTS

We found an inverse linear correlation between risk of PTB and $\Delta(\text{CL}) \geq 20\%$ at 28 weeks ($r = 0.14$). In case of $\Delta(\text{CL}) \geq 20\%$ the area under the curve (AUC) for PTB was 87.7%, in case of $\Delta(\text{CL}) \geq 25\%$ AUC for PTB was 89.4%. Our preliminary data confirm the association between PTB and a decrease in CL $\geq 20\%$ and 25% during subsequent ultrasound checks.

CONCLUSIONS

The presence of a $\Delta(\text{CL}) \geq 20\%$ and 25% has a good accuracy to predict PTB and its predictivity is higher than a single measurement of CL in multiple pregnancies.

ABS 17

PREGNANCY COMPLICATED BY GESTATIONAL DIABETES MELLITUS: IS PRETERM DELIVERY CORRELATED TO METFORMIN TREATMENT?

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INTRODUCTION

Gestational diabetes (GDM) is associated with an increased risk of adverse perinatal outcomes. Of interest, an increment rate of preterm delivery seems to be associated with metformin treatment, even if discordant results were reported in literature. The aim of our study is to evaluate if GDM treatment was associate to preterm delivery < 37 weeks.

METHODS

A retrospective study was conducted at MBBM Foundation, Milano Bicocca University, be-

tween 2009 and 2016. We included singleton pregnancies complicated by GDM (diagnosed according to NDDG guidelines until March 2010 and to IADPSG recommendations subsequently).

Exclusion criteria were multiple gestations.

In our institution, diet was the first line of therapy; if glycemic target was not achieved, metformin first, and, eventually, subsequently, insulin, were started.

We evaluated if pharmacological treatment was correlated to prematurity.

We also compared pregnancy and neonatal outcomes between preterm delivery (< 37 weeks) group and term delivery (≥ 37 weeks) one.

RESULTS

1,704 patients were included and divided according to gestational age at delivery: 1,560 women delivered at term (91.5%) and 144 delivered preterm (8.5%).

No differences in maternal characteristics were found (**Tab. 1**).

We reported similar rate of diet and metformin treatment between the two study groups (81 vs. 78%, 18 vs. 19%, respectively).

In preterm group, insulin use was more frequent compared to term one (1 vs. 4%).

Of interest in preterm delivery pregnancies, we found 8% of women in diet, 8.6% in metformin and 22.7% in insulin therapy.

In addition, preterm group presented a higher incidence of preeclampsia (PE), and premature preterm rupture of membranes (pPROM).

In both groups, vaginal delivery was most frequent, but in preterm group rate of cesarean section was significantly higher compared to term group.

Concerning neonatal outcomes in the preterm group there were a higher rate of Neonatal Intensive Care Unit admission, jaundice, hypoglycemia and respiratory distress syndrome. At a multivariate analysis, which considered, parity, ethnicity, GDM therapy, polyhydramnios, PE and pPROM, we found, as independent risk factors for preterm delivery, only PE and pPROM. Specifically, regarding GDM therapy, the insulin therapy resulted an independent risk factor for preterm delivery.

CONCLUSIONS

In our population, metformin therapy, similar to diet, was not associated to late prematurity; only a severe GDM requiring insulin therapy was related to a quadruplicate risk of preterm delivery.

Table 1 (ABS 17). Maternal, pregnancy, delivery and neonatal characteristics.

