

Lower socioeconomic conditions are associated with higher rates but similar outcomes in Sepsis in children

Condiciones socioeconómicas más bajas se asocian con tasas de sepsis infantil más altas pero con resultados similares

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What do we know about the subject matter of this study?

Sepsis is an important cause of pediatric morbidity and mortality. Globally, 2.9 million children under 5 years of age died annually from sepsis. Low- and middle- income countries have higher incidence and higher mortality.

What does this study contribute to what is already known?

Multi-centric study of 47 hospitals showing a decrease in prevalence and mortality of severe sepsis and pediatric septic shock in a low and middle income country over a 9-year period.

Abstract

Sepsis is an important cause of pediatric morbidity and mortality, especially in low-income countries. Data on regional prevalence, mortality trends, and their relationship with socioeconomic variables are scarce. **Objective:** to determine the regional prevalence, mortality, and sociodemographic situation of patients diagnosed with severe sepsis (SS) and septic shock (SSh) admitted to Pediatric Intensive Care Units (PICUs). **Patients and Method:** patients aged 1 to 216 months admitted to 47 participating PICUs with a diagnosis of SS or SSh between January 1, 2010, and December 31, 2018, were included. Secondary analysis was performed on the Argentine Society of Intensive Care Ben-

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chmarking Quality Program (SATI-Q) database for SS and SSh and a review of the annual reports of the Argentine Ministry of Health and the National Institute of Statistics and Census for the socio-demographic indices of the respective years. **Results:** 45,480 admissions were recorded in 47 PICUs, 3,777 of them with a diagnosis of SS and SSh. The combined prevalence of SS and SSh decreased from 9.9% in 2010 to 6.6% in 2018. The combined mortality decreased from 34.5% to 23.5%. Multivariate analysis showed that the Odds ratio (OR) of the association between SS and SSh mortality was 1.88 (95% CI: 1.46-2.32) and 2.4 (95% CI: 2.16-2.66), respectively, adjusted for malignant disease, PIM2, and mechanical ventilation. The prevalence of SS and SSh in different health regions (HR) was associated with the percentage of poverty and infant mortality rate ($p < 0.001$). However, there was no association between sepsis mortality and HR adjusted for PIM2. **Conclusions:** Prevalence and mortality of SS and SSh have decreased over time in the participating PICUs. Lower socioeconomic conditions were associated with higher prevalence but similar sepsis outcomes.

Introduction

Sepsis is implicated as the cause of 20% of global deaths, half of which are children mostly in low and middle income countries (LMICs).¹ The reasons for the inordinate contribution to death from LMICs are manifold and include unique diseases such as malaria, tuberculosis and HIV infections, comorbidities such as malnutrition, socioeconomic disparities, poor access to healthcare, poorly or non-resilient health systems and “social capabilities”, as was stated by Amartya Sen^{2,3}. However, these contributors are not present uniformly even in low income countries and hence outcomes may vary between and within regions in the same country. Moreover, in some upper and middle income countries, regional averages sometimes hide the existence of low resource settings by side high resource settings.⁴ Thus, the care offered and hence the outcome of a severely ill child with sepsis often depends entirely on context including geographical location and their socioeconomic status^{5,6}.

These factors underline the importance of understanding regional differences in outcomes such that interventions to decrease the burden and improve care and outcomes can be targeted to needs. Data relating to regional differences in sepsis is scarce in Latin America and lacking in Argentina.

SATI-Q (Sociedad Argentina de Terapia Intensiva-Quality) is a Quality Benchmarking program sponsored by the Argentine Society of Intensive Care (SATI). Its database has information prospectively collected of more than 50,000 admissions to public and private pediatric intensive care units (PICU) located in different regions of Argentina⁷. Public institutions comprise two sector blocks: hospitals dependent on the national or provincial Ministry of Health and others belonging to the social security system; they serve the poorest segment of the population and the formal workers, respectively. Private institutions operate based on an

agreement between a health service provider company and the beneficiaries.

To describe the prevalence and mortality of patients admitted with a diagnosis of SS and or SSh in those units affiliated to pediatric SATI-Q program, and to understand regional differences and trends over time, a secondary analysis of SATI-Q pediatric database was performed. Furthermore, we analyzed whether there was an association between the outcomes and regional socio-economic factors.

Patients and Method

Study Design and Data Source

An analysis of SATI-Q pediatric database was performed. This database includes data collected prospectively by the PICUs members of SATI-Q program between 1-1-2010 and 12-31-2018.

The SATI-Q program is a quality benchmarking and quality improvement initiative sponsored by SATI since 2003. Its aim is to optimize the care of critically ill patients in Argentina through the generation of a multicenter network of Intensive Care Units (ICUs) collecting data on an agreed set of quality indicators.⁷ Originally, an ICU network dedicated to adult patients, PICUs joined this initiative in 2005. This voluntary program is made up of both publicly and privately funded PICUs, located in both pediatric hospitals and in general hospitals in different regions of the country. The PICUs that are willing to join the SATI-Q program receive a free license to use the software as a data collection tool. All of the 130 PICUs in the country are eligible to join⁸.

The following variables are collected for each admission: demographic data, presence of chronic complex conditions, history, main and admission diagnoses, severity of illness on admission calculated by Pediatric Index of Mortality 2 (PIM2) score (See

supplementary material for equation and variables)⁹, use of invasive devices, procedures performed during hospitalization, predefined quality indicators (nosocomial associated devices infections, bedsores, falls, Standardized Mortality Ratio), length of stay in PICU, clinical course and outcome. The variables collected and their definitions are available in the SATI-Q data dictionary¹⁰. Diagnoses and procedures are recorded in a standardized format according to International Classification of Diseases 9 codes (ICD).

