

Selected Lectures of the 21st International Workshop on Neonatology and Pediatrics

EVOLUTION AND REVOLUTION IN NEONATOLOGY AND PEDIATRICS

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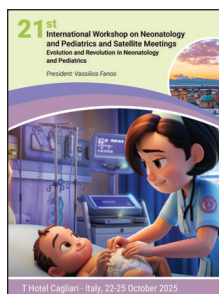
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LECT 1

OBESITY, GESTATIONAL DIABETES AND NEONATAL OUTCOME

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The pandemic of diabetes is increasing in developed countries, and it is definitely associated with a negative impact on reproduction and fertility. Obesity and gestational diabetes mellitus (GDM) drive most of the complications in perinatology. Epidemiology now certifies that preterm birth, GDM, preeclampsia and large for gestational age (LGA) babies are 2-5 fold increased in obese vs normal weight mothers [1]. Gestational weight gain (GWG) outside the appropriate ranges is a further factor increasing adverse perinatal outcomes [2]. Although pre-conceptional interventions are advisable (though difficult to implement), lifestyle intervention (LI) programs early in pregnancy are more suitable to be implemented and have been demonstrated to be able to reduce some of the above-described complications [3]. However, LI efficacy is closely related to adherence. We thus evaluate maternal metabolic changes in the third trimester in obese women receiving LI. Through a metabolomic approach, we find that the up-regulation of a set of maternal metabolites, mainly linked to oxidative stress and Krebs' cycle, predicts the birth of an LGA baby in such women, irrespective of BMI, GWG, GDM and central fat deposition.

Another nutritional approach to contain obesity-related complications could be done by using inositols (Ins), a family of endogenous insulin-sensitizing compounds. We previously reported that inositol triphosphate receptor-1 was up-regulated in the placenta of obese pregnant women, which also showed a depletion of Ins content. In a randomized controlled trial carried out in obese mothers, the supplementation of

myo-inositol reduced the risk of GDM by 70%, concomitantly decreasing preterm births and macrosomic babies [4].

Finally, apart from pregnancy complications and their management, the development of an appropriately grown fetus remains challenging to achieve in obese mothers, solely relying on LIs. Even metabolomic studies could help to address a better dietary approach; however, supplementation with metabolically active substances like Ins is currently more effective. Anyway, it is of paramount importance to challenge obesity and excessive GWG also through a healthy lifestyle, to support both maternal and neonatal well-being.

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LECT 2

ASSISTED REPRODUCTIVE TECHNOLOGIES (ART): A NEW PLAYER IN THE FETAL PROGRAMMING OF CHILDHOOD AND ADULT DISEASES?

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According to the theory of fetal programming of adult diseases proposed by David J.P. Barker, the analysis of the early phases of embryonic and fetal development represents a fundamental tool for risk stratification of newborns, allowing the identification of subjects who are susceptible or resistant to multiple diseases presenting later in life.

In this context, assisted reproductive technology (ART) represents a new entity to be analyzed accurately, to clarify its possible role in Barker's hypothesis. ART is an emerging field in medicine, which could play a key role in shaping a more sustainable future for humanity, halting declining fertility rates in many countries of the Western world. The recent introduction of artificial intelligence (AI)-driven models into ART allowed the development of more tailored and efficient treatment options, favoring the inclusion of ART into the essential levels of assistance in Italy since December 2024. On the other hand, ART procedures have been associated with possible consequences for mothers and newborns. ART procedures are not entirely risk-free: they have been associated with adverse outcomes that may occur in the perinatal period or even in childhood and adulthood. Here we will discuss the most recent data on the possible association between ART and cardiovascular, musculoskeletal, urogenital and other rarer congenital disabilities. Furthermore, the risk of developing neuropsychiatric sequelae later in life is discussed. In particular, the possible association between ART and the risk of autism spectrum disorders in childhood is analyzed.

All these data taken together, ART appears as a new player in the fascinating Barker's hypothesis, which is proving its value in multiple fields of medicine, particularly in neonatology, giving neonatologists a significant role in the prevention of various diseases of adulthood.

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LECT 3

PREVENTION OF RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION: STATE OF THE ART

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Respiratory syncytial virus (RSV) remains one of the leading causes of acute lower respiratory tract infections in infants and young children. Its clinical burden is especially significant among preterm newborns and in children with chronic lung disease, congenital heart disease, or immune deficiencies. Globally, RSV is estimated to cause more than 3 million hospital admissions and about 100,000 deaths every year in children under 5, with the highest toll observed in low- and middle-income countries [1].

For many years, preventive options were scarce. Palivizumab, a monoclonal antibody directed against the RSV F protein, represented the only available licensed strategy. However, its monthly dosing schedule and high cost restricted its use to selected high-risk infants.

A significant step forward has been achieved with the introduction of nirsevimab, a long-acting monoclonal antibody. A single intramuscular dose can protect for at least 5 months, effectively covering an entire RSV season. Clinical trials have shown that nirsevimab markedly reduces RSV-related hospitalizations in both preterm and term infants, with a very favorable safety profile [2]. Several countries are now adopting universal or targeted immunization programs with this antibody, and the first real-world data are confirming its effectiveness outside clinical trials.

Progress has also been made in maternal immunization. A recombinant prefusion F protein vaccine, administered during pregnancy, has been shown to induce transplacental antibodies that protect infants in the first 6 months of life, significantly reducing RSV-associated hospitalizations [3]. This approach complements existing maternal vaccination programs, such as those for pertussis and influenza, and provides early protection during the most vulnerable period of infancy.

The current landscape of RSV prevention now combines two complementary strategies: direct infant protection through monoclonal antibodies and early-life protection through maternal vaccination. Optimal implementation requires careful consideration of local epidemiology, cost-effectiveness, and healthcare system capacities. Equity of access remains a key issue, since the heaviest disease burden is concentrated in resource-limited settings.

In conclusion, RSV prevention has entered a new era. With long-acting monoclonal antibodies and maternal vaccines now available, pediatrics finally has practical tools to reduce the global impact of

RSV infection substantially. The challenge ahead will be to ensure timely, widespread, and equitable access to these interventions, thereby reshaping the management of a disease that has threatened child health for decades.

