Pedia Companion

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A study on assessing Angiopoietin-like protein 3 as a novel biomarker for nephrotic syndrome in children

Introduction-

Angiopoietin like protein 3 serves as a biomarker to identify the degree of nephrotic syndrome in children.

Nephrotic syndrome (NS) is characterized by presence of nephrotic range proteinuria, edema, hyperlipidemia, and hypoalbuminemia. The glomerulus, a highly specialised kidney structure, ensures that plasma is selectively ultra-filtered so that vital proteins are kept in the blood[1]. The two most typical causes of nephrotic syndrome in children are focal segmental glomerulosclerosis (FSGS) and idiopathic minimal change disease (MCD)[2]. In this study, the severity of the patients' diseases was evaluated along with the link between the levels of Angiopoietin-like protein 3 (ANGPTL3) in serum and urine of patients with nephrotic syndrome and proteinuria.

Methods –

In this prospective study, a total of 200 NS patients and 80 healthy controls were included. Patients with primary nephrotic syndrome (PNS, n-144) and those with NS with other causes (n-56) were separated based on the aetiology of NS. In order to measure the amount of ANGPTL3 using an ELISA (Enzyme linked immunosorbent assay), patients provided a total of 280 blood samples and 244 urine samples.

Results –

Results showed that ANGPTL3 levels in serum showed increased levels (Serum ANGPTL3: 62.113 µg/L vs. 47.466 µg/L) and in urine also there was an increased levels of ANGPTL3(0.0238 vs 0.0003ng/g) (Fig.1).

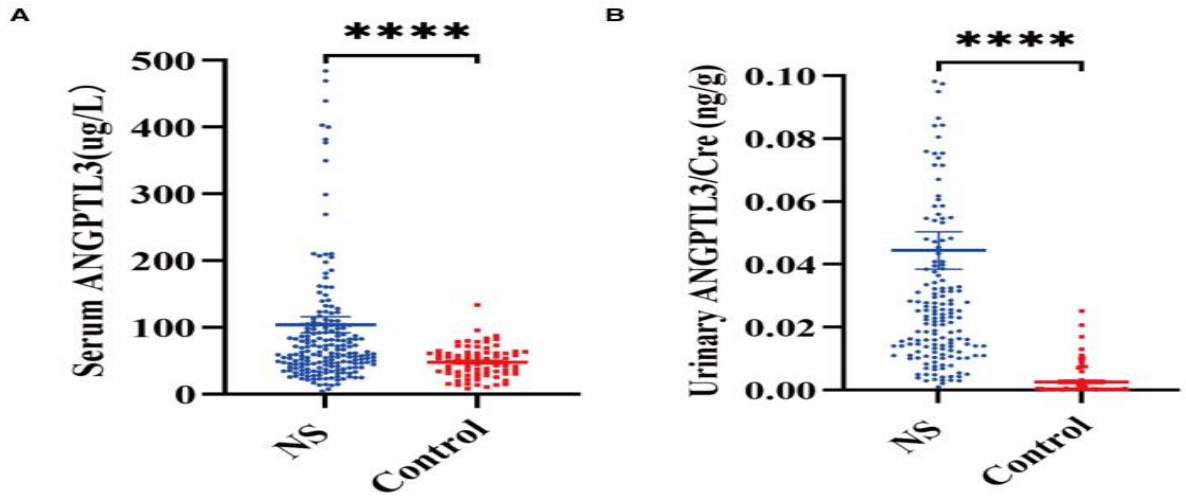

Fig-1. Comparison of ANGPTL3(A)- serum ANGPTL3 and (B) urine ANGPTL3 of NS patients and controls

Further analysis was made on protein positive NS patients and the results showed that serum and urinary ANGPTL3 may be helpful biomarker that distinguish NS patients with urine protein from control group. Serum ANGPTL3 and urinary ANGPTL3/Cre(Creatinine) expression were significantly elevated during the initial phase of NS, which was characterised by massive proteinuria, and decreased during the remission phase, when urinary protein decreased and returned to normal. As a result, the level of urine protein leakage in NS patients can be utilised as a marker to assess the disease's severity. Positive correlations were found between urine ANGPTL3/Creatinine and total cholesterol (TC), triglycerides (TG), and 24hour quantitative urinary protein (24h UPRO). In NS patients, a multivariate linear regression analysis revealed an independent relationship between urinary ANGPTL3/Cre and urinary PRO/CR and serum ALB (Albumin).