	Term delivery \geq 37 weeks (n = 1,560)	Preterm delivery < 37 weeks (n = 144)	p-value
GA at delivery (weeks; mean \pm SD)	39 \pm 1	34.4 \pm 2	
Maternal characteristics			
Ethnicity			
Caucasian	1,079 (69.2)	102 (70.8)	0.7
Non Caucasian	481 (30.8)	42 (29.2)	
Nulliparity	836 (53.6)	87 (60.4)	0.1
Maternal age (years)	33.7 \pm 5.2	33.6 \pm 5.5	0.9
Pregestational BMI (kg/m ²)	26.4 \pm 5.5	26.5 \pm 6.0	0.9
Pregnancy and delivery characteristics			
Hypothyroidism	207 (13.3)	16 (11.1)	0.5
Cholestasis	48 (3.1)	4 (2.8)	1.0
Polyhydramnios	255 (16.3)	13 (9.0)	0.02
Gestational hypertension	49 (3.1)	6 (4.2)	0.5
Preeclampsia	30 (1.9)	21 (14.6)	< 0.001
Preterm premature rupture of membranes	3 (0.2)	18 (12.5)	< 0.001
Oligohydramnios	27 (1.7)	2 (1.4)	1.0
Induction of labor	734 (47.1)	25 (17.4)	< 0.001
Mode of delivery			
Vaginal delivery	1,232 (79.0)	86 (59.7)	< 0.001
Cesarean section	328 (21.0)	58 (40.3)	< 0.001
Shoulder dystocia	4 (0.3)	-	NS
Neonatal outcomes			
Male	840 (53.8)	66 (45.8)	0.7
Large for gestational age	162 (10.4)	17 (11.8)	0.5
Small for gestational age	150 (9.6)	18 (12.5)	0.2
NICU admission	60 (3.8)	54 (37.5)	< 0.001
Jaundice	208 (13.3)	69 (47.9)	< 0.001
Hypoglycemia	17 (1.1)	23 (16.0)	< 0.001
Neonatal fractures	5 (0.3)	1 (0.7)	0.4
Respiratory distress syndrome	13 (0.8)	24 (16.7)	< 0.001
GDM therapy			
Diet (n = 1,369)	1,257 (80.6) ^a	112 (77.8) ^a	0.05
Metformin (n = 313)	286 (18.3) ^{a,b}	27 (18.8) ^{a,b}	
Insulin \pm Metformin (n = 22)	17 (1.1) ^b	5 (3.5) ^b	
		Preterm delivery	
Diet (n = 1,369)			112 (8.0)
Metformin (n = 313)			27 (8.6)
Insulin \pm metformin (n = 22)			5 (22.7)

Data are presented as number (%), and as mean \pm standard deviation.

GDM: gestational diabetes.

^{a,b}Bonferroni post hoc correction (each subscript letter denotes a subset of therapy category whose column proportion do not differ significantly).

ABS 18

MATERNAL HYPERTENSION AND SURVIVAL IN VERY PRETERM SINGLETONS AND TWINS: NOT JUST ONE ANSWER...

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INTRODUCTION

Studies examining the survival of very preterm infants born after maternal hypertension (MH) have yielded inconsistent results, in part due to differences in the analytic approach. We aimed to study how MH

