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LONGITUDINAL CHANGES OF BONE ULTRASOUND MEASUREMENTS IN HEALTHY PRE-SCHOOL CHILDREN: MATERNAL AND CHILD DETERMINANTS

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1. INTRODUCTION

Childhood is a critical period for bone development and the attainment of maximum bone mass, which largely determines the risk for osteoporosis. The aim of our study was to follow the longitudinal changes of bone mineral density (BMD) in healthy children up to 7 years of age and to identify key determinants of bone development during this period.

2. METHODS

The prospective cohort study followed 146 mother-child pairs up to the age of 7 years. Women's data (health status, anthropometry, QUS measurements, dietary assessment, vitamin D (VD) and adiponectin concentrations) were collected during the pregnancy to one year postpartum. The fatty acids composition of human milk was analysed. The children's data (health status, anthropometry, QUS measurements, and dietary assessment) were collected at birth, 1, 3, 12 months and 7 years of age. A speed of sound (SOS) value was used as an indicator of BMD determined by QUS. Chi-square tests, t-tests and Bonferroni adjustment were used for statistical comparisons between the groups.

3. RESULTS

Individuals with non-optimal BMD were detected among healthy preschool children. The longitudinal alterations in bone QUS measurements showed a decline in bone SOS values from birth to 3 months of age, followed by an upward trajectory until the age of 7. This decline was more pronounced in children with low bone SOS values at birth ($p < 0.01$). Maternal VD ($p < 0.01$) and thyroid gland dysfunction ($p < 0.05$) were associated with lower child's SOS values at birth, and the child's body mass index (BMI) was associated with SOS values throughout the pre-school years ($p < 0.01$ - $p < 0.04$). No association was found between offspring's BMD and maternal anthropometric, lifestyle and demographic characteristics, human milk fatty acids composition, or child's nutritional intake (all $p > 0.05$).

5. CONCLUSION

Longitudinal alterations of bone SOS values from birth till 7 years of age with transient physiological decline were detected by QUS. The risk factors for impaired bone health are maternal VD deficiency, thyroid gland dysfunction, and child's BMI. If there are individuals with low BMD in



healthy population, and the absence of other identified risk factors affecting bone development, genetic traits may be considered.

None declared.

		CHILDREN'S BONE MINERAL DENSITY SOS-VALUE				
		AT BIRTH (N=75)	AT 1 MONTH (N=141)	AT 3 MONTHS (N=141)	AT 12 MONTHS (N=146)	AT 7 YEARS (N=89)
MATERNAL HEALTH INDICATORS	Maternal age (years)	0.97	0.15	0.50	0.006	0.57
	Blood serum vitamin D	p<0.01	0.32	0.04	0.84	0.36
	Adiponectin plasma (µg/ml)	0.32	0.34	0.51	0.73	0.63
	BMI before pregnancy	0.38	0.27	0.61	0.59	0.36
	Body fat percentage at pregnancy	0.78	0.26		0.14	0.43
	Gestation mass gain (kg)	0.54	0.33	0.94	0.93	0.46
	BQUS SOS (m/s)	0.48	0.30	0.91	0.57	0.37
	Maternal Education level	0.72	0.06	0.70	0.65	0.25
	Residential environment : urban/rural	1.0	0.39	0.10	0.34	0.47
	Thyroid gland dysfunction	p<0.05	0.65	0.10	0.59	1.0
	Gestational diabetes	0.87	0.71	p<0.01	1.0	0.2
	Energy intake (kcal)	0.88	0.29	0.90	0.73	0.08
	Smoking during pregnancy	1.0	1.0	1.0	0.28	1.0
CHILD'S HEALTH INDICATORS	Body mass for age (Z-score)	0.46				0.05
	BMI for age (Z-score)	0.13	0.04	0.01	0.02	0.04
	Breastfeeding duration in total		0.99	0.45	0.30	0.75



	Consuming vitamin D at the age of 7 years					0.76
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Table 1