Discussion –

In this present study ANGPTL3 was identified as a diagnostic biomarker and indicator for severity of NS disease. Proteinuria is the main clinical findings in NS. It also showed that ANGPTL3 levels in serum and urine was positively correlated with TC level, TG level, PRO/Cre, 24h UPRO levels and negatively correlated with serum albumin in NS patients[1]. A study by Jiang S et al., says that ANGPTL3 is a potential biomarker to identify NS. It also showed ANGPTL3 causes podocyte injury through increasing podocyte movement and permeability eventually leading to glomerular disease and proteinuria. It also showed that ANGPTL3 is associated with the lipid metabolism[3].

Conclusion –

The study concludes that ANGPTL3 is correlated with proteinuria and serves a biomarker to assess the severity of NS in children.

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A study to evaluate relationship between Bronchopulmonary dysplasia grade and adverse neurodevelopmental risks in preterm infants born less than 30weeks of gestation

Pre-term infants with Bronchopulmonary dysplasia are at the risk of developing neurodevelopmental impairments.

Introduction –

Bronchopulmonary dysplasia(BPD) most prevalent respiratory condition affecting infants born very preterm. A very preterm lung exposed to many pathogenetic noxae develops the heterogeneous illness known as bronchopulmonary dysplasia[1]. Due to exposure to numerous prenatal and postnatal variables, BPD affects preterm children who are born at fewer than 32 weeks of gestation. BPD causes poor parenchymal and vascular growth and forces the immature lung to develop early[2]. The purpose of the current study is to assess the likelihood that preterm infants delivered at less than 30 weeks of gestation will experience unfavourable neurodevelopmental outcomes for each BPD grade.

Methods –

This is a retrospective study carried out on infants born less than 30weeks of gestation and had a respiratory data available at 36weeks post menstrual age (PMA) and who received formal neurodevelopmental assessment. A total of 250 infants were included in this study, out of which 89(35.6%) were graded as No BPD, 87(34.8%) as Grade-1, 65(20.6%) as Grade-2 and 9(3.6%) as Grade-3. Primary endpoint is to evaluate bronchopulmonary dysplasia in preterm infants. Descriptive analysis and regression models were used to evaluate the study.

Results- As the BPD grade increased, unfavourable neurodevelopmental outcomes, late pulmonary hypertension, small for gestational age (SGA), and dexamethasone administration became increasingly prevalent (fig.1).

