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SMART PEDI UPDATE

Pedismart Newsletter
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Pedi smart News Letter
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Dear Doctor,
Greetings from Micro Labs Limited. We are happy to bring you **"PEDI SMART"**which contain latest and interesting news in the field of Paediatrics.

This issue contains:

1. **Association between Lower respiratory tract infections in children and early mortality from respiratory diseases in adults**
2. **A case-control study on the risk factors for perinatal stroke in term infants.**
3. **The Impact of Dietary intake and Body Mass Index on the development of Islet autoimmunity in genetically at-risk children**
4. **A case study of the multisystem inflammatory syndrome in infant associated with the Bacille Calmette-Guérin scar.**

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Limited

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1. Association between Lower respiratory tract infections in children and early mortality from respiratory diseases in adults

Introduction:

Children are disproportionately affected by lower respiratory tract infections (LRTI), which are a major cause of morbidity and death globally. [1] Lower respiratory tract infections (LRTIs) in children are known to affect lung development and long-term lung health, but it is unknown if they also contribute to early adult mortality from respiratory illness.[2] The objective of the current study was to determine the likelihood and burden of premature adult mortality due to respiratory illness in association to early childhood LRTI.

Childhood lower respiratory tract infections (LRTI) was linked to a nearly two-fold higher risk of premature adult mortality from respiratory illness.

Methods:

Data from a nationally representative cohort recruited at birth in were utilised in this longitudinal observational cohort analysis. Researchers looked examined the relationship between early-childhood (age <2 years) lower respiratory tract infections (LRTI) and respiratory disease-related mortality from ages 26 to 73. Parents or caregivers reported an early childhood LRTI occurrence. The National Health Service Central Registry provided the death's cause and date. Early childhood LRTI hazard ratios (HRs) and population attributable risk were calculated using competing risks Cox proportional hazards models, adjusting for birthweight, sex, gender, childhood socioeconomic status, and childhood house overcrowding. Researchers compared the study cohort's mortality to overall mortality trends and calculated the approximate excess deaths that occurred across the country during the study period.

Results:

A total of 5362 participants began the research, and 4032 (or 75% of them) were still enrolled when they were 20 to 25 years old. Incomplete data on mortality (18 [1%]), smoking (57 [1%]), or early childhood (368 [9%] of 4032 individuals) resulted in the elimination of 443 people. The survival analyses from comprised 3589 subjects aged 26 (1840 [51%] male and 1749 [49%] female). The longest period of follow-up was 47.9 years. After adjusting for variables such as childhood socioeconomic position, childhood home overcrowding, birthweight, sex, and adult smoking, 913 (25%) of the 3589 participants who experienced an LRTI during early childhood were at an increased risk of mortality from respiratory disease by the age of 73 years compared to those who did not. (HR 193, 95% CI 110-337; p=0021). This result correlated with an increased mortality rate of 179 188 (95% CI 33 806-261 519) deaths, and a population attributable

risk of 20.4% (95% CI 38-298).

Discussion:

This study, which lasted eight decades, discovered that persons who had an LRTI by the age of two years old had a 93% higher risk of dying early from a respiratory illness as adults than those who did not. Early childhood LRTI was responsible for one-fifth (20.4%) of respiratory-related fatalities between the ages of 26 and 73.[2] Childhood LRTIs have been demonstrated to be connected to the development of adult lung function deficits, asthma, and chronic obstructive pulmonary disease. [3] Nevertheless, no prior study has had a long enough follow-up to prospectively relate these early childhood infections to adult mortality.[2]

Early childhood LRTI	
LRTI at age <2 years	913 (25%)
Number of LRTIs by age 2 years	
1	596/913 (65%)
2	162/913 (18%)
≥3	155/913 (17%)
Age when first LRTI occurred	
<1 year	648/913 (71%)
≥1 year	256/913 (28%)
Data missing	9/913 (1%)
Treatment of first LRTI	
Untreated	36/913 (4%)
Outpatient treatment	820/913 (90%)
Inpatient treatment	52/913 (6%)
Data missing	5/913 (1%)
Outcome by age 73 years	
Alive	2733 (76%)
Emigrated	182 (5%)
Died	674 (19%)

Overall outcomes of participants included in the survival analyses. *Data are n (%) ,Participants(n=3589)*

Conclusion:

According to study findings, early-life respiratory tract infection (LRTI) was linked to a nearly two-fold greater risk of premature adult mortality from respiratory illness, and this risk contributed for one-fifth of these fatalities. Early childhood LRTI may have a direct impact on the development or prognosis of adult respiratory diseases like chronic obstructive pulmonary disease. Preventive measures are needed in order to prevent the emergence of these adult illnesses.

