

Clinical Characteristics, Etiology, and Outcomes of Hypothermia in Well-appearing Children Referred to the Emergency Department

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ABSTRACT **Background:** Hypothermia, as a sign of serious bacterial infection (SBI) in children and infants older than 90 days is poorly characterized, especially in the post-pneumococcal vaccine era.

Objectives: To assess the prevalence of SBI in children and infants presenting to the pediatric emergency department (PED) with reported or documented hypothermia.

Methods: Retrospective data analysis was conducted of all well-appearing children aged 0–16 years who presented with a diagnosis of hypothermia at two tertiary PEDs from 2010 to 2019.

Results: The study comprised 99 children, 15 (15.2%) age 0–3 months, 71 (71.7%) 3–36 months, and 13 (13.1%) > 36 months. The youngest age group had increased length of stay in the hospital ($P < 0.001$) and increased rates of pediatric intensive care unit admissions ($P < 0.001$). Empirical antibiotic coverage was initiated in 80% of the children in the 0–3 months group, 21.1% in the 3–36 months group, and 15.4% in > 36 months ($P < 0.001$). Only one case of SBI was recorded and no bacteremia or meningitis. Hypothermia of unknown origin was the most common diagnosis in all age groups (34%, 42%, 46%), respectively, followed by bronchiolitis (26%) and hypoglycemia (13.3%) for 0–3 month-old children, unspecified viral infection (20%) and otitis media (7%) for 3–36-month old, and unspecified viral infection (23%) and alcohol intoxication (15.2%) in > 36 months.

Conclusion: There is a low incidence of SBI in well-appearing children presenting to the PED with hypothermia and a benign course and outcome in those older than 3 months.

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KEY WORDS: hypothermia, pediatric emergency department (PED), sepsis, serious bacterial infection (SBI)

Body temperature is regarded as a crucial indicator in assessing both health and illness [1]. While substantial data exist on fevers in children and infants as a sign of serious bacterial infection (SBI), there are scant data on hypothermia. Normal body temperature differs according to age; 36.5–38°C is considered normal. The World Health Organization defined hypothermia in infants as a temperature < 36.5°C. They classify hypothermia into three subgroups according to severity: mild 36.5–36°C, moderate 35.9–32°C, and severe hypothermia < 32°C [2]. The American Heart Association (AHA) definition for children with mild hypothermia is core temperature 32–35°C, moderate hypothermia 28–32°C, and severe < 28°C [3].

The etiology of hypothermia may be related to infections, intoxications, prolonged exposure to a cold environment [4], and/or thermoregulatory dysfunctions, which vary with age [5,6]. Hypothermia has historically been considered a sign of SBI or sepsis in the pediatric population, particularly in newborns [7] and young infants [6–9]. For this reason, patients undergo a thorough evaluation for a suspected infectious etiology and are empirically administered antibiotic treatment. Surprisingly, the role of hypothermia as an indicator of SBI in children and infants older than 90 days is poorly characterized, especially in the post-pneumococcal vaccine era when the incidence of SBI has further decreased [10].

In this study, our primary objective was to assess the prevalence of SBI in children and infants presenting at the emergency department with reported or documented hypothermia. Our secondary objective was to describe the etiology and outcomes including pediatric intensive care unit (PICU) admission, mortality, and long-term morbidity of these children.

PATIENTS AND METHODS

We conducted a retrospective cohort study at the Hadassah Hebrew University Medical Center and Shaare Zedek Medical Center, both of which are tertiary referral hospitals in Jerusalem, Israel. Data were collected from electronic medical records from January 2010 to December 2019. The sample was composed of all children aged 0–16 years with pediatric emergency department (PED) visits or a hospital discharge letter with a diagnosis of hypothermia with ICD-9 codes of 991.6, 780.65. Children with substantial co-morbidities and an ill-appearance at presentation were excluded. The data included demographics (age, sex), medical history, laboratory findings, hospitalization including length of stay (LOS), antibiotic coverage, PICU admission, long-term morbidity, and mortality. Ill appearance was established based on chart records according to the attending physician.

