

# Hyponatremia and Hypotonic Intravenous Fluids Are Associated With Unfavorable Outcomes of Bronchiolitis Admissions

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## ABSTRACT

**OBJECTIVES:** Hyponatremia has been associated with unfavorable outcomes when present at admission in children with bronchiolitis. Delayed hyponatremia may be a modifiable risk factor for severe disease that is influenced by intravenous fluid (IVF) tonicity. We hypothesized that both hyponatremia and prescription of severely hypotonic IVF are associated with unfavorable outcomes, and that prescription of severely hypotonic IVF is associated with subsequent hyponatremia.

**METHODS:** Data were retrospectively extracted for 1557 pediatric inpatients with bronchiolitis. Any day on which a subject was prescribed IVF with sodium  $<70$  mEq/L was termed “IVF  $<70$ .” All other days on which IVF was prescribed were termed “IVF  $\geq 70$ .” Any blood sodium  $\leq 135$  mEq/L defined hyponatremia for that day. All other days with sodium available were labeled normonatremia. Variables were compared with Spearman correlation, Wilcoxon rank test, or  $\chi^2$ . Significant results had  $P < .05$ .

**RESULTS:** Blood sodium levels correlated negatively with hospital length of stay ( $r = -0.477$ ,  $P < .0001$ ). On each of the first 4 days of hospitalization, significantly increased hospital length of stay was observed in patients with hyponatremia ( $n = 134$  [25.7% of subjects with available sodium data]) versus patients with normonatremia ( $n = 387$  [74.3%]), and in patients prescribed IVF  $<70$  ( $n = 348$  [46.3% of subjects prescribed IVF]) versus patients prescribed IVF  $\geq 70$  ( $n = 403$  [53.7%]). Patients prescribed IVF  $<70$  had increased rates of hyponatremia on the subsequent day versus patients prescribed IVF  $\geq 70$  (50.0% vs 26.9%,  $P < .001$ ).

**CONCLUSIONS:** In children hospitalized with bronchiolitis, hyponatremia may be a modifiable risk factor for severe disease that may be mitigated by avoiding use of severely hypotonic IVF.

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Bronchiolitis, a viral respiratory tract infection of young children, is the most common cause of hospitalization in children <2 years old.<sup>1-3</sup> In the United States, there are ~150 000 bronchiolitis admissions per year, with annual hospital costs exceeding \$1 billion.<sup>1-6</sup> Despite this heavy burden, there are no proven pharmacologic therapies for children with bronchiolitis and expert recommendations focus on preventive measures and support for associated complications, such as dehydration.<sup>7</sup> Some putative treatments (eg, bronchodilators and corticosteroids) are not recommended because numerous studies have revealed little benefit, whereas other commonly employed therapies (eg, intravenous fluid [IVF]) have been less robustly evaluated in bronchiolitis.<sup>7-9</sup>

Patients with bronchiolitis may be prescribed IVF for multiple indications, including to correct dehydration, to avoid the risk of aspiration during feeding, and to ensure an empty stomach in case endotracheal intubation is required. Traditionally, hypotonic IVFs such as quarter normal saline (0.2% NaCl) were prescribed to hospitalized children based on the work of Holliday and Segar.<sup>10</sup> The use of these traditional hypotonic IVFs has now been shown to promote hyponatremia in hospitalized children, likely related to increased blood levels of antidiuretic hormone (ADH) in bronchiolitis and other common pediatric illnesses.<sup>11-16</sup>

Hyponatremia has been defined as a blood sodium concentration of  $\leq 135$  mEq/L and is associated with unfavorable clinical outcomes in hospitalized adults and children.<sup>15,17-22</sup> In patients with bronchiolitis, hyponatremia near the time of hospital admission is associated with unfavorable clinical outcomes, including increased need for mechanical ventilation, prolonged ICU length of stay (LOS), and increased mortality.<sup>15,22-25</sup>

It is not established if hyponatremia later in the course of bronchiolitis is similarly associated with unfavorable outcomes. Delayed hyponatremia may be a modifiable risk factor for severe disease, especially because some experts still recommend the use of hypotonic IVF and many

practitioners report using them for infants with acute respiratory tract infections.<sup>26,27</sup> Although this practice increases the risk of hyponatremia, the use of hypotonic fluids has not been proven to negatively affect clinical outcomes like LOS.<sup>12,13</sup>

The objectives of this study are to (1) confirm the association between early hyponatremia and unfavorable outcomes in a larger patient cohort than those previously analyzed, (2) evaluate associations between later hyponatremia and unfavorable outcomes, and (3) evaluate if IVF composition is associated with unfavorable outcomes in bronchiolitis.