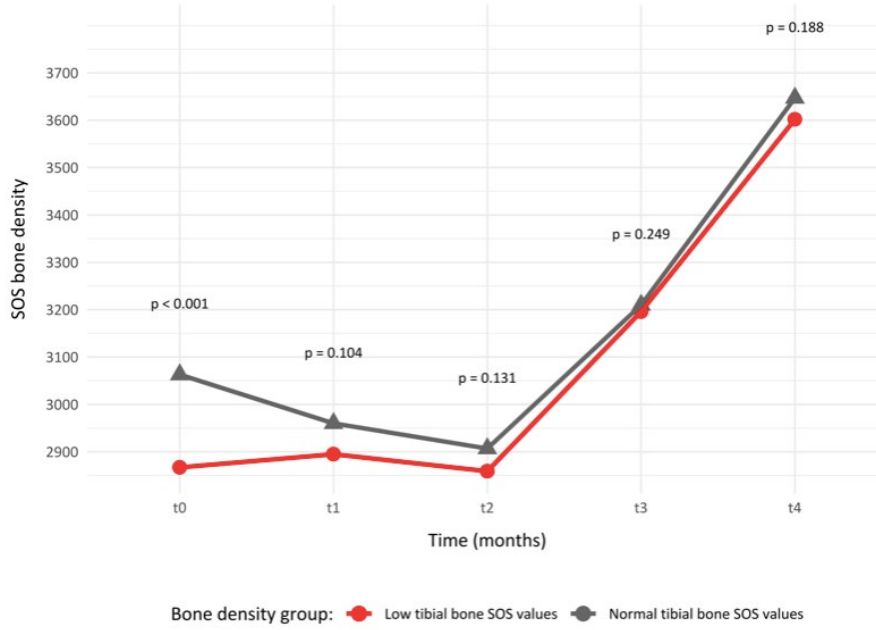


Figure 1



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EVALUATION OF NEONATES SCREENED FOR RETINOPATHY OF PREMATURITY IN THE NEONATAL INTENSIVE CARE UNIT

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INTRODUCTION: The objective of studies evaluating screening criteria for retinopathy of prematurity (ROP) is to reduce the number of infants requiring screening while ensuring that those with retinopathy receive treatment. This study evaluates the need for screening infants aged ≤ 32 -34 weeks and assesses the potential risks of the screening program.

MATERIAL AND METHODS: From 2017 to 2021, the records of 425 infants who underwent ROP screening were reviewed. The risk factors and ROP examination results were recorded. Infants were grouped based on ROP and treatment characteristics. The factors associated with ROP were evaluated. Multivariate logistic regression analysis was performed to identify the associated factors.

RESULTS: The study included cases with a mean gestational week of 30.71 ± 2.54 , and 246 (58%) of which were male. The frequency of PDA was 28%. Ninety infants out of 425 infants (21.2%) had any stage of ROP (group 2), while 335 infants (78.8%) did not have ROP (group 1). Among 10 patients who underwent ROP screening, all (2.3%) were treated with laser photocoagulation, and only one patient (0.2%) required vitrectomy. All patients who needed ROP treatment had a gestational age of < 30 weeks. The multivariate logistic regression analysis revealed that birth weight (BW), patent ductus arteriosus (PDA), and invasive mechanical ventilation (IMV) were independent risk factors for ROP [OR: 7.291 (95%CI:2.807-18.941), 2.619 (95%CI:1.080-6.353), and 3.891(95%CI:1.524-9.936), respectively). In the multivariate logistic regression analysis of infants with ≤ 32 weeks' gestation, BW, preterm rupture of membranes (PROM), and IMV were identified as independent risk factors for ROP (OR: 7.727 (95%CI:1.864-32.030), 6.039 (95%CI: 1.240-29.401), and 7.757 (95%CI: 2.678-22.471), respectively).

CONCLUSIONS: The incidence of ROP and the rate of ROP treatment in our unit were lower in the last five years (2017-2021) compared to previous years. Screening infants below 34 weeks gestational age or 1700 g BW does not result in missing any patients with any stage ROP. However, in our unit, it does not provide any additional benefit in terms of severe ROP. When screening older preterm infants for ROP, it is important to consider the presence of PDA, PROM, and IMV.

None declared.

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INVESTIGATING THE AWARENESS ABOUT THE LONG-TERM RESPIRATORY RISKS OF PREMATURE BIRTH AMONG PRETERM-BORN INDIVIDUALS WITH CHRONIC LUNG DISEASES: THE EMPOWER SURVEY PROTOCOL

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INTRODUCTION: Premature birth increases the risk of chronic respiratory disorders later in life, including asthma and chronic obstructive pulmonary disease (COPD). Whether preterm-born individuals consider early life events during their respiratory healthcare journey is unknown. The EMPOWER study (patiEnt journey of preterm born PeOple With rEspiRatory dysfunctions) aimed to investigate the level of awareness of former preterm-born individuals suffering from chronic respiratory diseases regarding the long-term respiratory risks associated with premature birth.