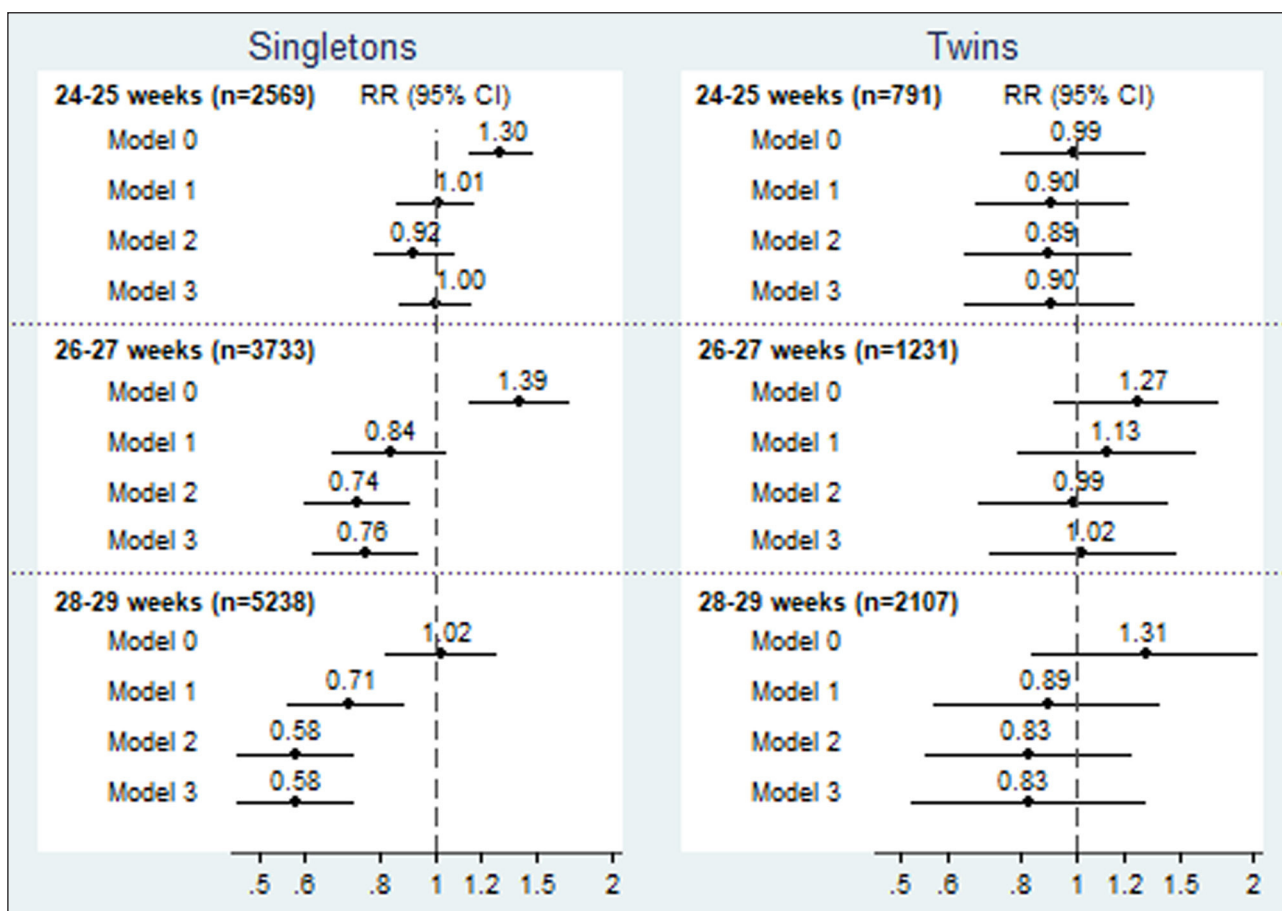


Figure 1 (ABS 18). Estimated relative risk and 95% confidence intervals of in-hospital death by maternal hypertension (MH), stratified by gestational age.

Model 0: no additional factor; model 1: + SGA; model 2: like model 1, but with birth weight (continuous, linear) instead of SGA; model 3: sex, antenatal steroids, inborn/outborn, race, mode of delivery (vaginal vs cesarean), and birth weight (continuous, linear). RR: risk ratios; SGA: small for gestational age.

is associated with mortality in very preterm singletons and twins, examining how including different predictors in the models influenced estimates.

METHODS

We fitted logistic regression models and estimated relative risks of in-hospital death in a cohort of 12,320 singletons (MH: 22.4%) and 4,381 twins (MH: 10.6%) born between 23 and 29 weeks in the Italian Neonatal Network (89 hospitals, 2008-2016).

RESULTS

Babies born following MH had comparatively higher gestational age at birth but were more frequently small for gestation (SGA). In unadjusted analyses, singletons and twins with MH had a 10-15% lower mortality than singletons without MH. Accounting for gestational age resulted in a reversal of the association; further inclusion of SGA yielded a null association in singletons, while twins had a higher mortality independently of MH. After stratifying by gestational age and twinning

(Fig. 1), singletons – but not twins – with MH had lower mortality from weeks 26-27 in models including size at birth (actual birth weight more than SGA). In all analyses, using birth weight instead of SGA yielded higher discriminatory power.

CONCLUSIONS

When predicting mortality after MH in very preterm infants, results depend on how gestational age and size at birth are accounted for. Although our findings cannot be interpreted causally, overall we saw evidence of a survival advantage associated with MH in singletons at higher gestational age, but not in twins. An effect modification by gestational age seems present in singletons. Using birth weight over SGA improves prediction.

ABS 19

CARDIOVASCULAR AND METABOLIC EFFECTS OF HYDROCORTISONE THERAPY

FOR BRONCHOPULMONARY DYSPLASIA IN PRETERM INFANTS

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INTRODUCTION

Hydrocortisone (HC) is used to facilitate the weaning from the ventilator of preterm infants at high risk of developing bronchopulmonary dysplasia (BPD). While most reports have focused on pulmonary benefits of HC treatment, data on cardiovascular and metabolic side effects are scanty. Aim: to assess the effects of HC therapy on blood pressure and plasma sodium concentration in preterm infants at high risk of developing BPD.