## METHODS

The Institutional Review Board of University Hospitals of Cleveland approved this retrospective study. Cases were identified and data extracted by using Population Explorer (Explorys, Cleveland, OH), automated data extraction software that is directly linked to our institution's electronic health record. As previously described, data for children admitted between January 2010 and July 2013 with a diagnosis of bronchiolitis were extracted into a limited data set.<sup>28</sup> Only the first admission in the data set for each subject was analyzed. Available data included race, sex, inpatient laboratory results, and inpatient IVF prescribed. To protect patient privacy, only birth year (not exact birth date) was available. Analysis was restricted to admissions with a diagnosis of bronchiolitis occurring during the same year as a child's birth or the next 2 years.

For each day of hospitalization in which a subject was prescribed IVF, they were categorized into 1 of 2 mutually exclusive categories. If the subject was prescribed any IVF with  $<70$  mEq/L of sodium (eg, 0.2% or 0.33% saline), they were categorized as having received IVF  $<70$  on that day. For the days during which all prescribed IVF had  $\geq 70$  mEq/L of sodium (eg, 0.45% saline or 0.9% saline), they were categorized as having received IVF  $\geq 70$ . If a subject was not prescribed IVF on a given day, they were not included in analyses of IVF category for that given day.

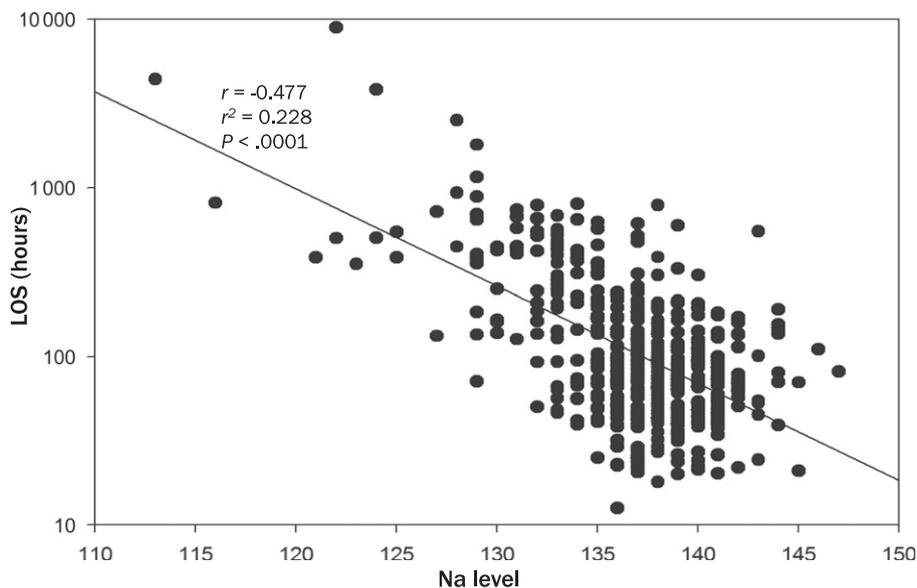
For each day of hospitalization in which a subject had a measurement of blood sodium, they were placed into 1 of 2 mutually exclusive categories. If the subject had any measurement of blood sodium that was  $\leq 135$  mEq/L, they were categorized as having hyponatremia on that particular day.<sup>15,22</sup> For the days during which all measurements of blood sodium were  $>135$  mEq/L, they were categorized as having normonatremia. If a subject did not have blood sodium measured on a given day, they were not included in analyses of blood sodium category for that given day.

