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Evaluation of the Relationship Between Age and Serum ATL-1 and ARX Levels in Cerebral Palsy

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Abstract

Cerebral palsy (CP) is a non-progressive neurological disorder caused by injury to the developing brain or abnormal brain development during the prenatal, perinatal, or early postnatal period. It is characterized primarily by motor dysfunction, impaired movement, and posture abnormalities, often accompanied by cognitive and sensory impairments. In recent years, increasing attention has been given to molecular biomarkers that reflect neuronal development and may provide insight into the underlying neurobiological mechanisms of CP. Among these biomarkers, Atlastin-1 (ATL-1) and Aristaless-Related Homeobox (ARX) are genes associated with neuronal growth, differentiation, and cortical development. The present study aimed to evaluate age-related variations in serum ATL-1 and ARX levels in children diagnosed with cerebral palsy. A total of sixty patients with CP were enrolled in this study and categorized into three age groups: 3 months–1 year (n = 24), 1–2 years (n = 17), and 2–3 years (n = 19). Serum levels of ATL-1 and ARX were measured using the enzyme-linked immunosorbent assay (ELISA) technique. Statistical analysis was performed to determine the differences in biomarker levels among the age groups.

The results demonstrated a significant increase ($p < 0.05$) in both ATL-1 and ARX levels in the 2–3 years age group compared with the younger groups. This elevation may reflect increased neuronal maturation and developmental processes occurring during early childhood in patients with CP.

Keywords: Cerebral palsy; ATL-1; ARX;; neurodevelopment; ELISA

Introduction

Cerebral palsy (CP) affects 2–3 per 1000 live births globally and is characterized by permanent disorders of movement and posture due to brain maldevelopment or injury during early life (5). Despite being non-progressive, the functional deficits in CP may evolve over time as the brain undergoes maturation.

Recent research has focused on molecular biomarkers that reflect neuronal development. **Atlastin-1 (ATL-1)** is a GTPase responsible for the homotypic fusion of endoplasmic reticulum (ER) membranes, which maintains ER morphology and supports intracellular signaling and calcium homeostasis in neurons (2,7). Dysfunction of ATL-1 can disrupt ER structure, impair synaptic function, and influence neuronal plasticity.

Aristaless-related homeobox (ARX) is a transcription factor involved in the development of cortical and GABAergic interneurons, regulating neuronal migration and synaptic connectivity during early brain maturation (6). Aberrant ARX expression is associated with epilepsy and neurodevelopmental disorders, highlighting its critical role in early neuronal network formation.

The first three years of life are characterized by rapid **synaptogenesis, neuronal circuit formation, and cortical maturation**, making this period particularly sensitive to neurodevelopmental disruption (4). Investigating ATL-1 and ARX in this age range may provide insights into the molecular mechanisms underpinning CP and identify potential biomarkers of neurodevelopmental status.

Methodology

Study Design: A cross-sectional clinical study was conducted to evaluate age-related variations in ATL-1 and ARX levels in children diagnosed with CP.

Study Population :Sixty children with clinically confirmed CP were recruited and divided into three age groups:

- **3 months–1 year (n = 24)**
- **1–2 years (n = 17)**
- **2–3 years (n = 19)**

Sample Collection: Venous blood was collected under sterile conditions. Serum was separated by centrifugation at 3000 rpm for 10 min and stored at −20°C until analysis

Biomarker Measurement Serum ATL-1 and ARX levels were measured using commercially available **sandwich ELISA kits** according to the manufacturer's instructions. Absorbance was read at 450 nm, and concentrations were calculated using standard curves.

Evaluation of biomarkers: The current study for level Atlastin, ATL1, Aristaless-related homeobox (ARX) were used ELISA PARAEDICAL, PKL, Microplate Reader

Kit form China company bioassay Technology Laboratory (BTLAB) cod number

Atlastin, ATL1 kit cod .NO, E7932Hu appendix1

Aristaless-related homeobox (ARX) kit cod NO,E7889Hu appendix2

Data are presented as **mean ± standard error (SE)**. Statistical comparisons among groups were performed using **one-way ANOVA** followed by **Tukey's post-hoc test**. A **p-value < 0.05** was considered statistically significant.

Results and discussion

1-Atlastin, ATL-1

The results in figure (1-1) refer to significant increase p<0.05 in ATL-1 level in age (2-3) years (1.062 ± 0.0902ng\ml) in comparison age (3month to 1 years) (0,7177 ± 0.0206 ng\ml) and less than (1-2) (0.6673±0.0487) ng\ml,The age 3 month to 1 years also show significant increase p>0.05 in comparison with age less of than (1-2) years