METHODS

Infants born between 24⁺⁰ and 31⁺⁶ weeks who received HC for BPD at Salesi Children's Hospital between 2004.01.01 and 2017.12.31 were studied. HC was administered at a starting dose of 5 mg/kg/d divided in 4 doses for 1 week and the dose tapered every 5 days. We retrospectively analyzed blood pressure (mean, systolic and diastolic) and sodium concentrations 7 days before vs 7 days after the start of HC. Statistical analyses was performed using paired t-test.

RESULTS

1,387 patients below 32 weeks were considered, 69 of the 1,387 received corticosteroid treatment for BPD and 44 were treated with HC. Blood pressure data were available for all study patients whereas sodium for 28 of them. Systolic, diastolic and mean blood pressure were statistically higher after HC (systolic, diastolic and mean blood pressure were 65 ± 7 vs 72 ± 6, 40 ± 4 vs 45 ± 4 and 50 ± 5 vs 56 ± 4 mmHg before and after HC, respectively; p = 0.000). Highest values were found after 5-day of HC treatment (mean: 48 ± 7; systolic: 74 ± 8; diastolic: 48 ± 7 mmHg). Sodium concentrations were increased after the start of HC compared to the 7 days before baseline values (135 ± 4 vs 137 ± 4 mEq/l; p = 0.008)

CONCLUSIONS

HC treatment in preterm infants at risk of developing BPD was associated with a statistically significant elevation of blood pressure and plasma sodium. The evaluation of other side effects of HC are in progress as well as the study of their predictors/associations.

ABS 20

DELIVERY AND NEONATAL OUTCOMES IN UNCOMPLICATED DICHORIONIC TWIN PREGNANCIES ACCORDING TO MODE OF CONCEPTION

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INTRODUCTION

Assisted reproductive technology (ART), including *in vitro* fertilization (IVF) with autologous oocyte (AO) or oocyte donation (OD), has been associated to increased odds of perinatal complications compared to spontaneous conception (SC) in singleton pregnancies. Whether this observation also applies to twin gestations is still unclear, mostly due to statistical limitations of previously published studies, such as limited sample size and lack of correction for confounding factors. The aim of our study was to compare delivery and neonatal outcomes of dichorionic twin pregnancies after IVF with AO, IVF with OD, and SC in a retrospective cohort of pregnant mothers with no pregestational disease or gestational complications.

METHODS

Observational retrospective study of twin pregnancies managed and delivered at our tertiary university maternal-fetal medicine center between 01/2010 and 07/2017. Inclusion criteria: dichorionic pregnancies without maternal pregestational disease and/or obstetric complications. Exclusion criteria: higher twin order, pregestational maternal disease (chronic hypertension, diabetes, other endocrine/autoimmune diseases), gestational complications (pregnancy induced hypertension, gestational diabetes), and monochorionic pregnancies. Assessed outcomes: gestational age at delivery, induction of labor, mode of and bleeding at delivery, birthweight, small for gestational age (SGA) neonate, umbilical gas analysis values, NICU admission, and composite neonatal outcome defined as at least one among the following: perinatal mortality, resuscitation ≥ 10 minutes, perinatal mortality, respiratory distress syndrome, intraventricular hemorrhage, bronchopulmonary dysplasia, leukomalacia, and retinopathy of prematurity.

RESULTS

During the study period, 18,153 women delivered at our department, 1,118 of whom were twin

gestations (6.2%). Final study population included 281 twin pregnancies and 558 newborns. There were 78 (27.8%) IVF with AO pregnancies, 21 (7.5%) IVF with OD pregnancies, and 182 (64.8%) SC pregnancies (**Tab. 1**). Four endouterine demises were diagnosed in ART group (AO and OD) whereas none was identified in SC group

($p = 0.02$). ART-pregnant mothers were more frequently nulliparous and older than SC women, with OD patients displaying the most advanced age among the 3 groups. OD group showed lower incidence of vaginal delivery and increased frequency of elective, pre-labor cesarean section than SC group. OD-twins had lower birthweight

Table 1 (ABS 20). Maternal, obstetric, delivery and neonatal characteristics.