References:

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2. A case-control study on the risk factors for perinatal stroke in term infants.

Introduction:

Perinatal stroke is a well-defined heterogeneous collection of illnesses characterised by a localised interruption of cerebral blood flow. The preterm brain contains unique vulnerabilities that predispose a newborn to stroke both in gestation and after delivery, despite the fact that perinatal stroke has generally been characterised as a condition of term infants.[1] Although there are a number of risk factors that have been discovered by earlier research, the aetiology is still poorly understood, making it challenging to identify the population that is most at risk. The challenge of identifying newborns at risk is exacerbated by the fact that several stroke risk indicators are also present in healthy infants. [3] This study's objective is to identify any previously unknown variables and prospectively confirm stroke risk factors.

Many risk factors have been connected to perinatal stroke. smoking, Neonatal infection, hypoglycemia, and a10 min Apgar score below seven were all independent risk factors..

Methods:

This was a case-control study of term infants with perinatal stroke (gestational age >37 weeks). Three healthy controls who were matched for gestational age and birth date (7 days) were included in the comparison group for each infant who had a stroke. Infants were those who experienced an acute perinatal stroke before 28 days after birth, as determined by brain magnetic resonance imaging (MRI) and the reporting doctor. Case reports were independently verified, and MRI brain scans revealed the types of perinatal strokes (ischemic, hemorrhagic, and cerebral sinovenous thrombosis, or CSVT) that had occurred. Researchers employed multivariable logistic regression models fitted with backwards stepwise variable selection, as well as univariate odds ratios (ORs), associated 95% confidence intervals (CIs), and multivariate odds ratios (ORs).

Results:

Ninety-five percent (57/61) of the 60 perinatal stroke cases reported had several risk factors. Resuscitation at birth ($P < 0.01$), low Apgar score (7) at 1, 5, and 10 min of age ($P < 0.01$), abnormal cord blood gas ($P < 0.01$), newborn infection/sepsis ($P < 0.01$), congenital heart disease ($P < 0.01$), and hypoglycemia ($P < 0.01$) were also revealed as significant risk factors by univariate analysis. A multivariate analysis revealed the following associations: smoking during pregnancy (OR: 1.48; 95% CI: 1.09-1.99), 1-min Apgar score 7, 10-min Apgar score 7, and hypoglycemia (OR: 1.49; 95% CI: 1.07-2.06).

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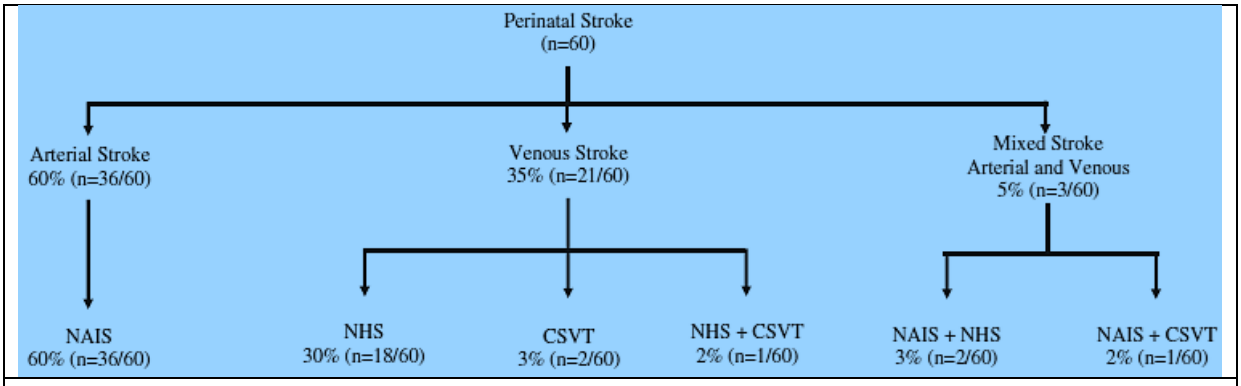

Types of perinatal stroke (n = 60). CSVT, cerebral sinovenous thrombosis; NAIS, neonatal arterial ischemic stroke; NHS, neonatal hemorrhagic stroke

Discussion:

In this study, researchers found that gestational diabetes was similar in both perinatal stroke infants and controls. Low birthweight, small and large for gestational age, and other characteristics that have been linked to risk in certain published studies did not show associations in this analysis.[3, 4] The risk of perinatal arterial ischemic stroke is significantly increased by congenital heart disease.[5] The univariate analysis of this study revealed that it was a significant risk factor, but the multivariate analysis was unable to take it into account due to missing data and a possible bias risk.