Children included in the study were both children with reported hypothermia by a caregiver prior to presentation and/or by the attending physician on presentation in the PED. The temperature of all children in the cohort was taken in the PED according to age recommendations for core temperature measurements. SBI was defined as a case of bacteremia, meningitis, or urinary tract infection (UTI).

This study was approved by the institutional review board (approval number: 0308-20 HMO).

STATISTICAL ANALYSIS

Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 25 (SPSS, IBM Corp, Armonk, NY, USA). Descriptive statistics for the demographic and clinical characteristics calculated the means, standard deviations, and ranges for the continuous variables, and frequencies for the discrete variables. Differences between subgroups and the clinical and demographic characteristics were assessed using Mann-Whitney or Kruskal-Wallis tests for the continuous variables, and chi-square and Fisher's exact tests for the discrete variables. Post-hoc analyses for the continuous variables were conducted using Mann-Whitney tests with a Bonferroni correction. Multivariate models for predicting well-appearing and hypothermia severity were conducted using logistic regressions. *P*-value < 0.05 was considered statistically significant.

RESULTS

Over the 10-year study period, 178 children < 16 years of age presented to the emergency department with a diagnosis of hypothermia. We excluded 79 children who manifested substantial co-morbidities and ill-appearance at presentation. The remaining 99 children were further classified into three groups: 0–3 months of age, 3–36 months of age, and older than 36 months of age [Figure 1].

The demographics and clinical characteristics are presented in Table 1. The mean age was 1.93 ± 2.75 years: 15 (15.2%) were 0–3 months old, 71 (71.7%) were 3–36 months old, and 13 (13.1%) were older than 36 months. Males predominated in all three groups with 9 (60%), 42 (59%), and 11 (84.6%), respectively.

Hypothermia was only measured at home prior to PED presentation in 6 children (40%) in the 0–3-month-old group compared to 63 (88.7%) and 11 (84.6%) in the 3–36-month-old and the > 36-month-old groups, respectively (*P* < 0.01).

Mean temperature at presentation to the PED was $35.36 \pm 1.25^\circ\text{C}$ in the 0–3-month-old group compared to $36.01 \pm 0.85^\circ\text{C}$ and $35.75 \pm 1.25^\circ\text{C}$ in the 3–36-month-old group and in the > 36-month group, respectively (*P* = 0.06).

The 0–3-month-old age group had the highest incidence of moderate to severe hypothermia 12 (80.0%), compared to 29 patients (42.0%) in 3–36-month-old group and 7 (58.3%) in the > 36 months group (*P* = 0.02). Most patients did not require active heating (87.3%). Four patients required passive heating (7.0%), three (4.2%) were warmed with a heating lamp, and one (1.4%) was warmed using warmed intravenous fluids. Three children (23.1%) in the 0–3-month-old group required hypothermia treatment, none in the 3–36-month

Figure 1. Flow chart of study population

*Substantial co-morbidities included prematurity < 32 weeks of gestational age, severe neurological deficits, and chronically ventilated children

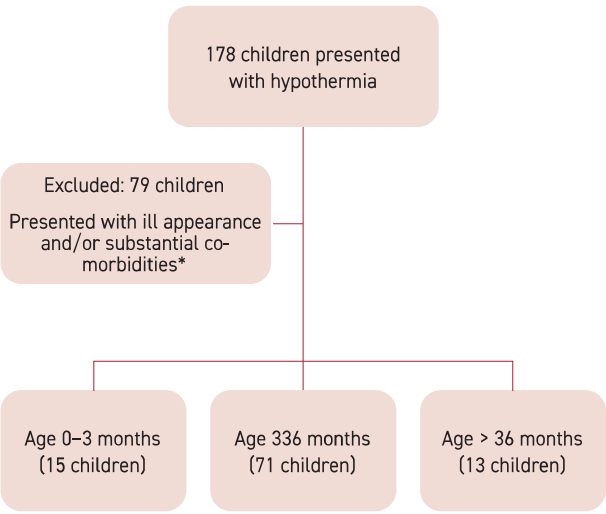


Table 1. Differences between age groups for demographic and clinical characteristics