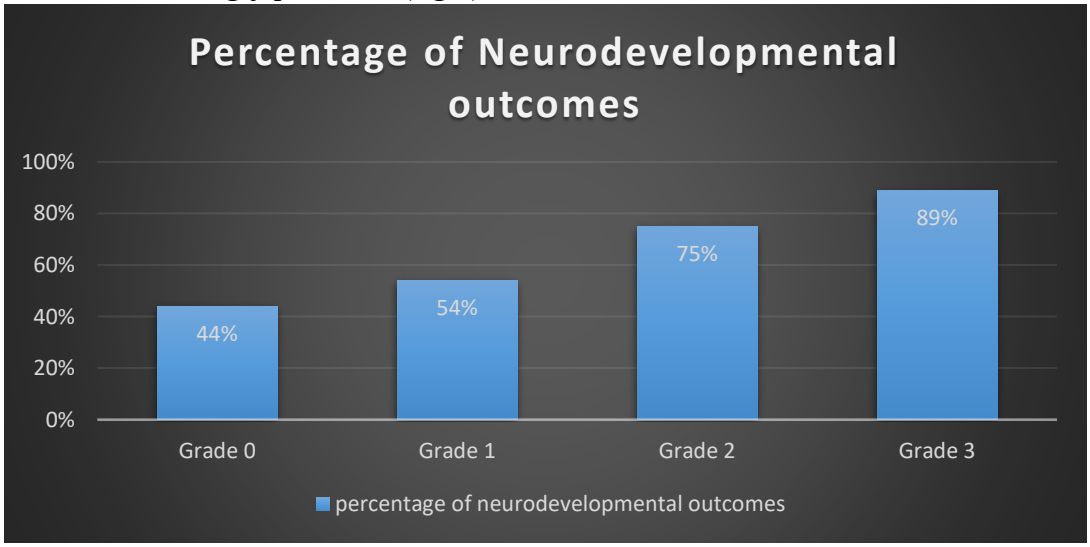

Fig.1 – percentage of neurodevelopmental outcomes in pre-term infants

When compared to BPD Grade 0, univariable logistic analysis revealed that BPD Grades 2, 3, but not Grade 1, were found to be substantially related with a worse composite

neurodevelopmental outcome. Additionally, it demonstrated a link between dexamethasone exposure and poor neurodevelopmental outcomes and birth gestation. After controlling for birth gestation and dexamethasone exposure, multivariable logistic analysis revealed that BPD Grades 2 and 3 remained strongly related with poor neurodevelopmental outcomes, with odds increases of 2.7 and 7.2-fold, respectively. According to a domain-specific analysis of the Bayley Scales for Infant and Toddler Development (BSID), higher grades were linked to lower scores in the cognitive, gross motor, and fine motor domains.

Discussion –

This study revealed that Grade 2 and 3, but not Grade 1 BPD were significantly and independently associated with an adverse neurodevelopmental outcome. Higher grades of BPD were associated with lower scores in cognitive, gross motor and fine motor domains[2]. A retrospective study by Gallini F et al., assessed the contribution of severity of BPD on neurodevelopmental outcomes and the results showed that infants with moderate to severe BPD are the risk of cognitive impairment[3]. Another study showed that 31% of the study's infant population had neurodevelopmental impairment and factors associated were low gestational age, low birth weight[4].

Conclusion – The study concludes that risk of neurodevelopmental outcomes increases with the increasing BPD grade.

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A study to evaluate association between cortisol levels and neonatal pain exposure in children born very preterm at age 18 months

Cortisol levels are associated with neonatal pain/stress and neurodevelopmental outcomes in infants born very pre-term

Introduction –

Cortisol is considered as the primary stress hormone in humans. In infants born very preterm, exposure to pain/stress is related to altered levels of cortisol from infancy to school age. In the Neonatal intensive care unit (NICU), early studies of pain/stress reactivity that lower cortisol reactivity to stress at 32 week's postmenstrual age was associated with higher number of invasive procedures since birth, after accounting for confounders such as early illness severity[1]. Very preterm babies spend their first few weeks to months requiring critical care in the NICU, when the brain is still being programmed and their stress response systems are still maturing[2]. The study aims to find the association between cortisol levels and neonatal pain exposure.

Methods –

This study is a longitudinal prospective cohort study carried out on 187 children's which includes 91 born at extremely low gestational age(ELGA), 58 very low gestational age(VLGA) and 38 healthy full term infants. Primary outcome is to evaluate cortisol levels in pre-term children and secondary outcome is to evaluate neurodevelopmental outcome associated with cortisol levels.

Results –

Results in cohort 1 found that 18 months corrected age (CA), children born ELGA, and VLGA had higher pre-test cortisol levels and greater neonatal pain exposure was seen among pre-term infants. In cohort 2 it was found that children born VLGA displayed higher pre-test cortisol levels than full term (FT) and greater cortisol output was related to more anxiety/depressive behavior's in children born VLGA(fig1).