Conclusion:

This comparative investigation established neonatal infection, exposure to smoking, and 10-min Apgar scores below seven as distinct risk factors for perinatal stroke. Other risk factors were requiring an emergency caesarean section, Resuscitation during childbirth, and having abnormal cord blood gas. This research also lends credence to the idea that the pathophysiology of perinatal stroke involves a variety of prenatal, perinatal, and neonatal risk factors.

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2. Roy B, Webb A, Walker K, Morgan C, Badawi N, Novak I. Risk factors for perinatal stroke in term infants: A case-control study in Australia. J Paediatr Child Health. 2023 Feb 14.
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3. The Impact of Dietary intake and Body Mass Index on the development of Islet autoimmunity in genetically at-risk children.

Introduction:

Type 1 diabetes is caused by the autoimmune destruction of pancreatic beta cells, which results in inadequate insulin production and subsequent hyperglycemia. Type 1 diabetes, even treated with insulin replacement, is a chronic condition that necessitates a considerable amount of effort from both the patient and their caregivers.[1] In many high- and low-income countries, the incidence of type 1 diabetes in children has been on the rise, with an estimated 3% yearly increase overall, suggesting a potential involvement for a number of environmental causes. Rapid growth and obesity are environmental factors that can contribute to the development of type 1 diabetesThe purpose of this study was to use body mass index (BMI), a prespecified mediator variable, to evaluate the impact of total energy and energy-yielding macronutrient consumption on the development of islet autoimmunity in genetically at-risk children between the ages of 2 and 8 years.

A greater BMI is associated with greater total calorie consumption, which increases the chance of developing islet autoimmunity (IA).

Methods:

The study population included were 8,676 genetically at risk infants in the prospective birth cohort known as The Environmental Determinants of Diabetes in the Young (TEDDY). In order to find the environmental causes of type 1 diabetes, children were enrolled in the research before the age of 4.5 months, and they were then monitored for 15 years. Anthropometric measures and 3-day food records were taken twice every year in genetically at risk children (n = 5,084) who were autoantibody negative at age 2 and were tracked until age 8. of these 495 (or 9.7%) had IA. A mediation analysis was carried out for the exposure (energy intake) and time-varying variables (BMI zscore). Sensitivity analysis was conducted using the Cox proportional hazard approach.

Results:

Researchers discovered an indirect effect of total energy intake (estimates: indirect effect 0.13 [0.05, 0.21]), energy from protein (estimates: indirect effect 0.06 [0.02, 0.11]), energy from fat (estimates: indirect effect 0.03 [0.01, 0.05]), and energy from carbohydrates (estimates: indirect effect 0.02 [0.00, 0.04]) (kcal/day) on the onset of IA. Protein had a direct impact on the generation of glutamic acid decarboxylase autoantibodies(GADA) as well as on daily kcal intake (direct effect estimates: 1.09 [0.35, 1.56] and 72.8 [3.0, 98.0]). Energy from protein intake (kcal/day) was linked to a higher risk of GADA in the sensitivity analysis; the hazard ratio was 1.24 (95% CI: 1.09, 1.53), and the p value was 0.042.

Discussion:

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This study supports prior findings that a higher BMI is linked to the onset of islet autoimmunity and that excessive energy intake (a higher energy intake than an increased energy expenditure over time) has a negative indirect influence on the outcome.[2] The majority of previous studies have found a link between childhood overweight and obesity and a higher risk of islet autoimmunity and type 1 diabetes. These studies have used a variety of weight gain and obesity measures, including rapid weight gain, length/height-for-age, BMI, and growth velocity.[3,4]