The day of hospital admission was defined as "hospital day 1." The primary outcome was hospital LOS. The use of mechanical ventilation was a secondary outcome. Wilcoxon rank test was used to test for associations between patient categories and LOS. We used the  $\chi^2$  test to analyze categorical variables and simple linear regression to test for associations between each patient's minimum measurement of

**TABLE 1** Patient Demographics

Variable	Median (IQR) or <i>n</i> (%)
Girl	644 (41.4)
Boy	913 (58.6)
Age definitively <12 mo <sup>a</sup>	529 (34.0)
African American	721 (46.3)
White	700 (45.0)
Other/unknown race	136 (8.7)
Tested positive for respiratory syncytial virus	899 (57.7)
Hospital LOS, d	2.5 (1.7-4.0)
Mechanically ventilated	59 (3.8)

<sup>a</sup> Exact age data are not available. These subjects all were admitted with bronchiolitis during their birth year, ensuring that they were <12 mo old.



**FIGURE 1** Linear regression shows that each patient's minimum sodium level during hospitalization is inversely associated with hospital LOS. Note logarithmic y-axis.

blood sodium and LOS. We performed subgroup analyses on the subset of children who were admitted with bronchiolitis during their birth year, ensuring that they were <12 months old. Analyses were performed by using SigmaPlot 12.5 (Systat Software, San Jose, CA). For all tests,  $P < .05$  defined statistical significance. Data are shown as  $n$  (%) or median interquartile range (IQR).

## RESULTS

We identified data for 1557 children meeting inclusion criteria. As shown in Table 1, most children were boys (913 [58.6%]) and nearly all were either African American (721 [46.3%]) or white (700 [45.0%]). More than half were identified as having respiratory syncytial virus infections (899 [57.7%]), and approximately one-third of the admissions occurred during the child's birth year (529 [34.0%]). The median LOS was 2.5 (1.7–4.0) days, and 59 subjects (3.8%) required mechanical ventilation.

More than one-third of the subjects (521 [33.5%]) had blood sodium measured at least once, and 134 (25.7%) of these subjects had hyponatremia. Among children with hyponatremia, the median minimum sodium measurement was 133 (131–135) mEq/L. Blood sodium measurement was more common among children admitted during their birth year (200 [37.8%] vs

321 [31.2%],  $P = .011$ ) and girls (238 [37.0%] vs 283 [31.0%],  $P = .016$ ), and was associated with longer LOS

(3.7 [2.3–7.1] vs 2.0 [1.4–3.1] days,  $P < .001$ ). There was a significant relationship between hospital LOS and the minimum

**TABLE 2** Associations Between Blood Sodium Levels and Clinical Outcomes

	<i>n</i>	Hospital LOS	<i>P</i>	Mechanical Ventilation (%)	<i>P</i>
Day 1			<.001		<.001
Normonatremia	287	3.1 (2.1–5.3)		18 (6.3)	
Hyponatremia	69	5.7 (2.8–10.2)		18 (26.1)	
Day 2			<.001		<.001
Normonatremia	166	3.9 (2.5–8.1)		24 (14.5)	
Hyponatremia	41	16.1 (6.3–20.4)		24 (58.5)	
Day 3			<.001		<.001
Normonatremia	82	7.3 (4.1–15.5)		24 (29.3)	
Hyponatremia	35	18.1 (14.7–27.1)		28 (80.0)	
Day 4			.02		.004
Normonatremia	47	13.1 (7.3–21.0)		21 (44.7)	
Hyponatremia	43	17.6 (13.0–27.1)		33 (76.7)	
Day 5			.927		.018
Normonatremia	38	18.3 (10.1–25.4)		21 (55.3)	
Hyponatremia	36	17.8 (14.4–23.4)		30 (83.3)	
Day 6			.677		.03
Normonatremia	36	18.2 (12.1–27.2)		20 (55.6)	
Hyponatremia	38	18.6 (15.7–24.7)		31 (81.6)	
Day 7			.665		.004
Normonatremia	24	17.2 (14.9–28.2)		12 (50.0)	
Hyponatremia	42	18.9 (16.1–26.9)		36 (85.7)	