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LECT 4

THE NEONATAL NEPHROLOGY STUDY GROUP (GSNN) OF THE ITALIAN SOCIETY OF NEONATOLOGY (SIN): 40 YEARS OF ACTIVITY (1986-2025)

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INTRODUCTION

Improvements in prenatal, neonatal, and pediatric care have led to increased survival rates, even for newborns with significant problems, many of which involve the nephrourological system, but also the function of other vital systems and organs. The spread of imaging in general, and ultrasound in particular, in pre- and postnatal studies has significantly changed the diagnostic potential for many neonatal and pediatric diseases, which have been recognized as having a significant effect on adulthood as well. The timeliness and accuracy of diagnosis are an essential basis for the effectiveness of therapy in a wide range of diseases.

AIM

To critically evaluate the research and training activities carried out by the Neonatal Nephrology Study Group (*Gruppo di Studio di Nefrologia Neonatale* – GSNN) of the Italian Society of Neonatology (*Società Italiana di Neonatologia* – SIN) since its foundation and to obtain recommendations for improving the effectiveness of care for children with nephrourological problems.

METHODS

Publications (conference proceedings and journal articles) relating to the activities of the GSNN since its creation (February 1986) – aimed at developing diagnostic and therapeutic protocols on topics of nephrourological pathology – were consulted, evaluating their usefulness also for the prevention of renal diseases.

RESULTS

The authors were able to demonstrate the effectiveness of data obtained through the following investigations carried out over the years by the GSNN:

1. urinary tract infections (UTI) in newborns (IPIVUN investigation), in collaboration with the Neonatology Centers of Lazio (1986-1987);
2. expansion of the IPIVUN investigation at the national level in collaboration with 65 Italian neonatal centers (1988-1989); 2,400 full-term and preterm newborns were studied, considered “at risk” for UTI according to anamnestic, clinical, and laboratory criteria: 428 newborns, 248 males and 180 females, 248 full-term and 180 preterm, were found to be affected by UTI;

3. since 1989, the Multicenter Survey on Polythelia and Malformative Uropathies in Newborns has demonstrated a significant frequency of malformative pathologies affecting various organs and systems, most notably in subjects in whom accessory glandular tissue was found in the supernumerary mammary areola;
4. between 1990 and 1992, a multicenter study was conducted on what at the time was known as acute renal failure (ARF) – later known as acute kidney injury (AKI) – in newborns, which confirmed, among other things, the role of asphyxia in determining ARF and the importance of N-acetyl-beta-D-glucosaminidase (NAG) as a marker of tubular hypoxic damage;
5. investigations into pre- and postnatal ultrasound diagnosis of malformative uropathies, with the participation of numerous Italian hospitals and university centers; the data collected between 1990 and 2000 were presented at national and international conferences on neonatology and perinatal medicine in Italy and abroad, and still represent the only national reference point for an objective assessment of the phenomenon of ultrasound screening for malformative uropathies in our country;
6. at the end of 1995, a multicenter study on renal function in preterm infants was proposed and carried out in collaboration with numerous second- and third-level neonatal pathology centers in hospitals and universities; the preliminary results of this survey were presented at prestigious international conferences, including the AAP-ASPR (American Academy of Pediatrics – American Society for Pediatric Research) conferences from 1997 to 2010 and the Meetings of the ESPN (European Society of Pediatric Nephrology); the results were published in the *Archives of Diseases in Childhood, Paediatric Nephrology*, and other prestigious journals.

Since 1988, the GSNN has organized an annual National Congress, now in its 22nd edition, and 18 International Workshops on Neonatal Nephrology, with the participation of the most representative experts in the field.

Among these: J.V. Aranda (USA), G.B. Avery (USA), R. Bracci (Italy), G. Bucci (Italy), L. Cataldi (Italy), R.L. Chevalier (USA), F. Dati (Germany), A. Edefonti (Italy), F. Emma (Italy), V. Fanos (Italy), J.B. Gouyon (France), J.P. Guignard (Switzerland), J.P. Langhendries (Belgium), A. Marini (Italy), G. Montini (Italy), K. Nicolaidis (UK), M. Mussap (Italy), Z. Papadopoulou Columbis (Greece), M. Plebani (Italy),

C. Romanini (Italy), G. Rondini (Italy), F.F. Rubaltelli (Italy), S. Salcedo Abizanda (Spain), U. Simeoni (France), E. Sulyok (Hungary).

National Congresses and International Workshops have always been followed with great interest by the audience.

Among the activities of the GSNN, it is worth mentioning over 20 editions of the Continuing Education Course in Nephrourological Ultrasound for Newborns and Infants and the 18 editions of the Advanced Course in Neonatal and Pediatric Nephrology (titled “Clinical, Laboratory, Instrumental Diagnostics, and Therapy of Nephrouropathies”), which from 1997 to 2017 were organized and reserved for a limited number of colleagues, many of whom participated in all editions of the courses.

In addition to the publications of the proceedings in scientific journals and volumes, the GSNN, in collaboration with the Italian Association for the Protection of Children with Nephrouropathies (AISERNUI), published 4 books on nephrourological topics in 1996 and 1997 [1-4]. The executive board elected in 2022 gave new impetus to the GSNN, enriching the page dedicated to the GSNN on the SIN website by publishing interesting clinical cases and reviews of articles from international literature.

A survey was also conducted on the state of knowledge and management of care for severely preterm infants in second- and third-level neonatal centers. The results are published on the GSNN page of the SIN website.

CONCLUSIONS

Based on the results of this research, the authors are confident that the activities of the GSNN have been efficacious, particularly in producing care recommendations that have been and continue to be a benchmark for the quality of care for newborns and children with nephrouropathy.

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LECT 5

WHAT ROLE DOES LUNG ULTRASOUND PLAY IN THE NEONATAL INTENSIVE CARE UNIT?

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Lung ultrasound (LUS) is one of the milestones in the more generally defined field of POCUS (point-of-care ultrasound) in the Neonatal Intensive Care Unit (NICU). Many recent studies underline that LUS is not only a qualitative evaluation of lung structure, but it can also add quantitative information on lung status through the LUS score. This score can be defined as a semiquantitative score derived from 6 different areas of the lungs (3 for each side) and can give the following grading:

0. normal air-filled lungs (predominant A Lines, with pleural sliding);
1. mild reduction in lung aeration (interstitial pattern);
2. moderate reduction in lung aeration (alveolar pattern);
3. complete lack of aeration (consolidations).