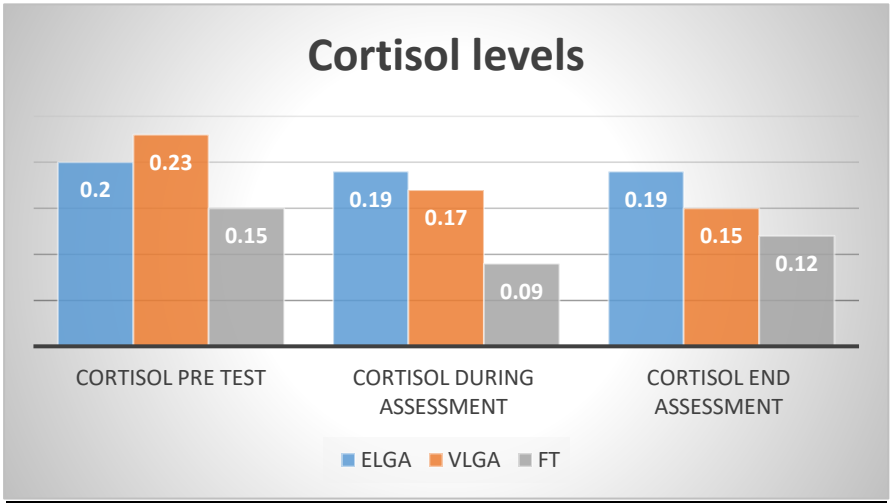

Fig.1 cortisol levels in infants born ELGA, VLGA and FT

In comparison with cohort 1, the children born ELGA in cohort 2 were less exposed to neonatal pain/stress, mechanical ventilation, and morphine. It was found that cortisol levels were related to neonatal pain/stress exposure in both cohorts. Hence children born extremely preterm showed altered HPA axis activity which is related to poorer neurodevelopmental and behavioral outcomes.

Discussion –

In this study children born extremely low term showed altered levels of HPA axis activity and responsiveness to cognitive challenge. In both cohort groups cortisol levels were elevated. While taking consideration of cohort 1 and cohort 2, cohort 2 group had less exposure to neonatal pain and had less elevated levels of cortisol[2]. A study Olszewska M et al., showed that increase in cortisol levels were seen in response to painful stimulus in very pre-term neonates[3]. Another retrospective study by Giordano V et al. revealed that neonatal pain exposure was linked to altered neurodevelopmental outcomes in infants born very preterm, and pain management should be taken into consideration to lower risk of neurodevelopmental outcomes[4].

Conclusion –

The study concludes that in infants born very pre-term cortisol levels are associated with the neonatal pain and altered HPA activity and responsiveness to cognitive challenge.

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A case report on secondary antiphospholipid syndrome with adrenal insufficiency as a rare manifestation

Introduction –

In children, secondary antiphospholipid syndrome manifests rarely as adrenal insufficiency. Antiphospholipid syndrome should be considered when hematologic problems like thrombosis are present.

A consistently positive antiphospholipid antibody (aPL) and pregnancy morbidity are two features of the acquired, systemic autoimmune illness known as antiphospholipid syndrome (APS). This syndrome known as paediatric APS if it is appearing before the age of 18. APS can be classified as primary (PAPS) when it manifests alone or secondary (SAPS) when it coexists with another autoimmune disorder[1]. These patients may experience adrenal insufficiency (AI) in the context of vascular conditions such as thrombosis and adrenal gland hemorrhage[2]. This case provides details on a child's antiphospholipid syndrome due to adrenal insufficiency.

Case presentation –

A 15 years old female patient presented to the endocrinology clinic with the complaints of irritability, abdominal pain, vomiting, salt craving and right thigh pain. Later patient was admitted to the hospital due to dyspnea, cough and fever with diagnosis of pneumonia and lung hydatid cyst. The left lower lobe of the chest showed a subpleural cystic formation spanning around 32×22mm, along with mild to severe bilateral pleural effusion. A hydatid cyst was confirmed by ELIZA. Surgery was necessary due to a burst infected hydatid cyst. Preoperative laboratory parameters were abnormal and surgery was cancelled and mebendazole was started. The treatment was successful and was discharged. Further patient was presented with hypotension, tachycardia, fever and generalized abdominal pain. Significant hyperpigmentation was seen in buccal mucosa, mouth, and extremities. Patient had limping. Edema and swelling on right lower extremities was seen (fig.1), for management patient was admitted to hospital.