	Age 0–3 months		Age 3–36 months		Age > 36 months		Chi-square	P-value
	Mean	N (%)	Mean	N (%)	Mean	N (%)		
Age in months	1.44		14		72.1		3.09	0.21
Sex: Male		9 (60.0)		42 (59.0)		11 (84.6)		
Hypothermia severity							7.49	0.02
Mild		3 (20.0)		40 (58.0)		5 (41.7)		
Moderate-severe		12 (80.0)		29 (42.0)		7 (58.3)		
Measured temperature at home (°C)	35.36 ± 0.30		34.96 ± 0.64		34.69 ± 0.82			0.19
Measured temperature at PED (°C)	35.36 ± 1.25		36.01 ± 0.85		35.75 ± 1.25			0.06
Oxygen saturation < 92% (number of patients)	4		0		0			0.00
Hospitalization length of stay	3.60 ± 2.29		0.75 ± 1.82		0.46 ± 0.88			0.00
Reported hypothermia at home		6 (40.0)		63 (88.7)		11 (84.6)	19.10	0.00
Complete Immunization coverage		4 (57.1)		57 (98.3)		8 (88.9)	17.08	0.00
Pediatric critical care unit admission rate		7 (46.7)		1 (1.4)		0	35.46	0.00

Continuous variables with sub-groups of fewer than 5 patients were excluded from the analysis and the table

PED = pediatric emergency department

Table 2. Demographic and clinical characteristics according to hypothermia severity.

	Mild hypothermia (N=49)		Moderate and severe hypothermia (N=48)		Chi-square	P-value
	Mean ± SD	N (%)	Mean ± SD	N (%)		
Age, in months	2.08 ± 2.64		1.76 ± 2.93			0.08
Sex: Male		27 (55.1)		34 (70.8)	2.57	0.11
Temperature at home	35.11 ± 0.57		34.79 ± 0.72			0.05
Temperature at intake	36.54 ± 0.37		35.09 ± 0.66			0.00
Hospitalization length of stay	0.14 ± 0.41		2.21 ± 2.56			< 0.01
Hypothermia at home		45 (91.8)		33 (68.8)	8.20	0.00
Positive urine culture		1 (16.7)		0	3.80	0.21
Spinal fluid culture taken		0		12 (25.0)	13.98	< 0.01
Blood culture taken		16 (33.3)		41 (85.4)	26.99	< 0.01
Positive blood culture		0		1 (2.3)	0.40	0.99
Empirical antibiotics		3 (6.1)		26 (54.2)	26.70	0.01
Pediatric intensive care unit admission		0		8 (16.7)	8.90	0.01
Hypothermia therapy		0		4 (10.5)	3.03	0.08

Continuous variables with sub-groups of fewer than 5 patients were excluded from the analysis and the table