For each day, hospital LOS was compared between groups by using Wilcoxon rank test and rates of mechanical ventilation were compared with  $\chi^2$ . Hospital LOS (days) is shown as median (IQR) and mechanical ventilation is shown as  $n$  (%).

blood sodium level measured, with lower sodium levels correlating with longer LOS (Fig 1). As shown in Table 2, LOS was significantly longer among children with hyponatremia compared with those with normonatremia on each of the first 4 days of hospitalization. Findings were similar when only subjects who were known to be <12 months old (those hospitalized for bronchiolitis during their birth year) were considered (Table 3). For each of the first 7 days of hospitalization, children who had hyponatremia had higher rates of mechanical ventilation versus those with normonatremia. Again, results were similar when only children who were definitively <12 months old were considered.

Thirty-six children had hyponatremia on hospital day 1 and had blood sodium measured on the next day of hospitalization. Among these patients, subjects with hyponatremia on day 2 ( $n = 14$ ) had longer LOS compared with children with normonatremia on day 2 (17.0 [10.0–27.6]

vs 6.4 [4.8–11.5] days,  $P = .007$ ). Use of mechanical ventilation was also significantly higher in the subjects with hyponatremia on both days (12 of 14 [85.7%]) versus those with hyponatremia only on day 1 (6 of 22 [27.3%],  $P = .002$ ). Forty-eight children had normonatremia on hospital day 1 and had blood sodium measured on day 2. Among these subjects, hyponatremia on day 2 ( $n = 7$ ) was associated with longer LOS compared with children with normonatremia on day 2 (18.1 [14.9–34.0] vs 5.6 [2.8–15.5] days,  $P = .021$ ). Use of mechanical ventilation was nonsignificantly higher in the subjects who developed hyponatremia on day 2 (4 of 7 [57.1%]) versus those who continued to have normonatremia (12 of 41 [29.3%],  $P = .311$ ).

Nearly half of all subjects (751 [48.2%]) were prescribed IVF on at least 1 day, and 46.3% ( $n = 348$ ) of these patients were prescribed IVF <70. The vast majority of children prescribed IVF were prescribed IVF for  $\geq 2$  days (663 [88.3%]). IVF prescription

was more common among children admitted during their birth year (277 [52.4%] vs 474 [46.1%],  $P = .022$ ) and girls (337 [52.3%] vs 414 [45.3%],  $P = .008$ ), and was associated with longer LOS (3.0 [2.0–4.9] vs 2.0 [1.3–3.1] days,  $P < .001$ ). There were 1237 unique orders for IVF  $\geq 70$  (0.45% saline = 1186; 0.9% saline = 43; lactated ringer's = 4; 154 mEq/L of sodium acetate = 4) and 714 unique orders for IVF <70 (0.2% saline = 708; 0.33% saline = 6; 50 mEq/L of sodium chloride = 2). As shown in Table 4, LOS was significantly longer among children who were prescribed IVF <70 versus those who were prescribed IVF  $\geq 70$  on each of the first 4 days of hospitalization. Findings were similar when only subjects who were hospitalized for bronchiolitis during their birth year were considered (Table 5). For each of the first 3 days of hospitalization, children who were prescribed IVF <70 had higher rates of mechanical ventilation versus those who were prescribed IVF  $\geq 70$ . Again, results were similar when only children who were definitively <12 months old were considered.

One hundred and thirteen children were both prescribed IVF on hospital day 1 and had a blood sodium level measured on day 2. Among these children, the rate of hyponatremia on day 2 was significantly higher among children who were prescribed IVF <70 on day 1 (19 of 52 [36.5%]) versus children who were prescribed IVF  $\geq 70$  on day 1 (5 of 61 [8.2%],  $P < .001$ ). In total, there were 363 instances in which a child was prescribed IVF on a given day and had blood sodium measured on the next day. Among these subjects, the rate of hyponatremia was significantly higher among children who were prescribed IVF <70 on the preceding day (94 of 188 [50.0%]) versus children who were prescribed IVF  $\geq 70$  on the preceding day (47 of 175 [26.9%],  $P < .001$ ). The rate of hyponatremia after prescribing IVF <70 was also significantly higher than the rate of hyponatremia after a day without IVF prescription (94 of 265 [35.5%],  $P = .003$ ).