	AO (n = 78)	OD (n = 21)	SC (n = 182)	p-value
Maternal characteristics				
Maternal age (years)	36.2 ± 3.9 ^a	43.2 ± 4.8 ^b	33.2 ± 5.0 ^c	< 0.001
Maternal age ≥ 40 years	6 (7.7) ^a	19 (90.5) ^b	13 (7.1) ^a	< 0.001
Nulliparity	53 (67.9) ^a	18 (85.7) ^a	91 (50.0) ^b	0.001
Pregestational weight (kg)	60.7 ± 10.4 ^a	61.9 ± 10.1 ^a	61.4 ± 11.2 ^a	1.0
Pregestational BMI (kg/m ²)	22.3 ± 3.7 ^a	23.0 ± 3.8 ^a	22.6 ± 4.1 ^a	1.0
Under-weighted woman	2 (2.6) ^a	0 ^a	14 (7.7) ^a	0.10
Over-weighted woman	4 (5.1) ^a	2 (9.5) ^a	20 (11.0) ^a	0.30
Obesity	3 (3.8) ^a	1 (4.8) ^a	8 (4.4) ^a	0.97
BMI at delivery (kg/m ²)	28.3 ± 3.8 ^a	28.6 ± 2.6 ^a	28.4 ± 4.0 ^a	1.0
Obstetric and delivery characteristics				
Fetal growth restriction	10 (12.8) ^a	4 (19.0) ^a	17 (9.3) ^a	0.33
Endouterine demise	3 (3.8) ^a	1 (4.8) ^a	0 ^b	0.02
Induction of labor	22 (28.2) ^a	1 (4.8) ^a	36 (19.8) ^a	0.05
Vaginal delivery after induction	14 (63.6)	1 (100)	31 (86.1)	
GA at delivery (weeks)	36.1 ± 3.0 ^a	35.2 ± 3.2 ^a	36.1 ± 3.1 ^a	0.23
Mode of delivery				
Vaginal delivery	26 (33.3) ^{a,b}	2 (9.5) ^b	89 (48.9) ^a	0.001
Elective cesarean section	27 (34.6) ^a	14 (66.7) ^b	57 (31.3) ^a	0.006
Emergent/urgent cesarean section	25 (32.1) ^a	5 (23.8) ^a	36 (19.8) ^a	0.10
Blood loss ≥ 1,500 ml	4 (5.1) ^a	2 (9.5) ^a	3 (1.6) ^a	0.08
Neonatal characteristics				
	AO twins (n = 153)	OD twins (n = 41)	SC twins (n = 364)	p-value
Gender (male)	75 (49.0) ^a	17 (41.5) ^a	196 (53.8) ^a	0.16
Birthweight (g)	2,324.7 ± 566.9 ^{a,b}	2,099.8 ± 565.7 ^a	2,333.1 ± 546.0 ^b	0.03
Small for gestational age	29 (19.0) ^a	10 (24.4) ^a	57 (15.7) ^a	0.36
pH ≤ 7.00	1 (0.7) ^a	0 ^a	1 (0.3) ^a	0.75
BE ≤ -12	2 (1.3) ^a	0 ^a	4 (1.1) ^a	0.78
NICU admission	32 (20.9) ^{a,b}	14 (34.1) ^b	59 (16.2) ^a	0.02
Fetal malformation	3 (2.0) ^a	1 (2.4) ^a	11 (3.0) ^a	0.78
Neonatal hypoglycemia	17 (11.1) ^a	4 (9.8) ^a	25 (6.9) ^a	0.25
Neonatal anemia	8 (5.2) ^a	3 (7.3) ^a	12 (3.3) ^a	0.36
Jaundice	32 (20.9) ^a	13 (31.7) ^a	68 (18.7) ^a	0.18
Adverse composite neonatal outcome ^e	20 (13.1) ^a	6 (14.6) ^a	47 (12.9) ^a	0.97

Data are presented as number (%).

AO: autologous oocyte; OD: oocyte donation; SC: spontaneous conception.

Chi-square and One-Way ANOVA with Bonferroni's post-hoc analysis to adjust for multiple comparison (shown as ^{a, b, c}).

^aDefined as blood loss ≥ 500 ml in case of vaginal delivery, and ≥ 1,000 ml in case of cesarean section.

^eDefined as at least one among perinatal mortality, resuscitation ≥ 10 minutes, respiratory distress syndrome, intraventricular hemorrhage, bronchopulmonary dysplasia, leukomalacia, retinopathy of prematurity.

and were more likely to be admitted to the NICU compared to SC twins. Yet, no differences were identified in gestational age at delivery, incidence of SGA, or likelihood of adverse composite neonatal outcome.