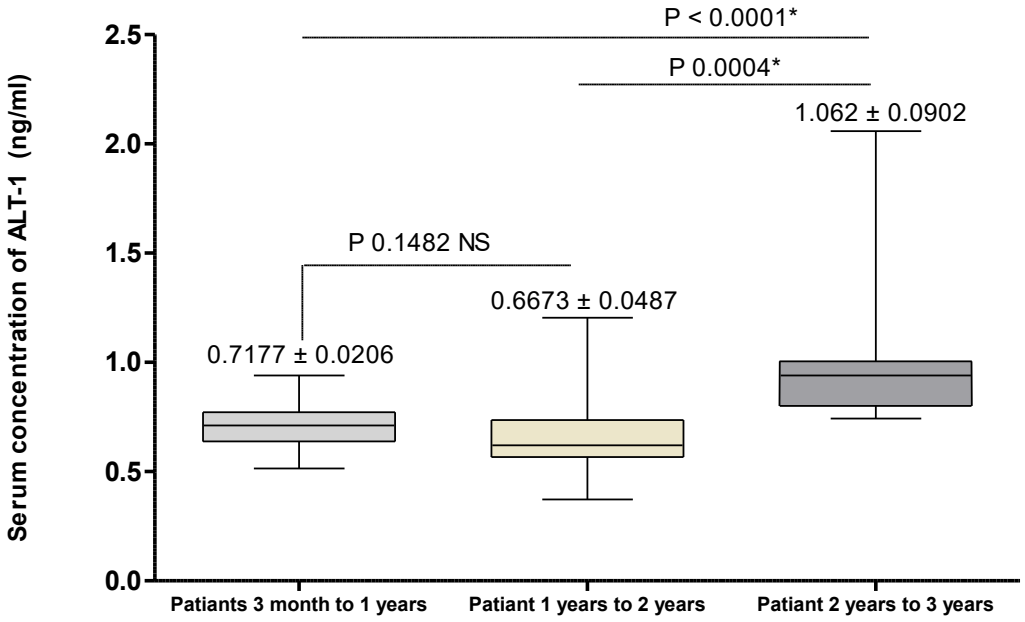

Figure (1-1) Effect of age on ATL-1 level in patient of cerebral palsy

3 month to 1 years =24 (1-2) years = 17 (2-3) years= 19 Different letters refer to significant differences at level p<0.05.

The results of figure (1-1) represent a highly significant increase in age(2-3)years in comparison with(3month to1 years) and less than (1-2)in patient of cerebral palsy current result, The age 3 month to 1 years also show significant increase p>0.05 in comparison with age less of than (1-2) years ,atlastin ATL-the ER has specialized characteristics likely to be crucial for proper neuronal function, including Ca^{2+} release channels that can increase or reduce synaptic efficacy distant from the stimulation site. (3).ER contact sites with the PM, have been implicated as intracellular signaling hubs in neuronal cell bodies. (7). The atlastin (ATL) GTPases mediate this fusion reaction and are critical for ER network maintenance.(2). with the absence of ATL causing disruptions to ER structure in mammalian cells.

2 Aristaless-related homeobox (ARX)

The results in figure (1-2) refer to significant increase p<0.05 in ARX level in age (2-3) years (1.300 ± 0.069ng\ml) in comparison age (1-2) (1.169 ± 0.040 ng\ml) and less than (3month to1years) (0.9881±0.052) ng\ml ,The age (1-2) years also show significant increase p>0.05 in comparison with age less of than 3 month to 1 years

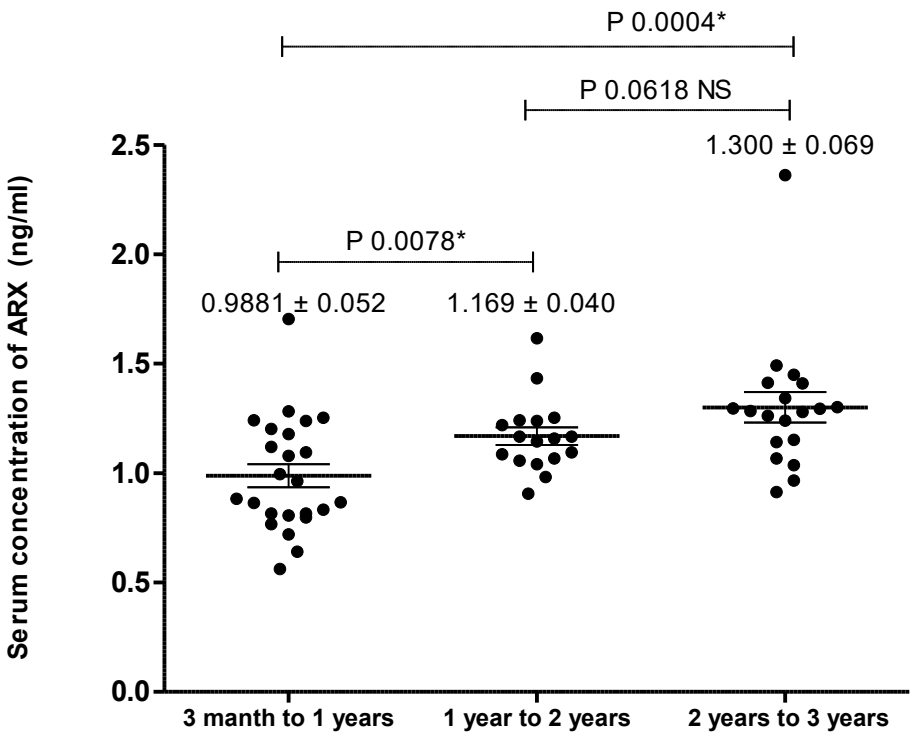

Figure (1-2) Effect of age on ARX level in patient of cerebral palsy

3 month to 1 years =24 (1-2) years = 17 (2-3) years= 19

Different letters refer to significant differences at level $p<0.05$.

The results in figure (1-2) refer to significant increase $p<0.05$ in ARX level in age (2-3) years in comparison age (1-2) and less than (3month to1years) The age (1-2) years also show significant increase $p>0.05$ in comparison with age less of than 3 month to 1 years ARX is a regulatory gene involved in cortical development and the differentiation of GABAergic and interneuron cells. It regulates neural migration during embryogenesis and from infancy to the newborn (6). ARX increases with age, and during the first few years of life (3 months to 3 years), brain regions undergo rapid maturation through synoptic formation and the rebalancing of light and inhibition. ARX changes further as the child grows older, driven by increased synaptic regulation (1,4).

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