ARTICLE IN PRESS
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Pediatrics and Neonatology xxx (xxxx) xxx

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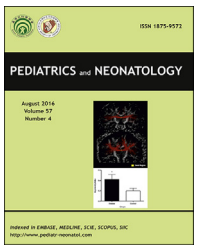
journal homepage: http://www.pediatr-neonatol.com



Original Article

Risk factors for hospitalization at the pediatric intensive care unit among infants and children younger than 5 years of age diagnosed with infectious diseases

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Received Feb 24, 2022; received in revised form Jun 2, 2022; accepted Jun 14, 2022
Available online ■ ■ ■

Key Words
children;
infectious disease;
intensive care;
PICU

Abstract *Background:* Children hospitalized with infectious diseases may develop severe, life-threatening conditions, often requiring admission to pediatric intensive care unit (PICU). The objectives of this study were to identify independent risk factors for PICU hospitalization with an infectious disease in children <5 years of age.
Methods: In southern Israel, two populations live side by side: the middle—high income Jewish population and the low-income Bedouin population, both receiving equal and free medical care at the only tertiary medical center in the area. The study population included all children born in southern Israel and hospitalized at PICU with an infectious disease during 1991—2012. Risk factors for PICU hospitalizations were retrospectively studied by Kaplan—Meier and Cox proportional hazard survival analyses.
Results: 9951 Jewish children and 18,002 Bedouin children were enrolled; overall, 1135 episodes of PICU hospitalizations with an infectious disease were recorded (879, 77.4% Bedouin and 256, 22.6% Jewish patients). Bedouin children had a higher risk for PICU hospitalization with an infectious disease compared with Jewish children (adjusted Hazard Ratio [adj. HR] 1.7, 95% CI 1.5—2.0); maternal multiparity and low-birth weight (<2500 g) were additional risk factors for PICU hospitalization with an infectious disease compared to firstborns (adj. HR = 1.2, 95% CI 1.0—1.5) or to children with a birth weight ≥2500 g (adj. HR = 1.5, 95% 1.2—1.9). Older age was a protective factor for PICU hospitalization (adj. HR = 0.98, 95% CI 0.97—0.99). Children hospitalized with a central nervous system infection had the highest risk of PICU hospitalization (adj. HR 6.8, 95% CI 5.5—8.4), followed by those with urinary tract

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https://doi.org/10.1016/j.pedneo.2022.06.012

Please cite this article as: J. Freedman, E. Leibovitz, R. Sergienko et al., Risk factors for hospitalization at the pediatric intensive care unit among infants and children younger than 5 years of age diagnosed with infectious diseases, Pediatrics and Neonatology, https://doi.org/10.1016/j.pedneo.2022.06.012

infections (UTI, adj. HR 3.1, 95% CI 2.5—3.8) and those with lower respiratory tract infections (LRTI, adj. HR 2.9, 95% CI 2.4—3.4).
Conclusion: Bedouin ethnicity, low birth weight, maternal multiparity and younger age were significant risk factors for PICU hospitalizations with an infectious disease. Among the infectious diseases analyzed, CNS infection had the highest risk for PICU hospitalization, followed by UTI and LRTI.

1. Introduction

Infectious diseases represent a serious burden on the medical system. Despite major medical advancements in the last few decades and a significant decrease in infectious disease morbidity and mortality in the 20th century, infectious diseases were the leading cause of primary care visits in the United States for children up to the age of 12 years.[1,2] Lower respiratory tract infections (LRTI) followed by urinary tract infections (UTI) were the main leading causes of infectious disease hospitalization across all age groups.[3,4]

The Pediatric Intensive Care Unit (PICU) admits critically ill or injured children requiring advanced medical care for potentially life-threatening medical conditions who are cared for by a multidisciplinary and highly qualified team. The conditions for PICU admission include, among many others, respiratory insufficiency, circulatory failure, neurological diseases, and infectious diseases leading to major organ dysfunction.[5]

The Negev region of southern Israel is populated by two distinct populations. The Bedouin Arab population has, in general, a low-income and is in transition from a semi-nomadic to a modern urban lifestyle. They reside in the city of Rahat or one of the 6 local councils, 12 Bedouin settlements or 22 Bedouin tribes-all in the Negev area. The Jewish population is considered a middle to high-income population and lives mostly in the city of Beer-Sheva and the surrounding Jewish settlements. Both populations receive free and equal medical care from the only tertiary hospital in the Negev region, the Soroka University Medical Center (SUMC) in Beer-Sheva.

