



ORIGINAL ARTICLE

Decreased Cystatin C—Estimated Glomerular Filtration Rate Is Correlated with Prolonged Hospital Stay in Transient Tachypnea of Newborn Infants



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Key Words

transient tachypnea
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glomerular filtration
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cystatin C

Background: Transient tachypnea of the newborn (TTN) is a benign disorder with a variable clinical course that often leads to hospitalization. The aim of this study was to assess and validate the relationship between the serum cystatin C level and symptom duration in infants with TTN.

Methods: Forty newborns presenting with TTN and who had undergone serum cystatin C (Cys C) tests on the first day of admission to the Kyung Hee University Hospital (Seoul, Korea) from 2009 to 2013 were included. The serum Cys C level, creatinine (Cr) level, estimated glomerular filtration rate (eGFR), and tachypnea duration were correlated retrospectively.

Results: The median gestation period was 37.8 ± 3.8 weeks and the mean birth weight was 3.2 ± 0.4 kg. Tachypnea duration was 3.3 ± 2.0 days. Serum Cys C and Cr levels were 1.7 ± 0.2 mg/L and 0.8 ± 1.2 mg/dL, respectively. Tachypnea duration was significantly positively correlated with the serum levels of Cys C and significantly negatively correlated with Cys C-based eGFR ($p = 0.016$), but was not significantly correlated with the serum Cr level or Cr-based eGFR. When tachypnea duration was compared between infants with Cys C level <1.6 mg/L ($n = 15$; Group A) and infants with Cys C level ≥ 1.6 mg/L ($n = 25$; Group B), the symptom duration was significantly shorter in Group A infants ($p = 0.011$).

Conclusion: Tachypnea duration was shorter with higher Cys C-based eGFR in infants with TTN. Copyright © 2015, Taiwan Pediatric Association. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

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1. Introduction

Transient tachypnea of the newborn (TTN), a clinical syndrome first described by Avery et al¹ in 1966, is accompanied by respiratory distress. Its pathogenesis is unclear, although it has been suggested that the development of TTN may be associated with a delay in the reabsorption of pulmonary alveolar fluid that prevents lung collapse during the fetal period.^{1,2} Most cases of TTN consist of benign self-limiting pulmonary disease, except for occasional severe cases that require laboratory tests, chest radiography, and admission into the neonatal intensive care unit (NICU) for intensive respiratory treatment. The incidence of TTN is ~1–2% in all neonates,³ and the average symptom duration is 2–5 days.⁴

Despite the relatively short hospital stay and benign course, TTN is associated with social and financial burdens because the affected infants are usually admitted to NICUs.⁵ Therefore, several studies pertaining to TTN symptom duration have been published. These studies have focused on fluid redistribution because some clinicians have used loop diuretics to treat patients with TTN. A recent study revealed no apparent advantage in using furosemide,⁶ although another study demonstrated a significant improvement in fluid-restricted TTN infants, which implicates an association between fluid balance and TTN symptoms.⁷

Because of its active effects on body fluid balance, the renal function of infants with TTN was analyzed in the current study to test the hypothesis that infants with a shorter symptom duration would have better renal function. Serum cystatin C (Cys C) and creatinine (Cr) were chosen for calculating the estimated glomerular filtration rate (eGFR) because they are representative markers of renal function.⁸ The aim of the current study was to evaluate the relationship between the eGFR, using serum Cys C, and symptom duration in infants with TTN.

2. Patients and methods

2.1. Participants

This retrospective study was conducted at a single tertiary care center—Kyung Hee University Hospital (Seoul, Korea)—and was based on medical chart reviews. Before the data were reviewed and analyzed, the Institutional Review Board of the Kyung Hee University Hospital approved the present study. Patients admitted to the NICU of the Kyung Hee University Hospital from January 2009 to July 2013 were screened with the following inclusion criteria: gestational age ≥ 37 weeks; birth weight ≥ 2500 g; a diagnosis of TTN without hyaline membrane disease, pneumonia, or pneumothorax, as confirmed through chest radiograph; and serum Cys C and Cr levels that were measured on the 1st day of admission. Infants were excluded that had renal failure (i.e., sustained plasma creatinine level ≥ 1.5 mg/dL)⁹ or oliguria (i.e., urine flow < 1 mL/kg/h).¹⁰ The Cys C level at the time of admission was not assessed because of renal impairment but as part of a routine serum chemistry battery.

2.2. Data collection

Individual medical records were transcribed into the case report forms and included sex, gestational age, and birth weight. Data pertaining to Apgar scores at 1 minute and 5 minutes, type of delivery, urine output, serum Cys C level on the 1st day of admission, and serum Cr were also collected. Mean urine output values measured every 1–3 hours during the admission period were used as a representative value of urine output. Serum levels of Cys C and Cr were measured by an automated chemical analyzer (Toshiba, Nasushiobara, Japan) using HiSens Cys-C LTIA (HBi Co., Ltd., Anyang, Korea) and serum Cr (Kanto Chemical Co., Tokyo, Japan), respectively. Serum Cr-based eGFR (Cr-eGFR) and serum Cys C-based eGFR (Cys-eGFR) were calculated using the following equations: (1) Cr-eGFR (in term neonates) = $0.45 \times \text{length (cm)}/\text{serum Cr (mg/dL)}$ and (2) Cys C-eGFR = $137/\text{Cys C} - 20.4$ (Bokenkamp A).¹¹ Based on the Cys C values, a cutoff of 1.6 mg/L (corresponding to Cys C-eGFR 65 mL/min/1.73 m²) was used to classify patients into two subgroups: (1) the low Cys C group (Group A; $n = 15$, Cys C < 1.6 mg/L, and Cys C-eGFR > 65 mL/min/1.73 m²) and (2) the high Cys C group (Group B; $n = 25$, Cys C ≥ 1.6 mg/L, and Cys C-eGFR ≤ 65 mL/min/1.73 m²).

2.3. Definitions

The time after admission to the resolution of tachypnea was recorded. The measured respiratory rates (RRs) were also reviewed from medical charts. Tachypnea was defined as a breath rate of more than 60 breaths/min. The RR was represented by the mean value of the RRs measured every 1–3 hours during the admission period of the patient. We assessed the average values of every 8-hour period. Resolution of tachypnea was defined as the day when the 8-hour period average RR was below 60 breaths/min in two or more consecutive periods.

2.4. Statistical analysis

The relationships between TTN symptom duration, serum Cys C level, serum Cr level, and eGFRs measured on hospital Day 1 were analyzed. The type of delivery, Apgar scores at 1 minute and 5 minutes, and average gestational period were also analyzed. All statistical analyses were conducted using SPSS version 20.0 software (SPSS Inc., Chicago, IL, USA). The data are expressed as the mean \pm the standard deviation. The Mann–Whitney *U* test was used to evaluate the differences between the low and high Cys C subgroups. Pearson's correlations and multivariate regression analyses were performed to examine the relationships between symptom duration, urine output, Cr, cystatin C, Cr-eGFR, and Cys C-eGFR. Statistical significance was set at $p < 0.05$.

3. Results

From January 2009 to July 2013, a total of 65 TTN patients older than 37 gestational weeks with a birth weight > 2500 g

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