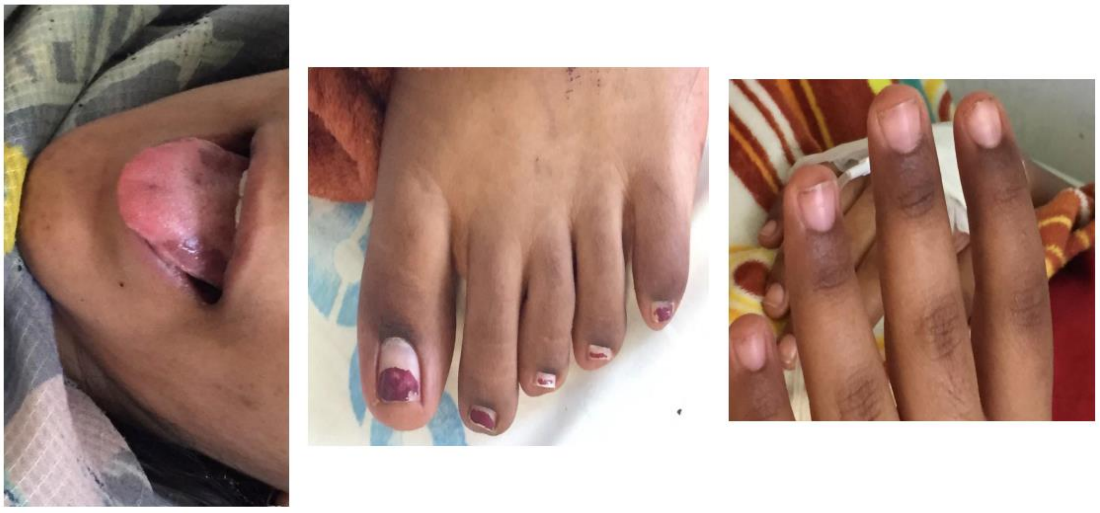

Fig 1. Hyperpigmentation

The right common femoral vein was thrombosed, as revealed by colour Doppler sonography (CDS) of the lower extremity veins. Laboratory results indicated adrenal insufficiency (AI), which was quickly treated with hydrocortisone and enoxaparin. Laboratory results indicated high ACTH 8 am and low cortisol level (Table 1).

ANA	Positive
Anti-ds DNA	221.6 IU/ml (positive)
Lupus anticoagulant	76.3s (28-43)
Anti-cardiolipin Ab	Positive
ACTH 8am	1180pg/ml (7.2-63.6)

Table 1. Laboratory parameters

Patient was prescribed with prednisolone (12.5mg PO TID), fludrocortisone (0.1mg PO QD), rivaroxaban (20mg PO daily), and hydroxychloroquine (200mg QHS) and discharged in good condition.

Discussion –

This report is based on a rare condition of adrenal involvement in secondary APS, especially in pediatric cases[2]. A study by Liu L et al., described a similar case report on school age girl whose laboratory and scanning reports revealed renal vein and inferior vena cava embolism and later on she was diagnosed with SLE (systemic lupus erythematosus) coexisting with APS[3]. Another study by Madison J A et al., says that thrombotic events was relatively common in both primary (40%) and secondary (45%) APS. Among patients with secondary APS and a concomitant rheumatic disease, most (82%) had a diagnosis of SLE[4].

Conclusion –

The current case concludes that APS is a significant contributor to fatal illness, particularly when thrombosis is present. If proper diagnoses are not done for AI, an adrenal crisis could occur, which is a lethal condition. As a result, an accurate diagnosis and prompt therapy can improve the condition of the disease.

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