The association between poverty and infectious diseases morbidity has long been established. Populations suffering from lower socioeconomic status were reported to suffer from higher infection rates.[6,7] This has been shown in Israel as well, with higher rates of infectious disease hospitalizations for Bedouin children. A study from the SUMC published in 1998 found that Bedouin children had higher rates of all infectious disease hospitalizations, with the highest risk for children younger than one year.[8] Bedouin children younger than 5 years also had higher rates of Norovirus-related gastroenteritis hospitalization than Jewish children, with a rate ratio of 2 (95% CI 1.6—2.3).[9] Similar findings have been published regarding Rotavirus, with a significant drop in both infectious and hospitalization rates post-vaccination against this agent in both Jewish and Bedouin populations.[10] However, the Bedouin children had higher hospitalization rates before and after the introduction of the vaccine, and the drop in hospitalization rates was less significant.[10] An association has also been found in the United States between ethnicity and PICU admissions, with African Americans shown to have a higher risk for PICU admission compared to non-Hispanic white Americans.[11] Children growing up in or around poverty had higher rates of PICU admissions.[12] In our geographic area, in respect to PICU admissions with infectious diseases, Bedouin children were shown to have a two-fold risk of ICU admission with community-acquired alveolar pneumonia compared with Jewish children (adj. OR = 2.67, 1.72—4.16).[13]

Despite the general knowledge of ethnic disparities in PICU admissions, the relationship between ethnicity and infectious disease PICU hospitalizations has not been extensively studied. The objective of our study was to identify independent risk factors for PICU hospitalization with an infectious disease in infants and children younger than 5 years of age while focusing on the differences between Bedouin and Jewish children living in southern Israel.

2. Material and methods

We conducted a population-based retrospective cohort study that included all Jewish and Bedouin children born at the SUMC who were hospitalized with an infectious disease at SUMC between the years 1991—2012.

The focus of our study was on analyzing the differences between Bedouin and Jewish children in respect to infectious disease PICU hospitalizations; therefore, the primary exposure was defined as Bedouin ethnicity.

We excluded from the analysis children who were not hospitalized with an infectious disease as well as all non-singleton births, perinatal deaths and patients with major congenital malformations (ICD-9 codes 740.0—757.9). Demographic, obstetric, and hospitalization information was obtained from the SUMC computerized database. For our study, the SUMC perinatal database of the obstetrics and gynecology department was merged with the SUMC pediatric hospitalization database for each study case. The hospitalization files included information on infectious disease hospitalizations from all pediatric wards, including the PICU.

The primary outcome was defined as the first PICU hospitalization from birth until the age of 5 years. Infectious diseases diagnoses were grouped in 4 major groups, according to their incidence among the pediatric population: lower respiratory tract infections (LRTI) (ICD-9 codes 466,

Table 1 Demographic, maternal and obstetrical characteristics: comparison between Jewish and Bedouin children (n = 27,953).

Demographic, maternal and obstetrical characteristics		Ethnicity		p value
		Jewish % (n) (n = 9951)	Bedouin % (n) (n = 18,002)	
Gender	Male	54.9 (5467)	56 (10,083)	0.083
	Female	45.1 (4484)	44 (7918)	
Birth order	Second or higher	71.9 (7153)	84.19 (15,141)	<0.001
	Firstborn	28.1 (2795)	15.9 (2857)	
Mother age (years, mean ± SD)		29.26 ± 5.60	27.31 ± 5.82	<0.001
Gestational age at time of birth (weeks, mean ± SD)		38.92 ± 2.13	38.99 ± 2.20	0.011
Birth weight <2500 g	Yes	6.6 (635)	7.4 (1278)	0.019
	No	93.4 (9002)	92.6 (16,096)	
Gestational Diabetes	Yes	6.6 (658)	4.2 (756)	<0.001
	No	93.4 (9293)	95.8 (17,246)	
Hypertension	Yes	6.4 (635)	5.2 (945)	<0.001
	No	93.6 (9316)	94.8 (17,057)	
Low APGAR score at 5 min (<8)	Yes	1.0 (95)	1.2 (207)	0.104
	No	99 (9771)	98.8 (17,396)	

481.0—488.89), acute gastroenteritis (AGE) (ICD-9 codes 005.9, 008, 009.2, 558), urinary tract infection (UTI) (ICD-9 codes 590.8, 595.0, 599.0) and central nervous system (CNS) infection (ICD-9 codes 003.21, 036.0, 047.8—048, 054.3, 054.72, 098.82, 320.0—320.9, 322.9). All other infectious diseases were grouped together for the statistical analysis. Infectious disease diagnoses were coded according to the ICD-9. Since we defined an infectious disease according to the main or secondary diagnosis from each hospitalization, the sum of infectious disease diagnoses added up to more than the total sum of hospitalizations.