Raimondi et al. [1] demonstrated that LUS not only allows for precise diagnosis of conditions such as consolidation, respiratory distress syndrome (RDS), or bronchopulmonary dysplasia (BPD), but also enables dynamic monitoring of the response to specific treatments, such as mechanical ventilation and surfactant administration. In preterm infants, LUS is the best diagnostic tool for an early diagnosis of RDS and the need for surfactant treatment.

Other applications of LUS in the NICU in the management of pulmonary diseases are transient tachypnea of the newborn, meconium aspiration syndrome, pneumonia, pneumothorax, BPD and bronchiolitis.

More recently, our Group underlined the role of POCUS in the management of neonates with congenital diaphragmatic hernia (CDH) [2, 3], proposing a standardized CDH-POCUS protocol in the NICU using functional echocardiography, lung ultrasound, splanchnic ultrasound and cerebral ultrasound. The protocol was based on the evaluation of the following parameters: 1) cardiac function and pulmonary hypertension, 2) lung volumes, postoperative pleural effusion or pneumothorax, 3) splanchnic and renal perfusion, malrotations and/or signs of necrotizing enterocolitis, 4) cerebral perfusion and eventual brain lesions. In particular, for LUS, we proposed a modified LUS score: we divided each lung into 6 areas and gave to each scan a value between 0 and 4 obtaining a total score range from 0 to 42. The CDH-LUS score was defined as mild (0-12), moderate (13-24), or severe (≥ 25).

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LECT 6

DECODING NEONATAL ELECTROCARDIOGRAPHY: FROM ARRHYTHMIAS TO CONGENITAL HEART DISEASE

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Neonatal electrocardiography (ECG) remains a cornerstone in the early diagnosis and management of cardiovascular disorders in newborns. Its interpretation is particularly challenging due to the unique physiology, ongoing postnatal adaptation, and transitional circulation that distinguish the neonatal heart from that of older children and adults. Typical neonatal ECG findings include higher heart rates, age-dependent variability in QRS and repolarization patterns related to myocardial immaturity and autonomic development, as well as transient changes associated with the closure of the ductus arteriosus. These factors necessitate age-specific interpretive criteria and careful clinical correlation.

NEONATAL ARRHYTHMIAS

The spectrum of neonatal arrhythmias extends from benign rhythm variants to critical disturbances.

- Premature atrial and ventricular contractions are frequent and often self-limited but may sometimes reflect structural or metabolic abnormalities.
- Supraventricular tachycardia is the most common clinically significant arrhythmia in neonates; its early detection is essential to avoid hemodynamic compromise.
- Bradycardia is frequently observed, especially in preterm infants, and may be associated with hypoxia, acidosis, or sinus node dysfunction. Severe bradycardia requires prompt evaluation.

- Conduction disorders, including first- and second-degree atrioventricular (AV) block, may occur in newborns born to mothers with autoimmune diseases or in neonates with congenital heart defects such as atrial septal defect. These conditions can progress to complete heart block.
- Abnormal P waves and PR intervals may also indicate atrial disease, pre-excitation syndromes (e.g., Wolff-Parkinson-White), or emerging AV nodal dysfunction, highlighting the importance of careful interpretation.

ECG IN CONGENITAL HEART DISEASE

Although echocardiography remains the gold standard for congenital heart disease, ECG offers valuable complementary insights.

- Conduction abnormalities such as prolonged PR intervals, bundle branch block, or altered P-wave patterns can provide early diagnostic clues.
- ST-segment and T-wave abnormalities may indicate repolarization disturbances linked to structural defects or altered ventricular loading.
- Signs of chamber hypertrophy or strain can suggest pressure or volume overload and guide further imaging.
- Postoperative monitoring relies on serial ECGs to assess recovery, detect arrhythmogenic substrates, and promptly identify complications such as junctional ectopic tachycardia or conduction blocks.

CONCLUSION

Despite advances in echocardiography and imaging, the neonatal ECG remains essential in Neonatal Intensive Care Units. Accessible and noninvasive, it helps detect arrhythmia, identify subtle signs of congenital heart disease, and guide both acute and long-term management. By combining expert interpretation with innovative analytic methods, ECG continues to enhance diagnostic accuracy, support therapeutic decisions, and improve neonatal cardiovascular outcomes.

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LECT 7

PLASTIC BRAIN OR PLASTICS IN THE BRAIN?

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This presentation explores the alarming presence and potential neurotoxic effects of micro- and nanoplastics (MNPs) in the human brain. Praised initially for their utility, plastics have now become a ubiquitous environmental contaminant; 44% of all plastic ever produced was manufactured between 2000 and 2015. Rivers, especially in Asia, serve as the primary channels for oceanic plastic pollution.

MNPs, derived from both primary (intentional) and secondary (degradation) sources, are detected across all ecosystems and even in human tissues – including the brain, kidneys, liver, and atheromas. They enter the body via ingestion, inhalation, or transdermal absorption and may cross the blood-brain barrier through endocytosis or other pathways. Alarming, brain tissue contains 30 times more MNPs than the liver or kidney, with polyethylene being the predominant polymer found.

Neuroscientific findings on neuroplasticity – the brain's capacity to reorganize and adapt – contrast sharply with the rising internal contamination by MNPs. The brain's plasticity, once thought to end after early adolescence, has been proven to persist throughout life and underlies recovery and learning. However, recent data suggest that this very “plastic” brain now contains real plastic, with implications for inflammation, oxidative stress, cognitive impairment, and neurodegeneration. Some studies have linked higher MNP accumulation with dementia, though causality remains unproven.

Notably, this contamination begins early in life. MNPs have been detected in the placenta, breast milk, amniotic fluid, and meconium, raising concerns for perinatal neurodevelopment. Multipotent stem cells in breast milk – which play a critical role in neonatal brain development – might serve as vectors for MNPs and endocrine-disrupting chemicals (EDCs), via a “Trojan horse” effect. EDCs further interfere with stem cell function through oxidative stress, epigenetic disruption, and hormonal pathway alteration.

The author advocates for standardized detection methods, mechanistic studies, and longitudinal human research, particularly in perinatal and

neonatal populations, to assess risks and guide prevention: to enhance brain plasticity, we must urgently reduce its plastic content.

