Pedia Companion

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Pedia Companion Newsletter

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Dear Doctor,
Greetings from Micro Labs Limited. We are happy to bring you "PEDIA COMPANION" which contain latest and interesting news in the field of Paediatrics.

This issue contains:

1. **Response to IL1-blockade and appropriateness of the standard of care in paediatric recurrent pericarditis**
2. **The study on lactate/albumin ratio as a predictor of in-hospital mortality in critically ill children.**
3. **A retrospective cohort study on the significance of screening for additional anomalies in patients with anorectal malformations.**
4. **A Case Report of Sickle Cell Disease in an Infant**

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. Response to IL1-blockade and appropriateness of the standard of care in paediatric recurrent pericarditis

Introduction:

A clinical syndrome known as recurrent pericarditis (RP) is characterised by recurrent attacks of acute pericardial inflammation. The morbidity may be severe, particularly in children and adolescents. RP has a number of possible aetiologies, the majority of which are autoimmune or auto inflammatory in nature.[1] Non-steroidal anti-inflammatory medications (NSAIDs) and low dosages of colchicine are recommended as the first-line treatments for acute pericarditis by the European Society of Cardiology (ESC). In individuals who do not respond to NSAIDs, guidelines recommend for the use of low dosages of steroids in combination with colchicine. In non-responder patients, a number of immunosuppressive medications were recommended as a third-line treatment, despite the fact that there was insufficient evidence of their efficacy.[2] In a cohort of paediatric patients with recurrent pericarditis (RP) who were receiving anti-IL-1 treatment, the purpose of this study was to examine the agent and dosage used as first-line therapy, the long-term efficacy of IL1-blockers, the proportion of patients who experienced a drug-free remission, and the presence of variables associated with drug-free remission.

The majority of paediatric patients with recurrent pericarditis who required IL-1 blockage were treated inadequately with first-line medications.

Methods:

A nationwide survey of patients with recurrent idiopathic pericarditis treated with IL1-blockers was conducted in Italian paediatric cardiology and rheumatology referral units in 2019. According to ESC recommendations, pericarditis was diagnosed when at least two of the following five signs or symptoms were present: (1) typical pericardial chest pain; (2) pericardial friction rub; (3) typical electrocardiographic changes (widespread ST-segment elevation or PR-segment depression); and (4) pericardial effusion on echocardiography. Data were gathered from the patient records. Using bivariate logistic regression analysis, the annualised relapse rate (ARR) was utilised to assess the effectiveness of the treatment.

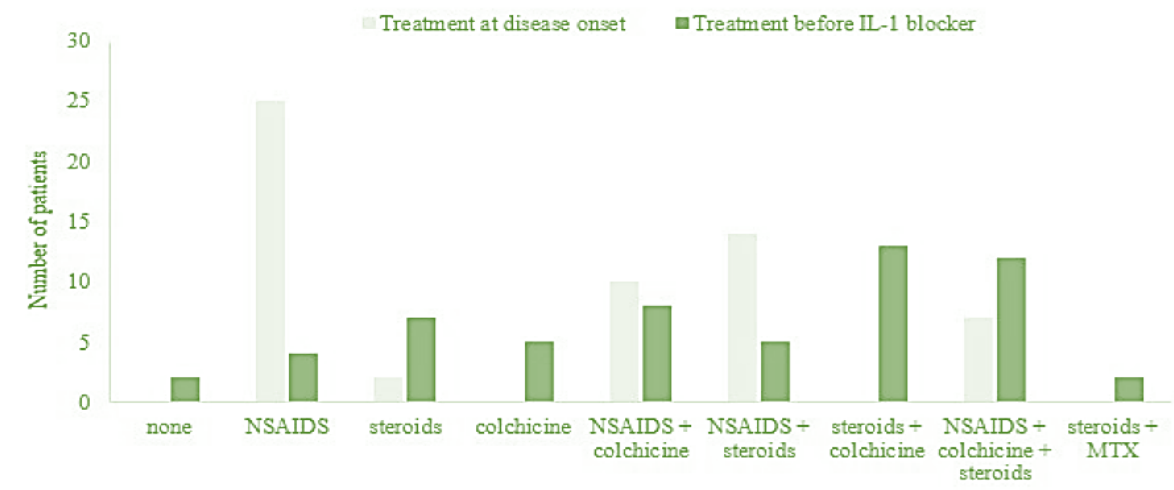
Results:

This was a multicentre and retrospective study, which had 58 patients treated between 2008 and 2018 (with an average follow-up of 2.6 years), 14 out of 56 patients who weren't respond to first-line medications had an inadequate dosage. 57 individuals had anakinra medication; the ARR before and during daily treatment was 3.05 and 0.28,

respectively (p <0.0001); an increase to 0.83 was seen following the reduction or termination of treatment (p<.0001). Canakinumab was switched from anakinra in five patients, and there was a slight increase in ARR (0.49 vs 1.46), but there was no statistically significant difference (p=0.215). Only 9 out of 58 patients had stopped all therapies at the most recent checkup. The only factor linked with drug-free remission was a shorter time of anakinra treatment due to the limitations of a retrospective investigation and the heterogeneity of the patients involved in the trial.

Discussion:

Prior to the use of IL-1 blockers, the majority of patients receiving traditional treatment for RP in children received insufficient doses of NSAIDs, particularly the most widely used medication, ibuprofen. Colchicine experienced the similar outcome, demonstrating the necessity to take into account NSAID and colchicine dosage in children before writing off the medications as ineffectual.[2] With regard to canakinumab's potential usefulness as an alternate anti-IL-1 therapy for recurrent pericarditis, this study adds to the body of evidence. A recent case of an idiopathic RP child who experienced anaphylaxis after using anakinra was recently described in paediatric patients. High dosages of canakinumab in conjunction with colchicine were successful in maintaining clinical remission in this instance, but in two other instances, this medication failed to reduce disease activity.[3,4]



Treatment of the patients included in the study at disease onset (first 28 days from the beginning of symptoms), at the time of initiation of anti-IL1 treatment

Conclusion:

This study demonstrates that the majority of paediatric patients with RP who required IL-1 blockage had inadequate management from first-line medications. This trial supports the efficacy of anakinra, but few patients experienced drug-free remission. The

differing rates of anakinra and canakinumab responses could indicate to a potential role for IL1 in the pathophysiology of RP.

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2.The study on lactate/albumin ratio as a predictor of in-hospital mortality in critically ill children.

Introduction:

In critically ill patients admitted to an ICU, an elevated lactate/albumin ratio was strongly linked to a poor prognosis. The lactate/albumin ratio may be a valuable, independent, and easily accessible indicator for risk stratification in critically ill patients.[1] It might be challenging for doctors in paediatric intensive care units (PICU) to manage critically ill patients with high mortality because they need to find the right prognostic biomarkers. Critically ill people can be accurately categorised using the lactate/albumin (L/A) ratio. But it's still unknown how the L/A ratio affects the prognosis of seriously ill children.[2] This study evaluated the predictive efficacy of the L/A ratio in predicting in-hospital mortality in critically ill patients from the PICU.

The L/A ratio was a clinical tool that was more accurate than lactate level alone for predicting in-hospital mortality in critically ill children.

Methods:

This retrospective single-center study. From the paediatric intensive care (PIC) database, clinical information on 8,832 critically ill patients between the ages of 28 days and 18 years was collected. The in-hospital mortality rate served as the primary outcome.The clinical information collected included details on the patient's characteristics, vital signs, laboratory findings, therapies (including the use of vasopressors such dopamine and epinephrine), and mortality results. When the patient was admitted to the PICU, the first blood sample was used to collect all laboratory data.