The study received the approval of the Institutional Review Board Committee of the SUMC (0046-13- SOR). Our study was a retrospective cohort database study and exempt from informed consent.

2.1. Statistical analysis

Statistical analysis was performed using SPSS software package version 26.0. Assumptions were two-sided with an $\alpha = 0.05$. Initially, we compared background, medical and obstetrical characteristics between the Bedouin and Jewish children. The Chi-squared test was used for categorical variables. Quantitative variables with normal distribution were compared using the independent t-test. Kaplan—Meier survival curves were used to compare PICU infectious disease hospitalization cumulative incidence between Jewish and Bedouin children. Survival and Hazard Functions were computed. The log-rank test was used to assess the differences between the two curves of Jewish and Bedouin Hazard Functions. Only the first PICU hospitalization was used for each case.

Multivariable survival analysis was performed using the Cox proportional hazards model. The independent variables were defined as follows: ethnicity (Bedouin/Jewish); mother's age (years); gestational age at the time of birth (weeks); gender (male/female), parity (firstborn/second-born or higher), weight at birth (<2500 g/2500 g/higher), APGAR score at 5 min (<8/8 or higher). Proportionality over time was tested for all independent variables.

3. Results

During the study period, a total of 27,953 children were enrolled, of whom 18,002 (64.45) were Bedouin Arabs and 9951 (35.6%) were of Jewish ethnicity. Of these hospitalizations, 8698 had a diagnosis of AGE, 7428 of LRTI, 2195 of UTI, 1046 of a CNS infection and 12,246 were diagnosed with another infectious disease.

Table 1 compares the background demographic, maternal and obstetrical data between the study groups. Excluding gender and APGAR score at 5 min, a significant difference was found in all background characteristics between the two groups. Bedouin mothers were younger at birth compared with Jewish mothers (mean age 27.31 ± 5.82 *vs.* 29.26 ± 5.60 years, respectively, $p < 0.001$). More Bedouin children had a low birth weight compared with Jewish children (7.4% vs. 6.6%, $p = 0.019$). More Bedouin mothers were multipara compared with Jewish mothers (84.1% *vs.* 71.9%, $p < 0.001$). Bedouin children had a significantly older gestational age at the time of birth compared with Jewish children (mean 38.99 ± 2.20 *vs.* 38.92 ± 2.13 weeks, $p = 0.011$).

A total of 1135 episodes of PICU hospitalizations with an infectious disease (from birth until the age of 5 years) were recorded during the study period. Table 2 presents a univariable analysis between children with a PICU hospitalization and those without a PICU hospitalization and

Table 2 PICU hospitalization rates by demographic, maternal and obstetrical characteristics: crude Hazard Ratio (HR) and 95% Confidence Interval (95% CI) for episode of pediatric intensive care unit hospitalization, from birth to the age of 5 years (n = 27,953).