## DISCUSSION

In this retrospective analysis of a large cohort of children hospitalized with

**TABLE 3** Associations Between Blood Sodium Levels and Clinical Outcomes in Children Admitted With Bronchiolitis During Their Birth Year

	<i>n</i>	Hospital LOS	<i>P</i>	Mechanical Ventilation (%)	<i>P</i>
Day 1			<.001		<.001
Normonatremia	107	3.5 (2.1–5.9)		7 (6.5)	
Hyponatremia	30	8.3 (3.0–18.0)		12 (40.0)	
Day 2			<.001		<.001
Normonatremia	60	4.8 (2.7–8.3)		10 (16.7)	
Hyponatremia	26	17.9 (11.5–24.8)		19 (73.1)	
Day 3			<.001		<.001
Normonatremia	33	8.4 (4.5–16.3)		11 (33.3)	
Hyponatremia	20	20.6 (17.8–28.0)		20 (100)	
Day 4			.007		.007
Normonatremia	18	12.5 (7.3–19.7)		9 (50.0)	
Hyponatremia	24	19.0 (16.2–28.1)		22 (91.7)	
Day 5			.326		.067
Normonatremia	19	22.8 (16.1–28.3)		12 (63.2)	
Hyponatremia	17	17.8 (15.5–22.7)		16 (94.1)	
Day 6			.977		.022
Normonatremia	19	22.8 (16.1–28.0)		11 (57.9)	
Hyponatremia	19	18.6 (16.9–30.0)		18 (94.7)	
Day 7			.45		.012
Normonatremia	13	22.8 (16.3–54.6)		8 (61.5)	
Hyponatremia	20	18.6 (16.3–27.2)		20 (100)	

For each day, hospital LOS was compared between groups by using Wilcoxon rank test and rates of mechanical ventilation were compared with  $\chi^2$ . Hospital LOS (days) is shown as median (IQR) and mechanical ventilation is shown as  $n$  (%).

**TABLE 4** Associations Between Prescribed IVF Composition and Clinical Outcomes

	<i>n</i>	Hospital LOS	<i>P</i>	Mechanical Ventilation (%)	<i>P</i>
Day 1			<.001		<.001
IVF ≥70	332	2.7 (1.8–3.9)		12 (3.6)	
IVF <70	247	3.6 (2.1–6.1)		32 (13)	
Day 2			<.001		<.001
IVF ≥70	390	2.9 (1.8–4.0)		17 (4.4)	
IVF <70	287	3.7 (2.2–6.1)		36 (12.5)	
Day 3			<.001		.02
IVF ≥70	243	3.6 (2.6–5.4)		18 (7.4)	
IVF <70	204	4.5 (2.9–7.5)		30 (14.7)	
Day 4			.049		.667
IVF ≥70	120	4.6 (3.7–7.1)		18 (15)	
IVF <70	129	5.7 (4.0–8.6)		23 (17.8)	
Day 5			.81		.638
IVF ≥70	75	6.8 (4.7–10.1)		16 (21.3)	
IVF <70	65	6.8 (4.8–9.9)		17 (26.2)	
Day 6			.348		.885
IVF ≥70	48	8.7 (6.3–14.7)		15 (31.3)	
IVF <70	40	8.6 (6.8–19.8)		14 (35)	
Day 7			.291		.66
IVF ≥70	35	9.2 (6.6–15.9)		12 (34.3)	
IVF <70	33	10.5 (7.9–20.8)		14 (42.4)	

For each day, hospital LOS was compared between groups by using Wilcoxon rank test and rates of mechanical ventilation were compared with  $\chi^2$ . Hospital LOS (days) is shown as median (IQR) and mechanical ventilation is shown as *n* (%). IVF <70 is defined as prescription of any maintenance IVF with <70 mEq/L of sodium on that given day. IVF ≥70 is defined as prescription of maintenance IVF on that day that exclusively contained >70 mEq/L of sodium.