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LECT 8

OPTIMIZING RENAL PROGNOSIS: 35 YEARS OF CONSERVATIVE MANAGEMENT OF FETAL-DIAGNOSED CONGENITAL ANOMALIES OF THE KIDNEY AND URINARY TRACT (CAKUT)

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Congenital anomalies of the kidney and urinary tract (CAKUT) represent a heterogeneous spectrum of malformations involving the kidneys, collecting system, bladder and urethra. They occur in approximately 2% of pregnancies and 1.5-2.5% of live births, accounting for up to 50% of congenital malformations detected during the neonatal period and nearly 40% of pediatric end-stage renal disease. Early embryological disturbances determine the severity of the phenotype, ranging from renal agenesis and dysplasia to obstructive uropathies such as vesicoureteral reflux or posterior urethral valves. Antenatal ultrasound, optimally performed between 16 and 20 weeks of gestation, is the gold standard for detection, allowing stratification of risk and prenatal counselling. Oligohydramnios is the most reliable predictor of impaired renal function and adverse outcomes, sometimes leading to the Potter sequence. Postnatal management requires a multidisciplinary approach aimed at preventing urinary tract infections and preserving renal function. Conservative management is generally preferred, with surgery reserved for selected cases with significant obstruction, recurrent febrile urinary tract infections, or declining renal function. Antibiotic prophylaxis may be considered in high-risk infants, although guidelines recommend a selective approach. Prognosis is highly variable, depending on the phenotype, timing of diagnosis, and adequacy of follow-up. Transitional care into adulthood is essential to reduce the long-term burden of chronic kidney disease. In conclusion, individualized counselling and early multidisciplinary

management are crucial to improve renal outcomes and quality of life in children with CAKUT.

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LECT 9

ETHICAL PROBLEMS IN NEONATOLOGY

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Neonatal intensive care has advanced significantly, enabling survival of extremely premature and critically ill infants, reaching a point that was difficult to imagine a few years ago. However, alongside these advances, this improvement has introduced new and complex ethical challenges. At this point, we must ask ourselves, as physicians, whether the usual key ethical principles – namely, autonomy, beneficence, non-maleficence, and justice – remain applicable within the neonatal context. The changing social attitude towards personal values makes the physician-relative dialogue increasingly complex whenever the newborn's best interests must be invoked as a central value in decision-making. Clinicians must navigate moral uncertainty and distress, particularly at the limits of viability, where decisions regarding resuscitation and palliative care are ethically complex. Shared decision-making with parents, transparent communication, and structured frameworks seem to be a possible answer to these burdensome questions. Withholding and withdrawing life-sustaining treatment are ethically equivalent when based on lack of benefit or excessive burden. Palliative care should prioritize comfort and dignity. Equity in access and outcomes remains a pressing concern, requiring systemic

reforms. Legal and cultural contexts, such as the Groningen Protocol in the Netherlands, highlight jurisdictional differences in end-of-life practices. Research ethics demand rigorous safeguards for vulnerable neonates. Ultimately, ethical neonatal care requires compassion, procedural clarity, and interdisciplinary collaboration to ensure that decisions serve the infant's best interests while respecting the family's values.

LECT 10

BEYOND THE FACE MASK: INTEGRATING SUPRAGLOTTIC AIRWAYS IN THE NEONATAL-PEDIATRIC AIRWAY CARE SETTINGS. EVIDENCE, ANAESTHESIOLOGY-GRADE PRACTICE, AND AN IMPLEMENTATION PLAN

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BACKGROUND

Delays to establishing adequate ventilation – not pharmacology – drive preventable harm in neonatal-pediatric resuscitation. When a two-hand mask seal fails within 60-90 s or intubation is not promptly feasible, a supraglottic airway (SGA)/laryngeal mask airway (LMA) provides a fast, reliable route to lung inflation that trained non-anesthetists can deploy. International guidance (ERC/ILCOR/NRP) recommends the use of SGA in newborns ≥ 34 weeks of gestational age (GA) and/or weighing ≥ 2 kg when mask ventilation is ineffective or intubation is delayed, and evidence shows a shorter time to adequate ventilation and fewer intubations in trained teams [1-3]. The question is no longer whether SGAs work, but how to ensure their performance is uniform across Delivery Rooms, Neonatal Intensive Care Units, Transport, and Perioperative Care.

INDICATIONS

The primary indication is failed mask ventilation despite corrective manoeuvres by two operators within 60-90 s, or when immediate tracheal intubation is not achievable. Early SGA placement limits desaturation, avoids repeated laryngoscopy, and creates a stable bridge to definitive airway control. SGAs are appropriate as a first-line device in experienced teams, as a conduit in anticipated or unanticipated difficult airways, and for short procedures in late-preterm/term infants where required pressures are modest. Caution is warranted in newborns < 34 weeks of GA

or < 2 kg (limited sizes/evidence) and in settings of high aspiration risk or need for very high inspiratory pressures; major craniofacial anomalies, suspected proximal tracheoesophageal fistula, and severe congenital diaphragmatic hernia remain indications for endotracheal intubation. Placement should be standardized, with objective confirmation by end-tidal CO_2 (EtCO_2) and a leak test; common problems (poor seal, gastric distension, malposition) are managed with the SEAL (Size, Ensure cuff pressure, Align airway, Leak check) loop.

IMPLEMENTATION

Impact depends on system design, not the device alone. We propose an anesthesiology-grade bundle:

1. protocolized decision flow: mask $\rightarrow$ SGA within 60-90 s; predefined escalation to intubation if ventilation remains inadequate;
2. standard kit: two SGA sizes per weight band, lubricant, capnography, cuff manometer where relevant, and a small-bore nasogastric tube for devices with a drain;
3. training and human factors: brief recurrent teaching aligned to newborn life support (NLS)/newborn resuscitation program (NRP), hands-on insertion skills, scenario-based simulation with closed-loop communication;
4. quality indicators: time-to-effective ventilation, proportion avoiding intubation, adverse events, and training coverage;
5. governance: documentation and audit of each use to refine thresholds and escalation rules.

This approach delivers the reliability, monitoring, and accountability expected in anesthesia while enabling safe deployment by neonatologists and other frontline teams.