Demographic and medical characteristics		Hospitalization in PICU with an infectious disease		p value (comparing hospitalization rates)	Crude HR (95% CI) p value
		No = 26,818 % (n)	Yes = 1135 % (n)		
Ethnicity	Bedouin	63.8 (17,123)	77.4 (879)		1.92 (1.67–2.21)
	Jewish	36.2 (9695)	22.6 (256)	<0.001	<0.001
Gender	Male	55.5 (14,880)	59.1 (670)	0.017	1.15 (1.02–1.29)
	Female	44.5 (11,938)	40.9 (464)		0.017
Birth order	Second or higher	79.6 (21,336)	84.4 (958)	<0.001	1.38 (1.17–1.62)
	Firstborn	20.4 (5475)	15.6 (177)		<0.001
Mother age in years (mean ± SD)[a]		28.00 ± 5.81	28.10 ± 6.09	0.598	1.00 (0.99–1.01)
				0.593	
Gestational age at time of birth in weeks (mean ± SD)[b]		39.00 ± 2.11	38.18 ± 3.21	<0.001	0.88 (0.86–0.89)
					<0.001
Birth weight	<2500 gr.	6.9 (1790)	11.9 (123)	<0.001	1.81 (1.50–2.19)
					<0.001
	≥2500 gr.	93.1 (24,191)	88.1 (907)		
Gestational Diabetes	Yes	5.1 (1355)	5.2 (59)	0.826	1.03 (0.79–1.34)
	No	94.9 (25,463)	94.8 (1076)		0.817
Maternal Hypertension	Yes	5.6 (1509)	6.3 (71)	0.369	1.12 (0.88–1.42)
	No	94.4 (25,309)	93.7 (1064)		0.354
Apgar score at 5 min	≤7	1.1 (279)	2.1 (23)	0.001	2.00 (1.32–3.02)
	≥8	98.9 (26,099)	97.9 (1068)		0.001
Age at time of hospitalization with infectious disease in months (mean ± SD)[c]		8.1 ± 12.29	5.0 ± 10.07	<0.001	0.97 (0.96–0.98) <0.001
AGE	Yes	31.7 (8501)	17.4 (197)	<0.001	0.45 (0.39–0.53)
	No	68.3 (18,317)	82.6 (938)		<0.001
LRTI	Yes	25.9 (6949)	42.2 (479)	<0.001	2.06 (1.83–2.32)
	No	74.1 (19,869)	57.8 (656)		<0.001
CNS infection	Yes	3.3 (893)	13.5 (153)	<0.001	4.23 (3.57–5.01)
	No	96.7 (25,925)	86.5 (982)		<0.001
UTI	Yes	7.5 (2023)	15.2 (172)	<0.001	2.15 (1.83–2.54)
	No	92.5 (24,795)	84.8 (963)		<0.001
Other infectious disease	Yes	44.2 (11,845)	35.3 (401)	0.001	0.69 (0.61–0.78)
	No	55.8 (14,973)	64.7 (734)		0.001

[a] Risk is measured per one-year increase in mother age.
[b] Risk is measured per weekly increase in gestational age at time of birth.
[c] Risk is measured per one-month increase in child age at time of hospitalization.

analyzes the background characteristics and risk factors for PICU hospitalizations with an infectious disease. Overall, Bedouin children were at a higher risk for PICU hospitalization with a crude hazard ratio (HR) of 1.92 (95% CI 1.67–2.21); males were at a higher risk compared with females (crude HR 1.15, 95% CI 1.02–1.29) and second-born children or higher were at a higher risk compared to first-borns (crude HR = 1.38, 95% CI 1.17–1.62). Children born with low birth weight were at a higher risk for PICU hospitalizations (crude HR = 1.81, 95% 1.50–2.19). Older gestational age at birth was a protective factor against infectious disease hospitalization (crude HR = 0.881, 95% CI 0.864–0.899), as was older age at time of hospitalization with an infectious disease (crude HR = 0.97, 95% CI 0.96–0.98). Mother's age at the time of birth, gestational diabetes and maternal hypertension were not found to be significantly associated with PICU hospitalization in both study groups. The risk of PICU hospitalization for each group of diseases (as the main or secondary diagnosis) was computed: LRTI (crude HR = 2.062, 95% CI 1.833–2.320),

CNS infections (crude HR = 4.233, 95% CI 3.570—5.019) and UTI (crude HR = 2.15, 95% CI 1.83—2.54) all presented a higher risk for PICU admission, while acute gastroenteritis (AGE) (crude HR = 0.458, 95% CI 0.393—0.534) and other infectious diseases (crude HR = 0.693, 95% CI 0.614—0.783) were protective factors against PICU admissions.

Kaplan—Meier survival analysis was computed and is presented in Fig. 1. The figure shows a significantly higher cumulative hazard for PICU hospitalization with an infectious disease in Bedouin children.

