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Urinary Nerve Growth Factor in full-term, preterm and intra uterine growth restriction neonates: association with brain growth at 30-40 days of postnatal period and with neuro-development outcome at two years. A pilot study, *Neuroscience Letters*,

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Abstract: Nerve Growth Factor (NGF) and Brain Derived Neurotrophic Factor (BDNF) are crucial for the peripheral and central nervous system development, respectively, and differential brain and blood levels in Intra Uterine Growth Restriction (IUGR) and prematurity have been found. As reduced growth of brain regions, measured at 30-40 days of postnatal period, has been demonstrated in preterm and IUGR neonates who showed impaired neuro-development at two years of age, in this study, the levels of NGF and BDNF were evaluated in the urine samples of 30-40 day-old subjects who were full-term, preterm and IUGR and showed a normal or an abnormal neuro-development at follow up after two years. Neurotrophins were measured concurrently with volumes of whole brain, thalamus, frontal cortex and cerebellum. Values were then correlated with later neuro-developmental outcome. Biochemical parameters and cerebral volumes were assessed using colorimetric ELISA kits and three-dimensional ultra-sonography (3DUS), respectively. Neuro-development was estimated using the Griffiths-II test. Urinary NGF and brain volumes significantly correlated and were in preterm and IUGR subjects characterized by poor neuro-development. No differences were seen in the case of BDNF. The present investigation demonstrates, for the first time, the strong and direct association of NGF with brain growth at the initial phase of the postnatal period and with neuro-developmental outcome in later life. Remarkably, urinary NGF may be suggested as an early prognostic indicator of high long-term risk of motor and cognitive impairment in IUGR and preterm neonates.

Keywords: Urinary neurotrophins; neuro-development outcome; prematurity; IUGR; 3D ultra-sonography cerebral volumes; Griffiths-II