CONCLUSION

SGAs are not a replacement for endotracheal skills; they are a high-value complement that shortens the path to adequate ventilation, broadens safe options in difficult or time-critical airways, and increases system resilience where an anesthetist is not immediately available. Embedding SGAs with anesthesiology-grade practice makes their use safe, reproducible, and measurable across neonatal-pediatric settings, aligning daily care with the global state of the art.

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LECT 11

SAFETY AND EFFICACY OF PREMEDICATION BEFORE ELECTIVE INTUBATION IN NEONATES

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Premedication before elective neonatal intubation has become an essential intervention in neonatal intensive care, as current evidence highlights its clinical importance. Intubation without analgesia or sedation can cause cardiovascular instability, pain, and potential long-term consequences. Over the last two decades, randomized trials and systematic reviews have consistently demonstrated that premedication significantly enhances procedural safety and improves outcomes [1]. Based on this evidence, clinical practice guidelines now recommend its use in all non-emergent cases.

Neonates receiving premedication exhibit greater cardiovascular stability, characterized by reduced fluctuations in blood pressure, more stable heart rates, and fewer episodes of desaturation, while the incidence of adverse events is minimized. Premedication also enhances the intubation process by reducing procedure time, decreasing the number of attempts required, and improving overall success rates. The drugs most commonly used include an opioid analgesic, an anticholinergic agent and a short-acting neuromuscular blocker [1]. These drug combinations provide analgesia, suppress vagal reflexes, and optimize conditions for safe and efficient airway management, while minimizing hemodynamic compromise and procedural complications.

The American Academy of Pediatrics and the Canadian Paediatric Society recommend premedication for all non-emergent intubations [2]. However, implementation of this practice remains variable worldwide. Premedication for elective intubations is often not administered due to drug safety concerns, lack of neonatal formulations, or absence of standardized protocols. These gaps highlight the need for the dissemination of evidence-based protocols and clinician training.

In summary, current evidence strongly supports the use of premedication before elective neonatal intubation. When appropriately administered, it improves clinical outcomes and procedural success with minimal serious complications. Areas for further investigation include the standardization of practices across Neonatal Units worldwide, ensuring equitable access to safe drug regimens, and evaluation of long-term outcomes [1].

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LECT 12

NEONATAL BRAIN INJURY: WHEN IT STARTS AND POSSIBLE OUTCOMES

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Newborn deaths account for nearly half of all deaths in children under 5, with 2.7 million lives lost each year. Newborn deaths represent a critical global health challenge, as most of these deaths are preventable, and inequities in access to care mean that newborns in fragile and vulnerable settings are disproportionately affected. Hypoxic-ischemic encephalopathy is a major contributor to this burden and remains a leading cause of neonatal death and long-term disability. Therapeutic hypothermia is the only proven therapy, though its benefits are not universal and its reach remains uneven across health systems. These combined limitations have accelerated research into novel and complementary neuroprotective strategies.

The purpose of this narrative review is to synthesize evidence on both established and emerging therapies for neonatal neuroprotection. Adjunctive care bundles that stabilize physiological parameters, control seizures, and optimize nutrition contribute to both short- and long-term outcomes. Pharmacological agents such as erythropoietin and melatonin have demonstrated anti-inflammatory and antioxidant potential, whereas stem cell-based therapies are characterized by

regenerative and immunomodulatory effects. Other experimental approaches, including magnesium sulphate, cannabinoids, and polyphenols such as curcumin and resveratrol, are under investigation but remain primarily in preclinical or early clinical stages. Non-pharmacological measures, including family-centered developmental care and kangaroo mother care, further enhance neuroplasticity and cognitive outcomes.

Neonatal neuroprotection is evolving toward integrated multimodal and holistic approaches that unite medical innovation with family-centered care. Future research must refine these strategies, close evidence gaps, and expand global accessibility to reduce disparities in neonatal survival and long-term neurological health.

LECT 13

PREMATURITY IN ALBANIA

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BACKGROUND

Preterm birth is the leading cause of neonatal mortality and is associated with long-term physical, neurodevelopmental, and socioeconomic effects. Preterm birth complications remained the top cause of under-5 child mortality globally in 2022, accounting for about 1 million neonatal deaths, similar to figures a decade ago. Understanding trends in preterm births (< 37 weeks of gestation) is essential for shaping perinatal health strategies. Unfortunately, Albania lacks consistent national data after 2015; however, global models (WHO/UNICEF) provide estimated trends up to 2020.

AIM

To describe the estimated trend of preterm birth rates in Albania during 2015-2020 based on global modeling, and to discuss implications for 2021-2024 in the absence of updated empirical data.

MATERIAL AND METHODS

We rely on the WHO Global Health Observatory's modeled estimates of preterm birth rates. The model projects national rates even when direct data is missing.

RESULTS

Key findings for the 2015-2020 trend

For most European countries, including Albania, prematurity rates have been stable over the decade 2010-2020, with no statistically significant

decrease. Globally, the annual rate of reduction was only -0.14%/year (2010-2020), implying minimal year-on-year change. Given that Albania follows the European regional pattern (typically < 8-9% of births), it is reasonable to conclude that the 2015-2020 trend is stable, with minor inter-year fluctuations.

2021-2024 gaps and interpretation

After 2020, there are no open official publications that provide an annual series of prematurity for Albania until 2024/2025. In their absence, the epidemiological judgment is based on the fact that no region has seen a sustained decrease in the last decade and that risk factors (increasing maternal age, multiple pregnancies/*in-vitro* fertilization, obesity/hypertension) have not changed drastically to expect a substantial decrease in prematurity in the country. Therefore, the 2021-2024 trend is likely to remain roughly flat, but this needs to be verified with national administrative data (maternity registries/INSTAT/PHI).

CONCLUSIONS

Given the minimal change over the prior decade, it is plausible that the trend remained flat unless substantial policy or demographic shifts occurred.

