

**PUBLISHED ABSTRACT**

# Correlation of Preterm Infant Salivary Cortisol Levels with Scores on the Neonatal Infant Stressor Scale

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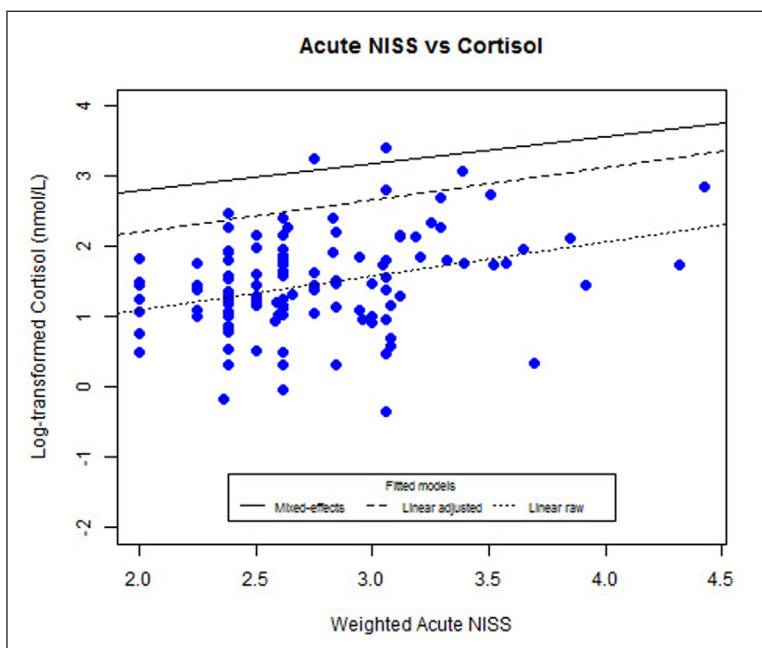
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Repeated stress during the early period of infant development is hypothesized to produce long-lasting effects on cognitive, behavioral, and somatic development. Despite efforts to nurture preterm infant development during the life-saving birth hospitalization, the neonatal intensive care unit (NICU) is a stressful environment. Variation in cortisol levels reflects multiple stressors during the neonatal period, potentially impacting development of immature hypothalamic, pituitary and adrenal axes. Assessing the stress response of neonates to noxious stimuli can be challenging. The Neonatal Infant Stressor Scale (NISS) is one tool used to quantify neonatal stress for clinical and research purposes. The scale consists of 35 acute items and 19 chronic items that are thought to capture stressful events that were chosen by NICU caregiver estimation of stressful events during the NICU hospitalization and. To our knowledge, scores on the NISS have not previously been compared to physiologic biomarkers of infant stress.

In this study, we compared acute and chronic NISS scores to an accepted biomarker of infant stress response, salivary cortisol, in a cohort premature infants born 28-0/7–32-6/7 weeks gestation through the course of the NICU hospitalization.

In preliminary analysis, we examined 143 salivary specimens from 68 patients. Using a Pearson correlation analysis and mixed-effects model we concluded that both acute and chronic NISS scores were significantly correlated with salivary cortisol (P-values < 0.001). The mixed-effects model with random coefficients for infant and family revealed significant



**Figure 1:** The plots show the NISS (x) and log-transformed cortisol concentrations (y). The three lines show three fitted models. The 'Linear raw' is the unadjusted linear regression model, 'Linear adjusted' is adjusted for PMA, and 'Mixed-effects' is adjusted for PMA as well as the random effect of subjects/families.

association between the weighted acute NISS score and salivary cortisol levels (adjusted  $\beta = 0.41$ , P-value = 0.02). No significant associations were found between the weighted chronic NISS score and the salivary cortisol levels (adjusted  $\beta = 0.88$ , P-value = 0.13). However, the association between the weighted chronic NISS score and cortisol levels was statistically significant with adjustment for lagged days of salivary cortisol collection (adjusted  $\beta = 0.88$ , P-value = 0.04).

Our results suggest that the Neonatal Infant Stressor Scale may provide an accurate noninvasive measure of neonatal stress. NISS scores may be used to monitor and reduce stress levels for premature infants.

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