For the multivariable analysis, we used the Cox proportional hazard model including the following variables: ethnicity, gender, parity, maternal age, gestational age at birth, low birth weight, age at time of hospitalization and the specific infectious disease diagnoses. A low APGAR score at 5 min, which was not a significant risk factor in the univariable analysis, was excluded from the final model. Table 3 summarizes the adjusted HRs and 95% CI for each of the variables. Bedouin ethnicity was a significant risk factor for PICU hospitalizations with an infectious disease, with an adj. HR of 1.7 (95% CI 1.5—2.0). Low birth weight and maternal multiparity were both independent risk factors for PICU hospitalizations with infectious diseases (adj. HR = 1.5, 95% CI 1.2—1.9; adj. HR = 1.2, 95% CI 1.0—1.5, respectively), while an older gestational age the time of birth was a protective factor (adj. HR = 0.94, 95% CI 0.91—0.98). Older age at time of hospitalization was a protective factor for PICU hospitalizations with an infectious disease (adj. HR = 0.98, 95% CI 0.97—0.99). Younger maternal age at birth and male gender lost their significance in the multivariable regression analysis. Regarding the diagnosis of infectious disease, a CNS infection presented the highest risk for admission to PICU with an adj. HR of 6.8 (95% CI 5.5—8.4), followed by UTI (adj. HR = 3.1, 95% CI 2.5—3.8), LRTI (adj. HR = 2.9, 95% CI 2.4—3.4) and other infectious diseases (adj. HR = 1.3, 95% CI 1.1—1.5). AGE lost significance in the multivariable model.

To test for potential confounding, we conducted sensitivity analyses to address the relationship between ethnicity and multiparity, and between ethnicity and low birth weight. For multiparty there was no difference on the effect of Bedouin ethnicity between primiparous (adj. HR = 2.1, 95% CI 1.4—3.3), multiparous (adj. HR = 1.7, 95% CI 1.1—2.6) and grand-multiparous (≥5 births) women (adj. HR = 1.9, 95% CI 1.4—2.5). In the sub analysis by low birth weight, Bedouin ethnicity lost significance in the low birthweight group (adj. HR = 1.5, 95% CI 0.99—2.5). There was no change in effect in the normal birthweight group (adj. HR = 1.7, 95% CI 1.5—2.0).

4. Discussion

Previous studies established that lower socioeconomic status is a risk factor for infectious disease hospitalization,[14] and specifically for PICU admission with an infectious disease.[13] Our study confirms these findings. We showed that Bedouin children, belonging to a low-income population living in southern Israel, had an almost twofold risk for PICU admission once hospitalized with an infectious disease. The meaning of this finding is that Bedouin children not only have a higher risk of infectious disease hospitalization, as previously shown,[8—10,13] but also the presentation of the disease is more severe compared to Jewish children. As our study focused on PICU hospitalizations, and therefore on children with more severe, life-threatening medical conditions, we conclude that the association between illness severity and lower socioeconomic status is real and not confounded by the possibility of a clinician's decision to hospitalize more children from a lower socioeconomic