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LECT 14

RARE DISEASE ASSOCIATED WITH CONGENITAL HEART DISEASE – CASE BY CASE

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INTRODUCTION

If a disease prevalence is less than 1 in 2,000, it is considered rare in Europe; in the USA, a disease

is considered rare if it occurs in fewer than 1 in 20,000 live births; 80% of these are based on genetic disturbances [1]. They can affect all parts of the human body, and a significant number are associated with congenital heart diseases (CHDs). CHDs can be the first presenting sign of a rare disease. In most cases, cardiovascular symptoms dominate the clinical manifestations of rare diseases and are the leading cause of morbidity and mortality, especially in childhood. The dysmorphic features may not be present, or the disease can have a wide range of phenotypic features, such as DiGeorge syndrome (22q11.2 deletion syndrome), which is detected in approximately 2% of all patients with CHDs and in 13% of patients with specific cardiac malformations. Therefore, risk management based on an accurate genetic diagnosis is necessary to effectively plan surgical and medical management, as well as follow-up, for these patients. In addition, multidisciplinary approaches and care for the combined extra-cardiac anomalies may help to reduce mortality and morbidity accompanied by CHD [3].

AIM

The purpose of this presentation is to present some cases of rare diseases diagnosed in Kosovo, associated with CHDs, where the leading clinical symptoms are from CHDs.

METHODS

Retrospectively, we analyzed recorded data of some children diagnosed with rare diseases associated with CHDs.

CASES

In this presentation, we present few children with rare diseases, accompanied by CHDs. In all cases, clinical and genetic examinations were conducted, and for a detailed cardiological diagnosis, additional examinations were performed to verify the disease and assess the possibility of effective treatment. The first case was with primary hypertrophic cardiomyopathy, which was the cause of loss of consciousness and severe heart rhythm disorders. The second child had restrictive cardiomyopathy, diagnosed in the neonatal period. The third child had developed primary pulmonary hypertension. The fourth presented child belongs to the group of mesenchymopathies with Loeys-Dietz syndrome, accompanied by giant dilation of the ascending aorta.

CONCLUSION

CHD is the leading cause of congenital disabilities and is a significant cause of morbidity and mortality during infancy and childhood. CHD is a

multifactorial disorder associated with both genetic and environmental influences. Approximately 30% of CHD is thought to be related to genetic syndromes accompanied by extra-cardiac anomalies. Understanding genetic etiology in a particular patient with both CHD and other anomalies can help clinicians to effectively plan a patient's surgical and medical management and their follow-up. All the presented children belong to the group of children with rare diseases, and in the clinical presentation, are dominated by the symptomatology of associated CHDs.

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LECT 15

THE RIGHT TO LIFE OF INFANTS BEFORE AND AFTER BIRTH IN THE REGIONS OF KYRGYZSTAN

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INTRODUCTION

The lecture studies the frequency of premature births in regional health organizations of Kyrgyzstan, with an assessment of antenatal care for screening and treatment of isthmio-cervical insufficiency, prevention of fetal distress, neonatal sepsis and neuroprotection with magnesium sulfate in pregnant women, and an assessment of the impact of the method of delivery.

RELEVANCE

Miscarriage and prematurity remain one of the main medical and social problems in Kyrgyzstan. Every year, 15 million premature births occur in the world (more than 60% in Asian and African countries: *WHO Bulletin* 2013). At the international congress of FIGO (International Federation of Gynecology

and Obstetrics) in 2018 there was a report that over the past 60 years there has been no decrease in the frequency of premature births in the world: it is 9.5% of all births (with slight differences between economically more and less wealthy countries); 15 million premature babies are born annually.

MATERIAL AND METHODS

The objective of this study was to examine the frequency of premature births in 7 regional health organizations of the country, and to determine the relationship between antenatal care (screening, progesterone, obstetric pessary and cervical sutures, diagnosis and treatment of vaginitis/vaginosis, tocolysis, prevention of fetal distress syndrome and neonatal sepsis, neuroprotection with magnesium sulfate, adequate delivery, proper resuscitation and care of the premature infant) and levels of perinatal morbidity and mortality in premature infants.

RESULTS

According to the data of the Center for Electronic Health of the Ministry of the Kyrgyz Republic for 2022-2024, there is a high level of infant mortality. Up to 70% of the causes of infant mortality are pathologies of the perinatal period. Over the past 3 years, relatively high levels of perinatal mortality have been noted in the Chui, Issyk-Kul, and Jalal-Abad regions.

In regional Maternity Wards, depending on the population density of the region and the service area, the proportion of premature births was from 4.5% to 10.6%. The estimated level of use of obstetric pessary in health care organizations is no more than 5%, the level of operations with sutures on the cervix is no more than 1%, the level of antenatal prophylaxis of fetal distress syndrome is no more than 70%, the level of prevention of neonatal sepsis is no more than 50%, neuroprotection is no more than 5-10%, the level of use of surfactant is no more than 10-15%, vitamin K is no more than 60% (centralized purchases of vitamin K were very low). According to the level of antenatal neuroprotection with magnesium sulfate among women with premature births in those organizations where this level was raised to 80% (Central Center for General Practitioners of Balykchy), there were no cases of intraventricular hemorrhage (IVH). Where neuroprotection was performed, almost every second woman had a decrease in instances of IVH (Central Center for General Practitioners of Kyzyl-Kiya from 6 cases to 0). There are hospitals with an insignificant frequency of premature births with a relatively smaller number of infants with low body weight (less than 1,500 grams), but have up to 10 cases of

IVH with infant mortality (Talas and Naryn Regional Hospitals). There are regions with a relatively moderate level of antenatal neuroprotection for 3 years (Batken Hospital – 35.2-47.1%); however, cases of IVH with infant mortality are more common due to the large proportion of premature babies with low body weight, up to 50%. The most significant number of cases of IVH was noted over 3 years in the Jalal-Abad Hospital – 737 (34.9%), while the level of antenatal neuroprotection with magnesium sulfate was very low – 8.9%. In the Chui Regional Hospital, the level of antenatal neuroprotection was up to 2.5% at the beginning of 2022, and at the end of 2024, it rose very slightly to 7.5%. Perhaps the low level of neuroprotection is due to both the timely diagnosis and prognosis of premature birth, as well as the knowledge and skills of healthcare workers in implementing this technology. If, in the first direction, there is no level of combined diagnostics involving biochemical tests and cervicometry in state organizations, then, in the second direction, an anonymous survey was conducted among health workers, and an analysis of the reasons for the low level of antenatal neuroprotection with magnesium sulfate was conducted. Among the anonymously surveyed healthcare workers, 58 gynecologists (82.9%) and 12 midwives (17.1%) indicated a lack of knowledge on antenatal neuroprotection in preterm birth – 70%, the absence of updated national thematic clinical guidelines – 92.8%, the absence of standards of operational procedures for antenatal neuroprotection – 60%, the absence of assessment and analysis by the compulsory health insurance fund and insufficient clinical audit – 60%, lack of resources for drugs and medical devices – 41.4%, lack of conditions on the part of the patient due to an emergency – 30%, the presence of conditions on the part of the patient for neuroprotection with magnesium sulfate in preeclampsia – 40%, the presence of side effects for refusing treatment with magnesium sulfate – 24.3%, unwillingness to conduct antenatal neuroprotection with magnesium sulfate – 37.1%.