bronchiolitis, there are 3 main findings. First, our findings support the association between hyponatremia early in the course of bronchiolitis hospitalizations and unfavorable outcomes that has been reported from previous smaller cohorts.<sup>15,22–25</sup> Second, we establish that hyponatremia later in the course of bronchiolitis admissions is also associated with unfavorable outcomes: specifically, prolonged hospitalization and the need for mechanical ventilation. Third, we identified associations between prescription of IVF with sodium <70 mEq/L and these unfavorable outcomes. Moreover, our data suggest that hyponatremia is a modifiable risk factor for severe disease that may be mitigated by avoiding use of severely hypotonic IVF.

Among our cohort, there were 304 patient-days that included hyponatremia among 134 subjects, which is 25.7% of the subjects who underwent blood sodium testing during

the study period. This is similar to the 33.8% cumulative rate of hyponatremia among the 716 subjects included in 5 previous reports of hyponatremia in bronchiolitis.<sup>15,22–25</sup> Those previous studies were also all retrospective and primarily focused on blood sodium levels near the time of hospital admission. Our analysis confirms their findings of associations between hyponatremia early in the course of bronchiolitis with increased mechanical ventilation and prolonged duration of illness. Our analysis also establishes that hyponatremia on later days of hospitalization is also associated with unfavorable outcomes and that more severe hyponatremia is associated with progressively longer hospital LOS (see Fig 1).

There are few proven therapies to improve the outcome of bronchiolitis inpatients, so establishing a modifiable risk factor for severe disease would be important.<sup>7</sup> Our

data suggest that hyponatremia may be such a modifiable factor. Among children who had hyponatremia on the day of hospital admission, outcomes were better when the blood sodium levels corrected by hospital day 2. Furthermore, among children who had normonatremia on the day of admission, outcomes were worse when hyponatremia developed the day after. These retrospective associations require prospective interventional study to confirm that active prevention and/or treatment of hyponatremia improves outcomes.

Hyponatremia in bronchiolitis may directly contribute to unfavorable outcomes by promoting fluid shifts into the lungs and brain, resulting in pulmonary and/or neurologic dysfunction.<sup>24,29,30</sup> Hyponatremia may also be an indirect marker of underlying disease severity. Increased levels of ADH are common in bronchiolitis, and may be especially high in sicker patients when severe lung hyperinflation reduces venous return to the right atrium, further stimulating ADH release.<sup>14–16</sup> High ADH levels predispose children to hyponatremia, especially if hypotonic IVFs are administered.

Indications for IVF prescription are common in bronchiolitis. In 2 recent interventional trials, ~30% to 40% of hospitalized children with bronchiolitis could not safely tolerate oral hydration, a rate similar to the use of IVF in our cohort.<sup>31,32</sup> In the original report by Holliday and Segar, it was suggested that IVF with ~30 mEq/L of sodium is appropriate, citing the sodium content of human breast milk and cow's milk.<sup>10</sup> It has now been well established that traditional hypotonic IVF cause increased rates of hyponatremia in hospitalized children, and hyponatremia has been proposed as a factor in many reports of unexpected poor outcomes, including cardiorespiratory arrests.<sup>12,13,33</sup> Despite these concerns, some experts still continue to recommend the use of hypotonic maintenance IVF in hospitalized children.<sup>27</sup> Prospective trials of fluid tonicity have been designed to measure impact on blood sodium and not clinical outcomes, so the impact of mitigating hyponatremia on patient outcomes is less well established. In

**TABLE 5** Associations Between Prescribed IVF Composition and Clinical Outcomes in Children Admitted With Bronchiolitis During Their Birth Year