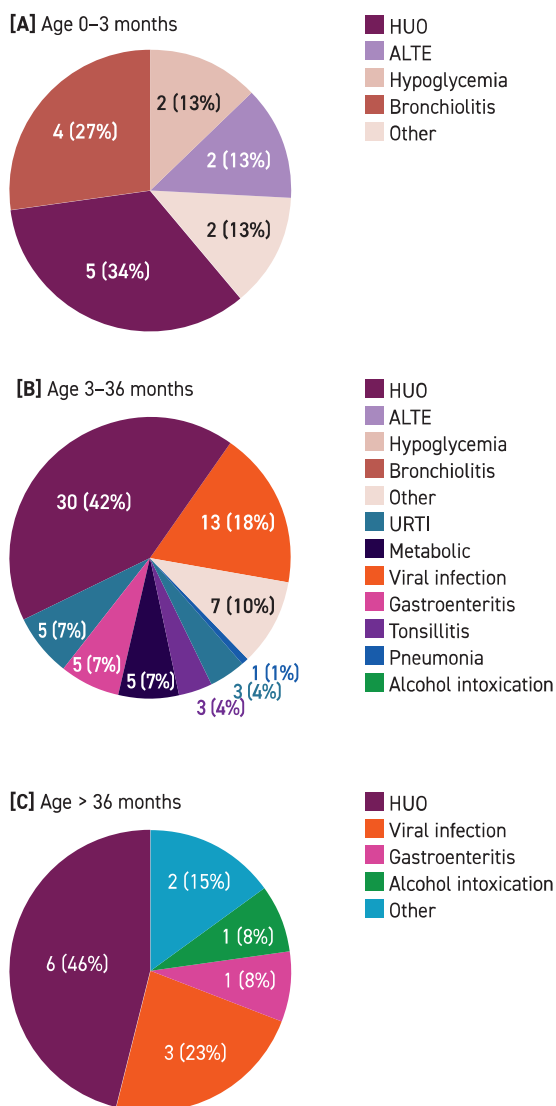
group, and one in the > 36-month group ($P < 0.001$). LOS in the 0–3-month-old group was 3.60 days ± 2.29 and was longer compared to the 3–36-month-old and > 36-month-old groups, in which the mean LOS was 0.75 days ± 1.82 and 0.46 days ± 0.88, respectively ($P < 0.001$). PICU admissions were recorded for 7 children (46.7%) in the 0–3-month-old age group compared to 1 (1.4%) in the 3–36-month-old and none in the > 36-month-old groups ($P < 0.001$).

The mean white blood cell counts (WBC) were within normal values adjusted for age in all three groups. C-reactive protein levels were 2.54 mg/dl ± 4.28, 2.6 mg/dl ± 2.59, and 1.47

mg/dl ± 2.12 in the 0–3-month, 3–36 month, and > 36-month-old groups, respectively ($P = 0.07$). Urine culture was collected in 12, 25, and 7 children, respectively. Blood cultures were performed in 13 (86.7%), 40 (57.1%), and 7 (53.8%), respectively. A lumbar puncture was performed in 12 (80%) of the 0–3-month-old group, but not in either of the other groups. Two cases of bacterial growth in the urine cultures were recorded in the 3–36-month-old group, one of which was considered a contamination with polymicrobial growth. No cases of meningitis were recorded. There were two cases of bacterial growth in the blood cultures, and both rendered contaminants

Figure 2. Age groups and diagnosis at discharge

ALTE = apparent life-threatening event, AOM = acute otitis media, HUO = hypothermia of unknown origin, URTI = upper respiratory tract infection



(*Staphylococcus epidermitis* and *Micrococcus luteus*). The serious bacterial infection incidence was 1.01%.

Empirical antibiotic coverage was initiated in 12 (80%) of the children in the 0–3-month-old group, 15 (21.1%) in the 3–36-month-old group, and 2 (15.4%) in the > 36-month-old group ($P < 0.001$).

Diagnosis at discharge is shown in Figure 2. The most common diagnoses at discharge in the 0–3-month-old group were hypothermia of unknown origin in 5 (33.3%) cases, bronchiolitis in 4 (27%) cases, and hypoglycemia in 2 (13.3%) cases. In the 3–36-month-old group, hypothermia

of unknown origin was diagnosed in 30 (42%) cases and unspecified viral infection in 13 (18%) cases, otitis media in 5 (7%), and acute tonsillitis in 3 (4.22%). In the > 36-month-old group, hypothermia of unknown origin was diagnosed in 6 (46.2%) cases, unspecified viral infection in 3 (23%) cases and alcohol intoxication in 2 (15.2%) cases.