There are recommendations from the American College of Obstetricians and Gynecologists from 2024 on the preference for cesarean section for the delivery of a premature infant after 26 weeks of gestation. The differences after 26 weeks are reliable: the morbidity of newborns with surgical termination of pregnancy is significantly better than with spontaneous preterm birth; stillbirth (mostly intrapartum fetal death) with spontaneous preterm birth is 40%, with cesarean section, 1.9%. Early neonatal mortality is, respectively, 30% and 7.9%. Therefore, perinatal

mortality in preterm birth can be reduced by delivering by cesarean section. Still, it remains problematic to influence the morbidity of children, especially with low and extremely low body weight, according to many authors. According to our data, in only 3 regional maternity hospitals, the caesarean section rate was within 24-25% (Naryn, Issyk-Kul and Osh Regional Hospitals). Unfortunately, in other regional maternity hospitals, where the caesarean section rate is about 10-12% for premature births, the neonatal mortality rate was 13-18.5% (Jalal-Abad, Chui and Batken Regional Hospitals). If we consider stillbirths after vaginal births, this figure may be even higher. We considered the proportion of deceased children with low gestational age and low body weight less than 1,500 g in the specified regional maternity organizations, and it ranged from 33% to 70%, with an average of about 45-50%. Immaturity of other systems may have affected survival in the low-birth-weight preterm infants' group. Still, in the group of infants over 1,500 g, there were infants with severe IVH who died and whose mothers did not receive the necessary antenatal care neuroprotection with magnesium sulfate.

CONCLUSION

Thus, based on scientific views and recommendations, it is necessary to develop local perinatal programs on priority issues, including early prevention and early correction of preterm birth prerequisites (for example, adequate gestagenic support, treatment of recurrent vaginitis/vaginosis, screening for cervical insufficiency with obstetric cerclage of the cervix, patient routing and an antenatal care package), development and implementation of a new clinical guideline on preterm birth by professional associations.

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LECT 16

BIRTH RATE AND BIRTHPLACE

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Falling birth rates are a global issue today. This phenomenon is observed all over the world, from the United States to China, from Italy to Finland, and has been known for decades. Since many countries have fertility rates below 2.1 children per woman (Europe below 1.38), it means that these populations are going to decrease in size in the following decades. Italy (like South Korea) is the country with the most severe demographic threat. The leading causes of this phenomenon are: higher costs of living, later economic independence, higher educational level with more career opportunities for women, and a later age for the first child. However, the main reason is the simple "not willing to have a baby".

The ISTAT (Italian national registry) data are: Italian birth rate, 9.8 births per thousand people, year 2004, and 6.4, year 2023 (possibly 6.2, year 2024); Italian fertility rate, 1.19 in 1995, and 1.18 in 2024. As we can see the problem was already present 30 years ago; however, 156,000 births more than year 2024 were counted in 1995, this because of the "shrinking number of fertile women mechanism". Another ominous statistic is the average age at delivery, 32.6 years. Italy is getting older and older, the rate "population < 10 years / population > 80 years" is now < 1, it was 2.5 (25 years ago), and 9 (50 years ago). The demographic changes determine some clinical changes: more clinically complex patients with chronic illnesses. The so-called "demographic winter" also has severe potential economic consequences: first, we will have a smaller workforce, then less paid taxes, and subsequently less money available for retirement plans, social security, and healthcare systems.

The last published CEDAP (Italian certificate of attendance at delivery) report for 2023 data shows: a total of 389 birth centers (BCs), with 61.7% of births taking place in BCs with more than 1,000 births (34.4% of the BCs). A total of 8.0% of births take place in BCs with < 500 births/year (about 30% of BCs). A total of 116 Neonatal Intensive Care Units (NICUs) are counted, 95 of them in BCs with more than 1,000 deliveries, and 8 in BCs with fewer than 800 deliveries. In 2015, 500 BCs were counted; 126 BCs had fewer than 500 deliveries, and 6.7% of births occurred in BCs with fewer than 500 births.

If we consider variable and fixed costs of births, it is not so easy to calculate the amount of euros per single birth. However, in the Trento province, the Court of Accounts applied the diagnosis-related group (DRG) system. It noted that the cost of a

single birth was 20,980 euros in two birth centers with less than 500 births/year (Cles and Cavalese) and 5,200 euros in Trento (a BC with NICU and more than 2,700 births/year) and 4,823 euros in Rovereto (a BC with more than 900 births/year).

CONCLUSIONS

The falling birth rate will be a universal issue for the following decades, posing a severe threat to economic systems. Therefore, strong and decisive decisions will be needed to ensure the sustainability of national healthcare services, particularly in Italy.

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LECT 17

THE OLD AND NEW FRONTIERS OF VITAMIN D

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Vitamin D derives mainly from sun exposure (90-95%) and to a lesser extent from diet (5-10%). It is crucial for bone growth and mineralization, preventing rickets. Osteoporosis is characterized by reduced bone mass and fragility with a risk of fractures. There are primary forms (e.g., osteogenesis imperfecta) and secondary forms (e.g., those induced by glucocorticoids). Bone density loss occurs early and is related to the dose and duration of therapy.