Exposure variable	Outcome	Total effect	Direct effect Estimates (95% CI)	Indirect effect
Total energy intake (kcal)	IA positivity (≥1)	0.89 (−1.43, 2.20)	0.76 (−1.63, 2.20)	**0.13 (0.05, 0.21)**
	IAA	−0.25 (−2.47, 1.87)	−0.39 (−2.49, 1.84)	**0.14 (0.00, 0.20)**
	GADA	1.15 (−0.48, 2.28)	1.03 (−0.55, 2.22)	0.12 (−0.01, 0.26)
Energy intake from protein (kcal)	IA positivity (≥1)	0.83 (−0.41, 1.45)	0.78 (−0.47, 1.41)	**0.06 (0.02, 0.11)**
	IAA	−0.09 (−1.31, 0.91)	−0.08 (−1.31, 0.87)	0.04 (−0.03, 0.12)
	GADA	**1.14 (0.36, 1.56)**	**1.09 (0.35, 1.56)**	0.06 (−0.03, 0.14)
Energy intake from fat (kcal)	IA positivity (≥1)	0.22 (−0.32, 0.54)	0.19 (−0.35, 0.53)	**0.03 (0.01, 0.05)**
	IAA	−0.06 (−0.61, 0.38)	−0.10 (−0.64, 0.38)	0.05 (−0.04, 0.08)
	GADA	0.27 (−0.21, 0.54)	0.26 (−0.29, 0.56)	0.01 (−0.05, 0.09)
Energy intake from carbohydrates (kcal)	IA positivity (≥1)	0.06 (−0.41, 0.29)	0.04 (−0.44, 0.28)	**0.02 (0.00, 0.04)**
	IAA	−0.07 (−0.48, 0.24)	−0.06 (−0.51, 0.25)	0.03 (−0.03, 0.16)
	GADA	−0.01 (−0.30, 0.22)	−0.02 (−0.35, 0.24)	0.01 (−0.05, 0.09)

Estimates (95% conFdence interval) for total e6ect, direct e6ect, and indirect e6ect for islet autoantibody development (outcome) in children (n =5,084), using BMI z-score as the mediator in all analyses

Conclusion:

This study confirms that a greater total calorie consumption is linked to a higher BMI, which in turn raises the likelihood of developing islet autoimmunity. In addition, nutritional analysis reveals that a diet with a larger percentage of protein-based energy has a direct impact on the emergence of GADA.

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4. A case study of the multisystem inflamatory syndrome in infant associated with the Bacille Calmette-Guérin scar

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Introduction:

Coronavirus disease (COVID-19) is an infectious disease brought on by the SARS-CoV-2 virus. The chief clinical symptoms of coronavirus disease 2019 (COVID-19) include a wide range of respiratory tract infections, from an asymptomatic carrier status (15.5-20% of patients) and a mild influenza-like illness to severe interstitial pneumonia and acute respiratory distress syndrome. Many nonspecific dermatological signs might exist and represent the only sign of the infection.[1] The WHO noted a noticeable rise in Kawasaki disease frequency in nations where Kawasaki disease was uncommon during the Coronavirus Disease of 2019 (COVID-19) pandemic. Unlike ordinary Kawasaki disease, this newly identified disease tends to manifest in later years, has notable gastrointestinal symptoms, higher rates of myocarditis and coronary artery involvement, and a larger necessity for intensive care unit hospitalisation (ICU). Rarely, the Bacillus Calmette-Guerin (BCG) scar had become inflammatory during the multisystem inflammatory syndrome (MIS-C).[2] This 1-year-old child with MIS-C is the second instance of erythema and induration of the BCG scar that has been documented.

The BCG scar changes that occurred following SARSCoV-2 infection may be a defining characteristic of MIS-C, as evidenced by the MIS-C case of a 1-year-old boy with erythema and induration of the BCG scar displaying Kawasaki symptoms.

Case Presentation:

A 1-year-old boy who has no notable medical history is the patient. Yet, he had continuous contact with his parents, who had been diagnosed with COVID-19 3 weeks before to hospitalisation. The patient's initial symptoms started while the family was away on vacation. He arrived at the hospital with a two-day history of conjunctivitis, erythematous lips, nausea/vomiting, diarrhoea, and a high-grade resistant temperature. He had a temperature of 38.9°C upon evaluation, which was his highest documented temperature throughout his hospitalisation. His physical examination revealed cracked erythematous lips and mucocutaneous sores on the tongue but no cervical lymphadenopathy. On the seventh day of his hospitalisation, he had erythematous induration of his BCG scar. On the tenth day after admission, he developed a diffuse maculopapular rash on his fingers and toes. His laboratory testing on the first day of hospitalisation revealed high CRP and WBC levels. The COVID-19 polymerase chain reaction (PCR) produced a negative result. He was originally given ceftriaxone and Intravenous hydration. His CRP and WBC levels increased on the third day. He continued to have a fever despite lower peak temperatures and less frequent episodes. He had a little cardiac murmur along with a regular heartbeat. The family initially opposed to the procedure; thus, doctors could not perform the echocardiogram on this day. On the fifth day, WBC and thrombocyte levels increased while CRP and haemoglobin levels marginally declined. The family gave their permission for an echocardiogram, which revealed a silent PDA, no coronary dilating, and regular heartbeats with an EF of 72%. The levels of troponin I, BNP, and NT-proBNP were normal. He maintained on antibiotics even though his CRP levels had started to steadily drop. On the seventh day, he developed a continuing fever and erythematous induration of his BCG scar.