Results:

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In non-survivors, the L/A ratio was higher than in survivors (P<0.001). The link between the L/A ratio and in-hospital mortality was shown to be statistically significant by logistic regression (OR 1.44, 95% CI 1.31- 1.59, P<0.001). In comparison to lactate level alone, the L/A ratio had a higher AUROC for predicting in-hospital mortality (0.74 vs 0.70, P<0.001). The L/A ratio and in-hospital mortality were significantly correlated in the age and primary disease categories, according to stratification analysis (P< 0.05).

	Model I			Model II		
	OR	95% CI	P	OR	95% CI	P
L/A ratio	2.02	(1.86, 2.19)	< 0.001	1.44	(1.31, 1.59)	< 0.00
Lactate	1.27	(1.23, 1.30)	< 0.001	1.16	(1.12, 1.21)	< 0.00
Albumin	0.90	(0.89, 0.91)	< 0.001	0.95	(0.93, 0.97)	< 0.00

Model I: non-adjusted model

Model II: adjusted for age, sex, ICU type, bacteremia, vasopressors use, WBC, PLT, hemoglobin, ALT, CK-MB, sodium, INR and CRP

OR odds ratio, *CI* confidence interval

Relationship between lactate/albumin (L/A) ratio, lactate, albumin and in-hospital mortality in diferent models of multivariable logistic regression

Discussion:

Early prediction of a critical illness' prognosis facilitates accurate stratification of various critical illnesses according to disease severity and allows for the selection of appropriate treatments. The results of the current study showed that for critically ill children and adolescents between the ages of 28 days and 18 years, the L/A ratio is a highly valuable predictive marker of paediatric ICU in-hospital mortality. In severely ill children, the non-survival group had greater L/A ratio, higher lactate, and lower albumin levels than the survivor group did. These developments, according to several research, were linked to a poorer prognosis for adult critical care patients.[3,4] This suggests that in addition to lactate, albumin, and the L/A ratio, prognosis may also be significantly predicted in critically ill children.

Conclusion:

In conclusion, the L/A ratio is a valuable predictor with excellent predictive performance for in-hospital mortality in critically ill children. Nevertheless, more prospective studies need be carried out to test the L/A ratio's ability to predict critical disease, as this study was retrospective in nature.

References:

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3.A retrospective cohort study on the significance of screening for additional anomalies in patients with anorectal malformations

Introduction:

A number of illnesses commonly referred to as imperforate anus fall under the umbrella term anorectal malformation. In patients with this diagnosis, the anal opening does not function normally; instead, a fistulous tract opens onto the perineum anterior to the anal muscle complex or onto nearby anatomical structures.[1] Additional defects within the VACTERL-association [vertebral (V) anorectal(A) cardial (C) tracheoesophageal (TE) renal and radial (R) and limb(L)] anomalies can manifest in children with anorectal malformations (ARM). For early identification and possible treatment, routine screening is crucial. However, there is a lack of homogeneity in screening procedures, and the literature has only described small cohorts. This study's objective was to evaluate and provide a summary of a very large cohort of ARM patients who had VACTERL screening during the newborn stage.

Most anorectal malformation patients (77%), who later progressed to 86%, had thorough screening to find other anomalies. However, around a quarter of individuals were not examined, which could have led to the loss of potential additional anomalies that could have had negative long-term consequences.

Methods:

It was a retrospective mono-center cohort study. Included were all newborns with ARM identified and tested for other abnormalities born between January 2000 and December 2020. Full screening included a physical examination for limb abnormalities, esophageal atresia, and ARM, as well as x-ray and ultrasound of the spine, heart, and renal ultrasonography. The EUROCAT definitions served as the predefined criteria for VACTERL classification.

Results:

A total of 216 patients were enrolled, 167 (77.3%) of whom had comprehensive VACTERL-screening (66% from 2000 to 2006, 82% from 2007 to 2013, and 86% from 2014 to 2020). At follow-up, the median age was 7.0 years (IQR 3.0e12.8). Additional abnormalities were found in 103/167 patients (61.7%). 35/216 patients, or 16.2%, met

the requirements for a type of VACTERL-association. There was evidence of a genetic aetiology or syndrome in 37/216 patients (17.1%).