Cutaneous synthesis of vitamin D is insufficient in winter and outside the central hours of the day, with modifiable factors of poor sun exposure, especially in adolescents. The newborn is at risk of hypovitaminosis D if not supplemented. Vitamin D acts on many tissues via the vitamin D receptor (VDR) and the CYP27B1 enzyme, influencing skin health, cell proliferation and differentiation, and the immune response, reducing the risk of infections such as bacterial pneumonia. The VDR is present in most tissues. It mediates the functions of calcitriol, the active form of vitamin D. Many tissues also

contain the CYP27B1 enzyme, which converts calcidiol to calcitriol, suggesting a role for vitamin D beyond calcium regulation, influencing various tissues. Most immune cells possess receptors and enzymes for vitamin D, which stimulates the production of antimicrobial peptides, such as cathelicidin LL-37 and beta-defensin 2, both of which work at the skin level. A vitamin D deficiency (< 10 ng/mL) is associated with an increased risk of bacterial pneumonia, highlighting the protective role of vitamin D in infections. Ceramides, produced by sphingomyelin thanks to vitamin D, are essential for the skin barrier and skin health. In infants, especially preterm infants, ceramide deficiency increases permeability and the risk of atopic dermatitis.

Definitions of vitamin D status vary: sufficiency is ≥ 20 ng/mL, hypovitaminosis is < 20 ng/mL, risk of rickets is < 12-15 ng/mL, and excess is > 100 ng/mL. The Endocrine Society no longer supports the sufficiency threshold of 30 ng/mL. Supplementation of 400 IU is recommended in early childhood and during pregnancy.

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LECT 18

ADVANCED NONINVASIVE VENTILATION IN TERM AND PRETERM INFANTS

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Respiratory distress syndrome (RDS) is a common condition affecting newborns and is a leading cause of morbidity and mortality in the neonatal period. Severely premature infants are particularly vulnerable to respiratory failure due to their immature lungs. Management of RDS often requires respiratory support, either via endotracheal intubation and invasive mechanical ventilation (IMV) or with various forms of noninvasive mechanical ventilation (NIV). In the last decades, noninvasive respiratory support has been recommended as the first-line treatment for newborns with RDS, as it can reduce the need for IMV and the risk of bronchopulmonary dysplasia (BPD). International guidelines recommend initiating support with nasal continuous positive airway pressure (nCPAP), both in the Delivery Room and during Intensive Care Unit stays, using various types and sizes of nasal cannulas and masks, which can be used even for infants with extremely low gestational age and weight. Alternatively, some centers adopt an even less invasive approach, i.e., humidified high-flow nasal cannula therapy (HFNC), although the evidence of efficacy compared to nCPAP is not always favorable. Over the years, other modalities have been added to provide noninvasive respiratory support, to provide the patient with artificial breaths with pre-set pressure or volume, in a controlled or assisted manner. Nasal intermittent positive airway pressure (nIPPV) is a noninvasive modality that applies continuous positive end-expiratory pressure plus intermittent positive inspiratory pressure, regardless of the infant's breathing pattern. Several studies have shown that nIPPV is associated with a reduced incidence of BPD and mortality compared to CPAP. However, as the support provided by nIPPV is not synchronized with the patient's respiratory effort, it can cause discomfort and patient-ventilator asynchrony. Thus, other modalities have been developed that ensure greater synchronization with the newborn's breathing pattern, such as nasal synchronized intermittent positive airway pressure (nSIPPV) and noninvasive neurally adjusted ventilatory assist (NIV-NAVA). The latter is a unique ventilation modality that uses the diaphragm's electrical signal to assist the patient's breathing proportionally. Another strategy that may offer advantages over conventional techniques is noninvasive high-frequency ventilation (nHFV), which operates at very high frequencies and low tidal volumes to ensure adequate gas exchange. Unlike conventional ventilation, which relies on significant changes in pressure and volume, nHFV

achieves this by operating at very high frequencies and low tidal volumes.

Despite significant advances in noninvasive respiratory support techniques, further research is necessary to determine the optimal ventilatory modalities and strategies for each newborn, considering local expertise and available resources.

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LECT 19

CHILDREN WITH SLEEP DISORDERS: FROM PAST TO METABOLOMICS

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Pediatric sleep disorders encompass a broad spectrum of clinical manifestations, ranging from respiratory disorders, such as obstructive sleep apnea (OSA), to neurological disorders, such as parasomnias. OSA are characterized by upper airway obstructions that determine a reduction in oxygen supply, triggering intermittent hypoxia phenomena with subsequent reoxygenation, capable of generating oxidative stress through the production of reactive oxygen species (ROS), responsible for damage to the entire organism due to systemic inflammation. For this reason, sleep-related breathing disorders are considered disorders with systemic impact and, if not adequately treated, are related to significant cardiologic, endocrinologic, and neurobehavioral comorbidities.

Recently, several studies have focused on the endothelial damage induced by intermittent hypoxia during sleep-disordered breathing. Similarly, studies have been conducted to evaluate the possible consequences of OSA on the intestinal microbiota, showing how intermittent hypoxia, altering normal intestinal permeability, creates imbalances in the microbiota in terms of microbial composition and abundance of species, the effects of which are still being studied.

Xu et al. [1] have shown how children with OSA show changes in the oral microbiota and present different metabolomic patterns compared to adults with OSA (in particular, metabolites associated with vitamin metabolism, the ornithine cycle, butanoate metabolism, and bilirubin metabolism), therefore suggesting that sleep-disordered breathing may have an effect all over human metabolism. Early recognition and treatment are mandatory to avoid systemic comorbidities.

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LECT 20

MATERNAL AND CHILD HEALTH CARE SERVICES IN ALBANIA

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Albania has made significant progress in maternal and child health care over the past three decades, marked by improved access to services, increased health system capacity, and declining mortality rates. Between 1990 and 2020, maternal mortality fell from 45 to 10 per 100,000 live births, and

under-5 mortality decreased from 45 to 11 per 1,000 live births, reflecting a commitment to health sector reforms and international health goals. The national health system provides free antenatal, perinatal, and postnatal care, with over 95% of births attended by skilled health personnel as of 2020. However, disparities persist across urban and rural areas, with rural women facing reduced access to specialized care and diagnostics. Immunization coverage remains high nationally (> 95% for key childhood vaccines), yet occasional vaccine hesitancy and logistical challenges hinder universal access. The integration of maternal and child health services within primary care and the adoption of the “Health for All” strategy, aligned with WHO guidelines, have been instrumental in improving service delivery. However, systemic challenges remain, including workforce shortages, limited health education, and underfunded infrastructure in remote regions. Continued investment in digital health tools, midwife training, and community outreach is essential to sustain gains and address remaining gaps. Strengthening monitoring and evaluation frameworks, with an emphasis on data quality and equity, will be key to achieving universal maternal and child health coverage in Albania.

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