CONCLUSIONS

In uncomplicated dichorionic twin pregnancies, ART appears to be associated with advanced maternal age, nulliparity, and increased odds of intrauterine demise and pre-labor cesarean section compared to SC.

ABS 21

ROLE OF GROUP B STREPTOCOCCUS ON PERINATAL OUTCOME IN PREGNANCY COMPLICATED BY PRETERM DELIVERY < 34 WEEKS

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INTRODUCTION

Group B Streptococcus (GBS) is the leading infectious cause of neonatal morbidity and mortality in high-income countries and the most common pathogen isolated from maternal and fetal tissues in midgestation spontaneous abortions. Whether GBS presence in the genitourinary tract of pregnant mothers also plays an etiological role in spontaneous

preterm delivery (sPTD) is less certain, although recently published preclinical and clinical data suggest so. The aim of our study was to assess the incidence of adverse perinatal outcomes according to GBS status in a cohort of pregnancies with sPTD < 34 weeks of gestation.

MATERIAL AND METHODS

Observational retrospective analysis of all sPTD < 34 weeks of gestation occurred at our tertiary university maternal-fetal medicine center (FMBBM, University of Milan-Bicocca) from January 2006 to December 2015. Patients with iatrogenic PTD (iPTD) were excluded from the analyses. Cervico-vaginal swabs, vagino-rectal swab for GBS, and urine culture were performed in all patients at hospital admission according to our institutional protocol. Antibiotic therapy was administered in case of pPROM or if delivery was deemed to be imminent. Assessed gestational and perinatal outcomes were mean birth weight and birth weight < 1,500 grams, mean pH, Apgar score at 5 minutes < 5, neonatal death.

RESULTS

During the study period, January 2006-December 2015, 615 deliveries < 34 weeks of gestation occurred at our Hospital. Final analysis was performed on 180 (29.3%) cases of sPTD. GBS infection was identified in 21% (38/180) of patients. Women with evidence of GBS infection were less likely to experience pPROM and more frequently delivered neonates with smaller birth weight at lower gestational ages (**Tab. 1**). In addition, GBS-positive patients showed higher

Table 1 (ABS 21). Obstetrical and perinatal characteristics in the GBS-positive patients and in controls.

	GBS + n = 38	GBS - n = 142	p-value
pPROM	16 (44.7%)	89 (63%)	0.03
Mean GA at pPROM (weeks)	26.5 ± 5.4	26.5 ± 4.7	1
Mean latency (days)	20.1 ± 26.2	20.2 ± 26.3	1
Latency > 7 days	7/16 (43.7%)	50/89 (56.2%)	0.36
Abruptio placentae	3 (8%)	12 (8%)	1
Fetal heart trace abnormalities	2 (5%)	25 (17.6%)	0.06
Mean GA at delivery	27.6 ± 3.1	29.1 ± 2.7	0.005
Mean birthweight	1,145 ± 478	1,348 ± 460	0.02
Birthweight < 1,500 grams	32 (84%)	85 (60%)	0.01
Mean pH	7.30 ± 0.8	7.30 ± 0.9	0.94
Apgar at 5' < 7	10 (26.3%)	38 (26.7%)	1
Clinical chorionamnionitis	2 (5%)	15	0.53
Histological chorionamnionitis	27 (67.5%)	70 (44%)	0.01
Histological villous alteration	9 (22.5%)	12 (7.5%)	0.02
Neonatal death	5 (13%)	17 (12%)	1

GBS: *Group B Streptococcus*.

incidence of histological chorioamnionitis and placental villi abnormalities, although frequency of antibiotic treatment did not differ from GBS-negative women. We did not identify any difference between the 2 groups for incidence of neonatal death.

CONCLUSIONS

In patients with sPTD < 34 weeks of gestation, GBS infection correlates with lower gestational age at

delivery, smaller birth weight, higher incidence of histological chorioamnionitis and villous alterations. On the other side it is not directly correlated with the incidence of pPROM. We may suppose a direct association between GBS infection and placental alterations leading to preterm labour, with or without intact membranes; but further studies on specific GBS-related lesions of the placenta will be performed.