Type of ARM	Total screening		Vertebral screening		Cardial screening		Renal screening	
	No	Yes	no	yes	no	yes	no	yes
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Recto-perineal fistula, n = 96	24 (25.0)	72 (75.0)	14 (14.6)	82 (85.4)	15 (15.6)	81 (84.4)	5 (5.2)	91 (94.8
Recto-vestibular fistula, n = 43	9 (20.9)	34 (79.1)	2 (4.7)	41 (95.3)	8 (18.6)	35 (81.4)	0	43 (100.
Recto-urethral fistula, n = 36	4 (11.1)	32 (88.9)	1 (2.8)	35 (97.2)	3 (8.3)	33 (91.7)	0	36 (100.
Recto-vesical fistula, n = 6	2 (33.3)	4 (66.7)	1 (16.7)	5 (83.3)	1 (16.7)	5 (83.3)	0	6 (100.0
Cloaca, n = 13	3 (23.1)	10 (76.9)	1 (7.7)	12 (92.3)	3 (23.1)	10 (76.9)	0	13 (100.
Anal stenosis, n = 3	3 (100.0)	0	2 (66.7)	1 (33.3)	2 (66.7)	1 (3.3)	1 (33.3)	2 (66.7)
Imperforate anus without fistula, n = 12	2 (16.7)	10 (83.3)	1 (8.3)	11 (91.7)	2 (16.7)	10 (83.3)	0	12 (100.
Rare/regional fistula, n = 6	2 (33.3)	4 (66.7)	2 (33.3)	4 (66.7)	2 (33.3)	4 (66.7)	1 (16.7)	5 (83.3)
Type of fistula unknown, n = 1	0	1 (100.0)	0	1 (100.0)	0	1 (100.0)	0	1 (100.0
Total, n = 216	49 (22.7)	167 (77.3)	24 (11.1)	192 (88.9)	36 (16.7)	180 (83.3)	7 (3.2)	209 (96.

Screening requiring additional imaging studies according to type of ARM.

Discussion:

In the current study sample of 216 ARM patients, 77% of the patients received comprehensive screening in accordance with the Amsterdam UMC screening standard to find any potential related anomalies. The screening percentages significantly grew over time.[2]In this study, 23% of the patients who were included did not receive a complete screening for other anomalies. This percentage is low when compared to other cohort studies that were comparable, since some authors found that 40 to 89% of the population had insufficient screening. There is frequently no standard screening procedure in place for these studies. [3,4] This study's screening protocol has led to a high percentage of fully screened patients, which increased over time to 86% in 2014–2020. This can be explained by natural progress over time, an increase in cardiac and genetic screening over time

Conclusion:

The majority of ARM patients (77%), which increased to 86% with time, had thorough screening to find other anomalies. However, just about 25 percent of individuals were examined, potentially missing significant additional anomalies that could have negative long-term effects. Genetic or VACTERL-association forms were discovered in 16% and 17% of cases, respectively. This study emphasizes the significance of regular screening.

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4.A Case Report of Sickle Cell Disease in an Infant

Introduction:

Sickle cell disease (SCD) is a term for a group of genetic conditions that affect the way that red blood cells carry haemoglobin (RBCs). It is brought on by a beta globin chain autosomal recessive mutation that codes for defective haemoglobin S rather than haemoglobin A.[1] Sickle cell disease (SCD) is the most prevalent hereditary disease and a multisystem disorder. Vasoocclusive events can harm any organ system, including the bones, spleen, liver, brain, lungs, kidneys, and joints, causing tissue ischemia, acute and persistent discomfort, and organ damage.[2] The uncommon early-infancy presentation of SCD is discussed in this study. Here is a report of SCD at 2 months old with severe symptoms necessitating hospitalisation.