MATERIAL AND METHODS: The EMPOWER study consisted of a 34-item online questionnaire distributed to adult preterm-born individuals from France, Spain, Germany, the UK and the US. The questionnaire is divided into three sections: A) Screening (5 items), B) Sociodemographic and Medical Profile and Preterm Awareness (24 items), and C) Patient Care Journey (5 items). The EMPOWER study questionnaire has been co-developed with 2 patient experts and with the support of the European Foundation for the Care of Newborn Infants (EFCNI) and Adult Premies.

RESULTS: The EMPOWER questionnaire was approved by the Institutional Review Board (IRB) on February 20, 2024, and the study subsequently started on March 5. The EMPOWER study targets recruiting at least 300 former preterm-born adults (135 with asthma, 135 with COPD and 30 with asthma and COPD), homogeneously distributed in each country. The results will be available by September 2024 and will be combined with those from the preceding PRE-TELL survey (PREmatures Towards Effective Lifelong Lung Care), which investigated the awareness of the medical community (neonatologists, paediatricians, allergologists and pneumologists) on the same topic. PRE-TELL found the need to address awareness gaps on the long-term respiratory risks of prematurity and to develop evidence-based guidelines for the follow-up of premature babies.

CONCLUSIONS: The EMPOWER study will help evaluate the impact of preterm status on chronic respiratory disease management and quality of life, providing insights into how healthcare professionals consider preterm status along the patient journey. The EMPOWER study and the PRE-TELL survey will provide a full picture of the different stakeholders' awareness regarding the respiratory risks associated with premature birth.

- The first 4 authors (Bianco, Costa, Ispas, Meshchenkova) are employees of Chiesi Farmaceutici S.p.A.



- Authors from 6 to 9 (Dalton, Ingledow, Lee, Quaglia) have collaborated as patient experts with Chiesi Farmaceutici for the development of the questionnaire and received a fee for this collaboration.



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WHAT DOES AFFECT THE DEVELOPMENTAL STATUS OF PRETERM INFANTS?

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INTRODUCTION

The role of stress as a modifier of brain development in preterm neonates is being discussed. Therefore, the aim of this research was to study the relationship between the stress experienced by preterm infants in the NICU and developmental status in the follow up, and to establish factors, associated with their neurodevelopment.

MATERIAL AND METHODS

The first stage of research involved measuring stress markers (cortisol, melatonin) in infants (n=56) during their NICU stay; the second phase assessed the developmental status at the corrected age of 24-30 months.

RESULTS

Melatonin level was positively correlated with the total ASQ-3 scores ($r=0.31$; $p=0.026$), communication ($r=0.36$; $p=0.009$), problem solving ($r=0.30$; $p=0.033$) and personal-social skills ($r=0.32$; $p=0.022$). Cortisol was negatively correlated with ASQ-3 communication ($r=-0.31$; $p=0.043$) and personal-social scores ($r=-0.35$; $p=0.022$).

The ROC-curve analysis revealed that a decrease of melatonin below 3.44 ng/ml and 3.71 ng/ml during the neonatal period can predict communication and problem-solving disorders respectively. An increase in cortisol above 0.64 mcg/dl is predictive in personal-social disorders.

Negative correlation was identified between the NICU and total hospital stay duration and ASQ-3 communication scores in the follow-up ($r=-0.27$; $p=0.049$ and $r=-0.41$; $p=0.002$, respectively). The duration of mechanical ventilation was negatively correlated with gross motor scores ($r=-0.46$; $p=0.043$). Apgar scores were positively correlated with ASQ-3 communication ($r=0.29$; $p=0.032$) and personal-social scores ($r=0.28$; $p=0.034$); maternal age – with ASQ-3 total ($r=0.29$; $p=0.034$), communication ($r=0.37$; $p=0.006$), and personal-social scores ($r=0.29$; $p=0.041$). Positive correlations were observed between gestational age and communication scores ($r=0.28$; $p=0.033$).

Infants who suffered neonatal sepsis had significantly often disorders of communication ($p=0.014$) and gross motor skills ($p=0.016$). Children who required mechanical ventilation were more likely to have communication disorders ($p=0.034$).