Table 2 presents the groups according to hypothermia severity. Patients with moderate or severe hypothermia had longer hospitalizations than patients with mild hypothermia with $2.21 \text{ days} \pm 2.56$ versus $0.14 \text{ days} \pm 0.41$ respectively ($P < 0.01$). In patients with mild hypothermia, fewer blood cultures were drawn in comparison to patients with moderate or severe hypothermia: 16 children (33.3%) vs. 41 children (85.4%) respectively ($P < 0.01$). Lumbar puncture was performed only in cases where severe hypothermia was recorded in 12 cases (25.0%, $P < 0.01$). PICU admissions only took place in the severe hypothermia group with 8 (16.7%) children admitted to the PICU ($P < 0.01$). No mortality was recorded in our cohort. Patients with mild hypothermia were less likely to be treated with empirical antibiotics than patients with moderate or severe hypothermia; namely, 3 children (6.1%) versus 26 children (54.2%) respectively, $P < 0.01$.

DISCUSSION

This study highlights the benign outcomes of well-appearing children above the age of 3 months who present with hypothermia recorded at home or with low body temperature measured at presentation to the emergency department.

Hypothermia has been recognized as a sign of sepsis and SBI in infants and children and thus is included with fever in the criteria for diagnosis of systemic inflammatory response syndrome [7]. While several studies of infants below the age of 3 months have reported low body temperature in conjunction with SBI [11–16], others have failed to find correlations and concluded that the prevalence of SBI in hypothermic young infants in the PED is low [17].

The findings of this study show an absence of SBI in hypothermic 0–3-month-old children but an increased incidence of desaturation on presentation, metabolic derangements (e.g., hypoglycemia) as well as an increased rate of admissions to the PICU and increased LOS in the hospital. Infants below the age of 3 months presenting with hypothermia were also more likely to have a full sepsis workup ($P < 0.001$) and to receive empirical antibiotic treatment ($P < 0.001$) compared to older infants and children. Interestingly, in 41% of the cases in this age group, no cause of hypothermia was found. Four infants in this group were eventually diagnosed with bronchiolitis, highlighting the association between bronchiolitis and hypothermia, as

previously reported [18,19]. Limited research exists concerning hypothermia in healthy infants and children over the age of 3 months. For our study, complete blood counts and blood and urine cultures were obtained in 71% of the children in this age group. Empirical antibiotic treatment was initiated in 31.4%. However, no case of bacteremia or meningitis and only one case of UTI were recorded. In this age group as well, the most common diagnosis was an unknown cause of hypothermia, followed by unspecified viral infection and trivial bacterial infections such as otitis media and tonsillitis. Full recovery and a short admission stay characterized this age group.

Note that therapeutic measures to correct hypothermia, including external rewarming methods, may be harmful in severe hypothermia and may be ineffective in patients without spontaneous circulation [20]. These measures were uncommon and were used in only four patients.

This study has several limitations. The retrospective nature of this study prevented the collection of all the relevant data missing from the charts. In addition, children with hypothermia might not have been included if they did not have an ICD code for hypothermia. In addition, the sample was relatively small since the study excluded ill-appearing, severely injured, and/or hemodynamically unstable children. No outpatient clinic follow-up was documented; thus, the results apply solely to well-appearing children presenting with hypothermia. While the decision to include reported hypothermia at home by the caregiver might represent a limitation as few children with normothermia were eventually included in the cohort, we believe that including those children is important as many attending pediatricians will address it as true hypothermia similarly to reported fever by caregiver and normothermia at presentation.

CONCLUSIONS

These findings portray the common etiologies of hypothermia in well-appearing infants and children over a 10-year period of admissions to the PED in two tertiary hospitals in Israel. They highlight the low incidence of SBI and the benign course and outcome in infants and children older than 3 months. These study results do not support the use of ancillary laboratory tests and empirical antibiotic treatment in the case of well-appearing children over the age of 3 months presenting to the emergency department.

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