	<i>n</i>	Hospital LOS	<i>P</i>	Mechanical Ventilation (%)	<i>P</i>
Day 1			<.001		.01
IVF ≥70	83	2.9 (1.7–4.2)		4 (4.8)	
IVF <70	134	4.0 (2.3–8.1)		24 (17.9)	
Day 2			.001		.054
IVF ≥70	91	3.0 (1.9–4.9)		7 (7.7)	
IVF <70	156	4.2 (2.7–7.6)		27 (17.3)	
Day 3			.093		.331
IVF ≥70	52	4.0 (2.9–7.1)		7 (13.5)	
IVF <70	108	5.1 (3.2–9.2)		23 (21.3)	
Day 4			.942		.975
IVF ≥70	28	6.8 (3.8–12.0)		7 (25)	
IVF <70	72	5.9 (4.1–9.8)		16 (22.2)	
Day 5			.553		.826
IVF ≥70	23	7.1 (6.3–11.9)		6 (26.1)	
IVF <70	37	6.8 (4.5–12.7)		10 (27)	
Day 6			.06		.542
IVF ≥70	17	7.1 (6.3–10.4)		4 (23.5)	
IVF <70	21	9.3 (7.2–23.5)		8 (38.1)	
Day 7			.128		.691
IVF ≥70	12	8.1 (6.4–15.6)		4 (33.3)	
IVF <70	19	14.8 (8.2–23.0)		9 (47.4)	

For each day, hospital LOS was compared between groups by using Wilcoxon rank test and rates of mechanical ventilation were compared with  $\chi^2$ . Hospital LOS (days) is shown as median (IQR) and mechanical ventilation is shown as *n* (%). IVF <70 is defined as prescription of any maintenance IVF with <70 mEq/L of sodium on that given day. IVF ≥70 is defined as prescription of maintenance IVF on that day that exclusively contained >70 mEq/L of sodium.

our subjects, use of IVF with <70 mEq/L of sodium was associated with unfavorable outcomes when it was prescribed on any of the first 4 days of hospitalization. In addition, subjects in our cohort prescribed IVF <70 were more likely to have hyponatremia on the subsequent day compared with both children given higher tonicity IVF and children not prescribed IVF (and presumably given enteral nutrition). These findings support recommendations that severely hypotonic fluids such as quarter normal saline or third normal saline (0.2% and 0.33% NaCl) be used cautiously, if at all, in bronchiolitis inpatients.<sup>7</sup>

Our study has several limitations. It is a retrospective, single-center study that can test for associations but not causation. Exact ages were not available, so we could not adjust our analyses for age. It is possible that the youngest children may

have been preferentially prescribed IVF <70, which could bias our results against IVF <70, because neonates are more likely to have severe disease. However, our findings were similar when analyses were restricted to children who were known to be <12 months old. Other potential confounders include that our center's ICU more typically used isotonic IVF during the study period, which could bias our results against IVF ≥70. Our database only includes inpatient data, so prehospital IVF and laboratory results could not be evaluated. The database does not contain physical examination findings (eg, adventitious lung sounds, work of breathing, etc) or relevant comorbidities (eg, prematurity, congenital heart disease). Our findings may have differed if we had been able to adjust our analyses for such risk factors for severe disease.<sup>34–36</sup> However, we found that both sodium measurement and IVF prescription

were associated with unfavorable outcome; therefore, we excluded less severely ill patients from each analysis by excluding subjects who did not require blood sodium measurement or IVF prescription on that particular day. The definition of hyponatremia varies in the literature. We chose a definition of blood sodium ≤135, which has been used in multiple previous studies.<sup>15,22</sup> Some of our patients were >1 year old, and some experts exclude children >1 year old from bronchiolitis studies.<sup>37–39</sup> However, we repeated our main analyses by using children known to be <12 months old and found similar results.

## CONCLUSIONS

This single-center retrospective study of more than 1500 children hospitalized with bronchiolitis reaffirms that hyponatremia early during hospitalization is associated with unfavorable clinical outcomes, further establishes that later hyponatremia is also associated with unfavorable outcomes, and suggests that severely hypotonic IVF may worsen patient outcomes by promoting hyponatremia. Prospective studies are needed to confirm these findings and establish if the treatment and prevention of hyponatremia can improve outcomes. In the interim, we recommend generally avoiding severely hypotonic IVF in bronchiolitis inpatients and that hyponatremia should prompt close monitoring for clinical deterioration and consideration of corrective measures.

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