CONCLUSION

Neonatal stress was associated with developmental disorders in preterm infants at the corrected age of 24-30 months. This evidence was supported by correlations between the cortisol and melatonin levels determined in the neonatal period with communication, problem-solving and personal-social



development in the follow up. Factors as gestational age, duration of hospital and NICU stay, mechanical ventilation, neonatal sepsis were associated with more frequent disorders in communication, gross motor, and problems-solving skills.

The authors declare that they have no conflict of interest.



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THE NEONATOLOGICAL ASPECT OF CONGENITAL CYTOMEGALOVIRUS INFECTION

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Timing for diagnosis of CMV is one of the most important factors as positive CMV at birth or during the first 2 weeks of age reveals prenatal infection of the baby. It is detected by direct isolation of the virus in urine or saliva using electronic microscopy and it is the quickest and most reliable method for early verification of this infection. The diagnosis can be confirmed by the PCR method, as well.

To recognize congenital CMV without previous information about the mother's infection is very difficult but yet possible for experienced clinical neonatologists.

THE AIM of the study was to find out what are the most frequent clinical signs that were recognized at the ..first clinical assessment in children later diagnosed as congenital CMV infection.

MATERIALS AND METHODS It is a clinical study held at neonatal department of the Institute for Childrens and Youth Health care of Vojvodina in Novi Sad, Serbia over the course of 10 years.

CLINICAL CASES OR SUMMARY RESULTS There were 27 neonates with congenital CMV infection , meaning less than 19% of all hospitalised term newborn. All of them had been diagnosed after delivery. Clinical signs are very discrete. The most important signs are paleness or jaundice of the skin, rash, reduced fat tissue, reduced birth weight and length, microcephaly, hepatomegalia, poor feeding, hypotonia, lack of spontaneous motility, lethargic behaviour .The main reason for serological and PCR testing were- jaundice, reduced fat tissue, poor gaining in weight and pathological neurological neonatal assessment. The most characteristic signs were - small for Gestational age in 100 %, neonatal jaundice (88,88%) and hypotonia (85,18%). The leading clinical problem that induces their hospitalisation was poor feeding and poor gaining in weight (74,07%).

CONCLUSIONS It is of great importance to recognize discrete signs of illness as they can lead to proper DD and if congenital CMV is diagnosed, then a modern therapeutic approach and follow up together with neurostimulative treatment can prevent serious neurological problems and impair development.

KEY WORDS Cytomegalovirus, follow up, infection, neonatal



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Antenatal Steroids and Influence of Sex on Neurodevelopmental Outcomes of Late Preterm Infants

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Introduction: In recent years, ANS treatment is recommended for pregnant women who are at risk of delivery in the late preterm period. However, the influence of ANS on long-term neurodevelopmental outcomes is not yet fully elucidated. In this study, we aimed to evaluate the effect of ANS on neurodevelopmental outcomes at 18 months corrected age and to analyse possible influence of sex on outcome.

Material and Methods: Late preterm infants born between January 2019 and December 2020 were recruited from the delivery room records. These infants were divided into two groups as ANS (+): received antenatal betamethasone at 34 weeks' gestation or later and ANS (-) : received no antenatal betamethasone. A total of 152 infants, 82 (47 male, 35 female) in the ANS (+) group and 70 (41 male, 29 female) infants in the ANS (-) group, were included in this study.

Neurodevelopmental assessment was performed using the Bayley III developmental test at corrected age of 12-24 months. Developmental delay was defined as a Bayley score of less than 85. Outcomes were compared between groups by using logistic and linear regression, adjusted for social risk.



Results: The rate of developmental delay was similar between the groups in cognitive, language and motor domains. There was no significant difference between the groups in cognitive ($p=0,511$), language ($p=0,308$) and motor ($p=0,101$) domain scores.

Among those who received ANS, male infants had a tendency to worse developmental outcomes, with adjusted composite score mean differences of -6.7 (95%CI, -12.4 to -1.0) for cognitive development, -7.9 (95%CI, -15.1 to -0.6) for language development, and $-6,8$ (95%CI, -13.4 to 0.1) for motor development, compared with female sex. Among those who did not receive ANS, there was no significant association between sex and Bayley scores.

Conclusion: Our findings suggest that male sex is a risk factor for worse neurodevelopmental outcomes at corrected age of 12-24 months after ANS treatment in late preterm period. These results can be attributed to the different neurological and systemic effects of steroids according to gestational age and sex. Multicenter studies with larger groups should be conducted on its long-term neurodevelopmental effects.

None declared