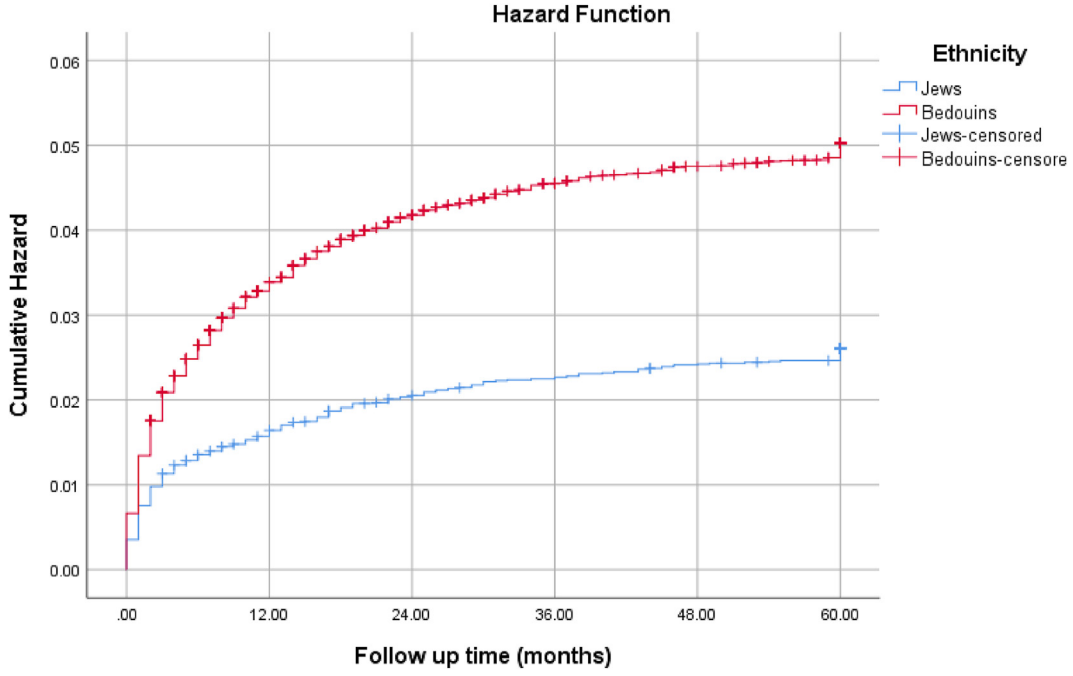

Figure 1 Comparison of PICU admissions with an infectious disease between Bedouin and Jewish children younger than 5 years of age.

Table 3 Cox proportional hazard model for the association between ethnicity and pediatric intensive care unit hospitalizations with an infectious disease, with adjusted Hazard Ratios (adj. HR) and 95% Confidence Intervals (95% CI) (n = 26,681).

Variables		Adj. HR	95% CI	p value
Ethnicity (Bedouin, Jewish)		1.7	1.5–2.0	<0.001
Birth weight< 2500 (Yes, No)		1.5	1.2–1.9	<0.001
Multiparity (Yes, No)		1.2	1.0–1.5	0.025
Gender (Male, Female)		1.1	0.9–1.2	0.074
Gestational age at birth (Weeks)[a]		0.94	0.91–0.98	0.008
Mother's age (Years)[b]		1.0	0.9–1.0	0.321
Age at time of hospitalization (Months)[c]		0.98	0.97–0.99	<0.001
Infectious disease diagnosis	CNS infection (Yes, No)	6.8	5.5–8.4	<0.001
	LRTI (Yes, No)	2.9	2.4–3.4	<0.001
	UTI (Yes, No)	3.1	2.5–3.8	<0.001
	AGE (Yes, No)	0.9	0.7–1.1	0.403
	Other Infectious disease (Yes, No)	1.3	1.1–1.5	0.001

[a] Risk is measured per weekly increase in gestational age at time of birth.
[b] Risk is measured per one-year increase in mother age.
[c] Risk is measured per one-month increase in child age at time of hospitalization.

background due to an inability to adequately follow-up with necessary care, as previously established.[12]

Among the infectious diseases, we found that CNS infection had the highest risk for PICU hospitalization. Meningitis, though rare, is a serious cause of morbidity, with a mortality rate of 1–8% due to neurological or hemodynamic impairment.[15] Although an uncommon disease, children who present with an infection of the CNS have a much higher risk of being admitted to the PICU due to the seriousness of the illness. In a large cohort of children with sepsis admitted to the PICU in 7 European countries, CNS infection was the most frequently diagnosed (23%), followed by pneumonia (19%).[16] In our study, LRTIs represented a large number of all hospitalizations, and the risk for PICU admission was three times higher than in children without an LRTI. In both cases of CNS infections and LRTIs, studies have shown that the largest burden is in children under the age of 5 years, and mostly from vaccine-preventable agents, including *Neisseria meningitidis* and *Streptococcus pneumoniae*.[17]

UTI is a common source of infection in children admitted to the PICU with fever and hemodynamic instability, particularly in those younger than 2 years of age, or in patients with immunosuppression and congenital renal anomalies.[18,19] In our study, we found that children with a diagnosis of a UTI had a higher risk for PICU admission, although our study excluded children with a congenital renal anomaly. Because UTI is a common infection in children and adults alike, most cases are treated in the community, and only a minority are severe enough to necessitate hospitalization, therefore explaining, most probably, the high risk for admission to PICU in this group.

Although AGE is a leading cause of mortality in low-income countries, it is less so in developed countries.[20] In our study, AGE was the single most common infectious disease diagnosis, and yet hospitalization with AGE was not significantly associated with PICU hospitalization. Despite the high prevalence of AGE in the pediatric wards, it is mostly a self-limiting, non-life-threatening illness, which explains our findings.