Expanding and sustaining newborn screening programmes for Sickle cell disease (SCD) in developing countries could help doctors and parents in making plans for early treatment, appropriate prophylaxis, and improved management of SCD complications.

Case Presentation:

A 10-week-old boy was sent to the hospital after having a history of (i) coughing for two weeks before to the visit, (ii) sneezing, (iii) refusing to breastfeed, (iv) intermittent fevers, and (v) general irritability and being challenging to console. His medical history showed that he was HIV exposed (HEI) and had been receiving neonatal prophylaxis from birth (Nevirapine 1.5 mL OD, Zidovudine/lamivudine 1.5 mL BD, Cotrimoxazole 2.5 mL OD). HIV DNA PCR testing was performed at 6 weeks, and the results were negative. The infant was born naturally through vaginal delivery at term, weighed 3.8 kg at birth, was exclusively breastfed, and was immunised according to age. There was no history of tuberculosis or positive tuberculosis contact in the family. Before being admitted to the hospital, the child had already received paracetamol and nasal saline drops at home, with little improvement. The infant appeared ill, was irritable, pale, febrile, and had a flaring nose upon examination. The infant had a temperature of 38.8°C, weighed 5 kg, had a heart rate of 142 beats per minute, a respiratory rate of 38 beats per minute, and an oxygen saturation level of 97% on room air. A chest exam revealed bilateral anterior coarse crepitations. The results of all other systemic tests were normal. Prior to investigations, an impression of pneumonia and severe anaemia due to malaria was formed, and the child was sent to the University Teaching Hospital for additional care. Blood tests showed bicytopenia

(Hemoglobin, HB 3.7 g/dL, White cell count, WCC 5.2x10^9 /L, Platelets 143x10^9 /L), red cell abnormalities, including sickle cells, target cells, poikilocytosis, anisocytosis, microcytosis, hypochromia, and mild macrocytic anaemia, as well as elevated liver function tests (bilirubin 38.7 mol/L, AST 43.3 IU/L, and protein 67.2 g/L). Blood testing revealed common levofloxacin, moxifloxacin, clindamycin, and linezolid susceptibility in Staphylococcus haemolyticus and Streptococcus pneumoniae. Additionally, ciprofloxacin, erythromycin, tetracycline, and co-trimoxazole were all ineffective against Staphylococcus haemolyticus. The findings of the haemoglobin electrophoresis test showed a 90.5% HbS percentage and a 2.9% HbF percentage. Following an assessment of the laboratory findings, sickle cell disease with sepsis and pneumonia was identified. He received two blood transfusions containing 160 cc of packed red blood cells, as well as oral analgesics, cefotaxime 200 mg IV TDS, and ciprofloxacin 100 mg PO BD, as well as intravenous crystalloid fluids and broad-spectrum antibiotics (paracetamol 80 mg PO TDS). The patient continued to recover successfully, with the cough and fever fading away and the HB level returning to 8.8 g/dL. Thirteen days after being admitted, he was sent home with haematinics (folic acid 5 mg daily) and medication to prevent malaria (deltaprim 1/4tab weekly). The child was readmitted two months after being released with a one-day history of fever, restlessness, and excessive crying. An irritable infant with oral thrush, extreme pallor, but no jaundice, was discovered during the examination. At the presentation, the following anthropometric data and vital signs were noted: weight 5.8 kg, temperature 37.4 °C, heart rate 165 b/min, respiratory 56 b/min, and oxygen saturation (95% on room air). With the exception of the child crying whenever he was raised, all other systems were normal. He was taking folic acid 5 mg OD, deltaprim 1/4 tab weekly, and his HIV post-exposure prophylaxis medicine in addition to these other medications. At this presentation, laboratory findings revealed significant anemia (HB 2.8 g/dL) and leucocytosis (WCC 56.2 x 109 /L), and MCV was 93.6 FL. The child was treated for vaso-occlusive crisis (VOC) with sepsis in SCD and oral candidiasis during the second hospitalization. He received oxygen through nasal prongs, intravenous fluids, a transfusion of two units of packed red blood cells (160 cc), 200,000 iu of Nystatin every other day, 290,000 iu of Benzyl penicillin every other day, and 2.5 mL of paracetamol syrup. The child's haemoglobin level was 9.2 g/dL when discharged after a 5-day admission. After receiving a second discharge, the child went back to the hospital two weeks later with a three-day history of weakness and decreased activity. His oxygen saturation on room air was 86%, his temperature was 37.9°C, and his pulse rate was 168 beats per minute. He was very pale, in discomfort with his breathing, and conscious. Other systems functioned normal. The child's laboratory tests during this admission revealed that he had malaria (P. falciparum) on RDT, HB 2.2 g/dL, WCC 50.9 x 10^9 /L, and MCV 90.1 FL (Table 4). He was given treatment for malaria and severe anaemia (hemolytic crisis) in SCD during his third admission. He was given two units of packed red blood cells (160 cc), Artemether-Lumefantrine (one tablet at first, one after eight hours, and one