Repeated polymerase chain reaction (PCR) results for COVID-19 remained negative, however IgG antibodies to SARS-CoV-2 were detected by serological testing and were found to be positive. Both his chest x-ray and abdominal USG were normal. A few echocardiograms revealed no new findings. His ongoing fever, together with other clinical symptoms, signs, and laboratory findings, led to the diagnosis of MIS-C. The use of antibiotics was stopped, and IVIG treatment was suggested but first rejected by the family. The patient's family gave their permission for him to undergo one 10-hour infusion of IVIG at a dose of 2g/kg on the seventh day after his hospitalisation. Contrary to what doctors expected, his fever and other clinical signs persisted. The family rejected the expected second dose. He was switched to methylprednisolone medication at 2 mg/kg per day and anti-inflammatory aspirin therapy at 80 mg/kg per day on the ninth day. After 48 hours of combination therapy, his temperature started to go down and the BCG scar began to diminish visibly. On the 14th day, the scar totally disappeared. On the 14th day after hospitalisation, methylprednisolone and aspirin medication were stopped since the patient's symptoms had subsided. He had aspirin medication for six weeks at a dose of 5mg/kg/day before being discharged on the fifteenth day after hospitalisation. On his return to his home country, the patient underwent an uneventful follow-up in an outpatient clinic. Three months following his discharge, doctors arranged a follow-up consultation in their clinic.

Day of admission	Day 1	Day 3	Day 5	Day 10	Day 15 (Discharge)
Leukocyte (× 10^3/μL)	19.7	21.3	22.9	13.6	11.5
Neutrophil (× 10^3/μL)	9.24	10.2	11	2.94	2.5
Lymphocyte (× 10^3/μL)	9.31	9.11	9.37	8.58	7.6
Hematocrit (%)	30.3	30.4	27.6	27.8	28.3
Hemoglobin (g/dL)	10.1	10.2	9.29	9.02	9.04
Platelets (× 10^4/μL)	434	442	614	1373	965
Albumin (g/dL)	4.2	4.1	3.9	3.4	3.8
Troponin I (pg/mL)	0.01	0.01	0.01	0.01	0.01
CRP (mg/L)	81.8	178.1	163.1	26.7	8.4
Aspartate aminotransferase (IU/L)	35	31	23	55	28
Alanine aminotransferase (IU/L)	10	9	6	24	19
Blood urea nitrogen (mg/dL)	5	7	7	9	7
Creatinine (mg/dL)	0.42	0.44	0.34	0.4	0.39
Sodium (mEq/L)	134	135	139	138	137
Potassium (mEq/L)	4.5	4.5	4.9	5.5	4.5
Procalcitonin (ng/mL)	0.72	2.67	2.45	0.75	0.45

Time course of laboratory findings

Discussion:

Pediatric infammatory multisystem syndrome temporally linked with SARS-CoV-2 infection (PIMS-TS) in Europe and multisystem infammatory syndrome in children (MIS-C) in the United States are the terms used to describe symptoms that are Kawasaki-like following SARS-CoV-2 infection.[2] Children with Covid-19 infection often have milder symptoms and get less testing than adults. The precise frequency of MIS-C in children who have SARS-CoV-2 infection is unknown as a result. Nonetheless, it appears to be a very uncommon COVID-19 consequence in children, affecting less than 1% of those with confirmed SARS-CoV-2 infection.[3]

Conclusion:

Although it's not a diagnostic criterion for Kawasaki, clinically, 30–50% of patients have a reaction at the location of the BCG injection. Researchers describe the case of a 1-year-old child who was diagnosed with MIS-C and who had erythema and induration of the BCG scar at the time of presentation. Additional research is required to investigate this clinical presentation, particularly in nations with BCG vaccination programmes, and to identify the causes of MIS-C.

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