We found that low birth weight was an independent risk factor for PICU admission. Previous studies have shown that low birth weight is an independent risk factor for PICU admission and respiratory support for children hospitalized with bronchiolitis.[21] In our study, older age at birth was associated with a lower chance of PICU hospitalization. This finding correlates with similar studies that showed that prematurity was a risk factor for PICU admission.[13] We used multiparity of the mother as an indicator of crowding at home, under the assumption that firstborn children would most likely live in surroundings without siblings, and subsequently born children would have siblings at home. Crowding is a well-established risk factor for infectious diseases,[14] although, to our knowledge, it has not been specifically associated with PICU hospitalizations in the past. Crowding is one of many physical living conditions that could explain the higher risk for hospitalization of children from low-income, low-socioeconomic households, where other factors (including environmental pollution and higher exposure to tobacco) are more common compared to higher socioeconomic areas.[12] In our study, older age at time of hospitalization with an infectious disease was a protective factor for PICU admission. These findings are similar to data presented in other studies that show a higher severity of infectious diseases in younger age groups.[6,8]

Male gender, an established risk factor for infectious disease morbidity,[3,22] and younger maternal age, which has also been shown to be an independent risk factor for infectious disease mortality,[23] were not significant risk factors for PICU hospitalization with an infectious disease in our study.

This study has some limitations, mainly related to the time period of the study completion. Our database included information on children born in the SUMC and hospitalized in the PICU between the years 1991 and 2012. Therefore, we could not evaluate the effects of two important vaccines, the pneumococcal and anti-rotavirus vaccines, which were introduced into the Israeli routine national vaccination program in 2009 and 2010, respectively. Although the efficacy of these vaccinations in reducing disease-related

hospitalizations has been established around the world,[24–27] previous studies have shown that lower socioeconomic status is still a risk factor for PICU admission,[12,13] and therefore we believe our findings retain their value remain of this limitation. More research is necessary to validate our findings during the years since the implementation of these two important vaccines.

Our data highlight the importance and potential impact of infectious diseases on health care utilization and health service needs of the pediatric populations in southern Israel. The findings of high rates of hospitalizations for infectious diseases at PICU in Bedouin infants are important from the viewpoint of health-related outcomes as well as from the viewpoint of the economic costs involved. Preventive measures such as introduction of additional and new vaccines should be considered, as well as improved sanitation and maternal education, in the attempt to reduce the disease burden from infectious diseases in general, and that of the Bedouin population in particular.

Funding

This research received no financial support or institutional funding.

Declaration of competing interest

None.