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more tablet after two days), folic acid (5 mg) by mouth every other day, and deltaprim (one-fourth tablet by mouth) once a week. On the seventh day after his admission, he was discharged with an HB of 12.5 g/dL.

Infant HIV DNA PCR:	**Negative**			
Full Blood count:				
White cell count	5.18×10^9/L			
Red blood cells	1.36×10^{12}/L			
Haemoglobin	3.7 g/dL			
Haematocrit	11.9%			
MCV	87.5 fL			
MCHC	31.1 g/dL			
Platelets	143×10^9/L			
Differential count:				
Neutrophils	45% 1.99×10^9/L			
Lymphocytes	50.1% 2.20×10^9/L			
Sickling test:	Positive			
Peripheral blood smear	Red cell morphology – Sickle cells, anisocytosis, poikilocytosis, microcytosis, hypochromic, schistocytes, target cells			
White cell morphology	Normal			
Platelet morphology	Thrombocytopenia noted on film			
Blood culture				
Organism identification	*Streptococcus pneumoniae* and *Staphylococcus hemolyticus*			
Antibiotic susceptibility	STRPN	STAHA	STRPN	STAHA
Ciprofloxacin	S	R	Quinupristin/dalfopristin	S
Levofloxacin	S	I	Nitrofurantoin	S
Moxifloxacin	S	S	STRPN, *Streptococcus pneumoniae*	
Erythromycin	S	R	STAHA, *Staphylococcus* haemolyticus	
Clindamycin	S	S	[S]usceptible [R]esistant [I]ntermediate	
Linezolid	S	S		
Tetracycline	S	R		
Co-trimoxazole	R	R		
Gentamicin		S		

Laboratory Results at First Admission

Discussion:

According to this report, the child initially showed signs of a pneumococcal infection. Even among individuals who have received the pneumococcal conjugate vaccine, invasive pneumococcal disease (IPD) has primarily been observed in children with SCD (PCV).[3] According to a comprehensive analysis of IPD among children with SCD, 61% of cases were septicemia, 39% were LRTI, and 9% were meningitis.[4] In a similar manner, Olufunke et al. showed in another study that children with SCD who had a good response to penicillin and strains not covered by PCV had a considerably greater incidence of the condition.[3] The infant in this instance responded nicely to broad-spectrum antibiotics and was unharmedly discharged from the hospital.

Conclusion:

Although unusual, the early onset of sickle cell disease and severe anaemia in this infant recognizes the significance of newborn screening programmes in endemic areas, particularly in developing nations. Regular SCD screening during the newborn or infant period may help to enhance clinical outcomes by promoting proactive care and disease management. Regardless of family history, attending clinicians should consider screening for SCD in infants who come with severe anaemia as early as 2 months of age.

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