References

1. Low M, Almog R, Balicer RD, Liberman N, Raz R, Peretz A, et al. Infectious disease burden and antibiotic prescribing in primary care in Israel. *Ann Clin Microbiol Antimicrob* 2018;**17**:26.
2. Cherry DK, Woodwell DA, Rechtsteiner EA. National Ambulatory Medical Care Survey: 2005 Summary. *Adv Data* 2007;(387):1–39.
3. Yorita KL, Holman RC, Sejvar JJ, Steiner CA, Schonberger LB. Infectious disease hospitalizations among infants in the United States. *Pediatrics* 2008;**121**:244–52.
4. Christensen KL, Holman RC, Steiner CA, Sejvar JJ, Stoll BJ, Schonberger LB. Infectious disease hospitalizations in the United States. *Clin Infect Dis* 2009;**49**:1025–35.
5. Frankel LR, Hsu BS, Yeh TS, Simone S, Agus MSD, Arca MJ, et al. Criteria for critical care infants and children: PICU admission, discharge, and triage practice statement and levels of care guidance. *Pediatr Crit Care Med* 2019;**20**:847–87.
6. Blakely T, Atkinson J, Kiro C, Blaiklock A, D'Souza A. Child mortality, socioeconomic position, and one-parent families: independent associations and variation by age and cause of death. *Int J Epidemiol* 2003;**32**:410–8.
7. Council on Community Pediatrics. Poverty and child health in the United States. *Pediatrics* 2016;**137**:e20160339.
8. Levy A, Fraser D, Vardi H, Dagan R. Hospitalizations for infectious diseases in Jewish and Bedouin children in southern Israel. *Eur J Epidemiol* 1998;**14**:179–86.
9. Leshem E, Givon-Lavi N, Vinjé J, Gregoricus N, Parashar U, Dagan R. Differences in Norovirus-associated hospital visits between Jewish and Bedouin children in southern Israel. *Pediatr Infect Dis J* 2015;**34**:1036–8.
10. Givon-Lavi N, Ben-Shimol S, Cohen R, Greenberg D, Dagan R. Rapid impact of rotavirus vaccine introduction to the National Immunization plan in southern Israel: comparison between 2 distinct populations. *Vaccine* 2015;**33**:1934–40.
11. Turner D, Simpson P, Li SH, Scanlon M, Quasney MW. Racial disparities in pediatric intensive care unit admissions. *South Med J* 2011;**104**:640–6.
12. Andrist E, Riley CL, Brokamp C, Taylor S, Beck AF. Neighborhood poverty and pediatric intensive care use. *Pediatrics* 2019;**144**:e20190748.
13. Feinstein Y, Greenberg D, Ben-Shimol S, Mimran M, Dagan R, Givon-Lavi N. Characterization of children younger than 5 Years of age with severe community-acquired alveolar pneumonia (CAAP) requiring Pediatric Intensive Care Unit (PICU) admission. *Pediatr Neonatol* 2020;**61**:406–13.
14. Thrane N, Søndergaard C, Schønheyder HC, Sørensen HT. Socioeconomic factors and risk of hospitalization with infectious diseases in 0- to 2-year-old Danish children. *Eur J Epidemiol* 2005;**20**:467–74.
15. Odetola FO, Bratton SL. Characteristics and immediate outcome of childhood meningitis treated in the pediatric intensive care unit. *Intensive Care Med* 2005;**31**:92–7.
16. Boeddha NP, Schlapbach LJ, Driessen GJ, Herberg JA, Rivero-Calle I, Cebey-López M, et al. Mortality and morbidity in community-acquired sepsis in European pediatric intensive care units: a prospective cohort study from the European Childhood Life-threatening Infectious Disease Study (EUCLIDS). *Crit Care* 2018;**22**:143.
17. Martinón-Torres F, Salas A, Rivero-Calle I, Cebey-López M, Pardo-Seco J, Herberg JA, et al. Life-threatening infections in children in Europe (the EUCLIDS Project): a prospective cohort study. *Lancet Child Adolesc Health* 2018;**2**:404–14.
18. Czech K, John E. Approach to pediatric patients with UTI in the PICU. *J Pediatr Intensive Care* 2016;**5**:64–8.
19. Schlager TA. Urinary tract infections in children younger than 5 years of age: epidemiology, diagnosis, treatment, outcomes and prevention. *Paediatr Drugs* 2001;**3**:219–27.
20. Liu L, Oza S, Hogan D, Chu Y, Perin J, Zhu J, et al. Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the sustainable development goals. *Lancet* 2016;**388**:3027–35.
21. Mecklin M, Heikkilä P, Korppi M. Low age, low birthweight and congenital heart disease are risk factors for intensive care in infants with bronchiolitis. *Acta Paediatr* 2017;**106**:2004–10.
22. Holman RC, Folkema AM, Singleton RJ, Redd JT, Christensen KY, Steiner CA, et al. Disparities in infectious disease hospitalizations for American Indian/Alaska native people. *Public Health Rep* 2011;**126**:508–21.
23. Person MK, Esposito DH, Holman RC, Mehal JM, Stoll BJ. Risk factors for infectious disease death among infants in the United States. *Pediatr Infect Dis J* 2014;**33**:e280–5.
24. Ben-Shimol S, Givon-Lavi N, Leibovitz E, Raiz S, Greenberg D, Dagan R. Near-elimination of otitis media caused by 13-valent pneumococcal conjugate vaccine (PCV) serotypes in southern Israel shortly after sequential introduction of 7-valent/13-valent PCV. *Clin Infect Dis* 2014;**59**:1724–32.
25. Farnham AC, Zimmerman CM, Papadouka V, Konty KJ, Zucker JR, Nattanmai GV, et al. Invasive pneumococcal disease following the introduction of 13-valent conjugate vaccine in children in New York City from 2007 to 2012. *JAMA Pediatr* 2015;**169**:646–52.
26. Lamberti LM, Ashraf S, Walker CL, Black RE. A systematic review of the effect of rotavirus vaccination on diarrhea outcomes among children younger than 5 years. *Pediatr Infect Dis J* 2016;**35**:992–8.
27. Troeger C, Khalil IA, Rao PC, Cao S, Blacker BF, Ahmed T, et al. Rotavirus vaccination and the global burden of rotavirus diarrhea among children younger than 5 years. *JAMA Pediatr* 2018;**172**:958–65.