Each PICU sends its local data encrypted and anonymized on an annual basis to perform the quality benchmarking reports. For this study, we analyzed data from 47 PICUs. Each PICU provided data for an average of 4.7 years (SD 2.8).

Definition of cohort and variables of interest

For the purposes of this study, we analyzed the records of patients between 1 month and 216 months old admitted to the participating PICUs between 01-01-2010 and 12-31-2018 with a diagnosis of SS or SSh. Those patients still receiving PICU care by 12-31-2018 were excluded.

The diagnosis of SS or SSh was made by the bedside physician following admission and based on clinical evaluations and laboratory tests when indicated. The diagnosis was related to the database dictionary and classified either as the primary or secondary diagnosis. The definitions of SS and SSh, as outlined in the International Consensus Conference, was adopted as the diagnostic criteria by SATI-Q¹¹. Nonetheless, while the bedside physicians used the International Consensus Conference diagnostic criteria to diagnose SS and SSh, the individual variables leading to the diagnosis were not recorded.

The following variables were extracted from the database: age, gender, date of hospital and PICU admission, source of admission (pediatric ward, intermediate care unit, emergency department, operating room), reason for admission to PICU, diagnosis, presence of complex chronic condition, probability of death calculated by PIM2, duration of mechanical ventilation (MV), length of stay (LOS) and outcome at discharge from the PICU. The presence of complex chronic conditions (CCC) was defined according Feudtner et al¹² as any medical condition that can be reasonably expected to last at least 12 months (unless death intervenes) and involves either several different organ systems or 1 organ system severely enough to require specialty pediatric care and likely hospitalization in a tertiary care center.

Socioeconomic Indicators

Infant Mortality Rates (IMR) and the vaccination coverage by jurisdiction from 2010 to 2018 were obtained

from the annual reports of the Argentine Ministry of Health^{13,14}. The percentage of the population below the poverty line (%P) and the percentage of Illiteracy (%I) were obtained from the National Institute of Statistics and Censuses reports^{15,16}. Regional average of illiteracy was taken from the last National Census in 2010, because there is no official data since then¹⁶.

The poverty line refers to the minimum resources necessary to cover a basic food basket capable of satisfying a minimum threshold of energy and protein needs plus the value to cover non-food goods and services such as clothing, transportation, education and health¹⁵. In accordance with a decision made by the national authorities, the poverty data were not reported from the second half of 2013 to the second quarter of 2016¹⁶.

Human Development Index (HDI) is a composite index of life expectancy, education (Literacy Rate, Gross Enrollment Ratio at different levels and Net Attendance Ratio), and per capita income indicators. The United Nation Development Program adopted it as a way to measure a country's development and their influence on people's life¹⁷. Sub-national data were obtained from Global Data Lab® (Institute of Management Research, Radboud University, Nijmegen, Netherlands)¹⁸.

Healthcare Regions and PICU characteristics

According to the Argentinian Ministry of Health, Argentina is divided into five healthcare regions (HR): Central, Cuyo, Patagonia, Northwestern and Northeastern. All data was classified and analyzed based on these regions (table 1)^{19,20}.

Statistical analysis

Descriptive statistics was used to characterize the population. The prevalence of SS and SSh is expressed as the rate and 95% confidence interval (CI). Continuous variables are expressed as median and interquartile range (IQR) or mean and standard deviation (SD). Categorical variables are expressed as frequencies and percentages.

Univariate analysis was performed to assess the association between the presence of SS and SSh and characteristics and outcome of the patients. Continuous variables were compared with Student's t test or non-parametric tests according to their distribution. Categorical variables were compared using χ^2 test with Fisher's exact correction if applicable. Odds Ratio (OR) and 95% CI were used as a measure of association between categorical variables. A p-value < 0.05 was considered statistically significant. Multivariate logistic regression analysis was performed to assess the association between the presence of SS and SSh on PICU admission and mortality in the PICU adjusted for confounding factors.

Table 1. Participating PICUs characteristics according to Healthcare Regions

Healthcare Region	PICU, n	Public PICU, n	University associated PICU, n	PICU with Fellowship Programme, n	Healthcare Region General Population, n
1. Central	33	20	20	16	26327371
2. Cuyo	4	3	2	3	2883625
3. Patagonia	4	4	2	3	2406040
4. Northwestern	4	4	1	3	5076473
5. Northeastern	2	2	1	1	3672528

PICU: Pediatric Intensive Care Unit. Argentina has five healthcare regions (HR). Pediatric Intensive Care Unit (PICU) characteristics from every HR is shown. The PICUs were allocated preferential at most populated regions. Region 1 is the most developed, industrialized and richest one. Also, it's where the largest number of universities are. The country has PICU where medical students do their practices (pre graduate programs) and there are PICU with fellowship programs.

Ethical Considerations

Ethical and scientific aspects of the protocol were evaluated and approved by the Research Ethics Committee of Complejo Medico Churrua Visca with the approval number 6947, accredited by the Ministry Of Health And Social Development; Sub-Secretary For Quality, Regulation And Inspection; National Advisory Committee On Research Ethics. Each PICU complied with the administrative requirements and authorizations of their institution. In all cases, the need for informed consent was waived because collecting this type of data was routine practice in each PICU, the nature of the study was observational, and data protection requirements were met.

Results

The data represents 45,480 hospitalization records from 47 PICUs located in five HRs of Argentina.

During the study period, 3777 patients with diagnosis of SS and SSh were admitted. The characteristics of the whole population and its course in the PICU as well as the characteristics and outcomes of patients with SS or SSh are shown in table 2.

The median age for SS and SSh patients was 21 months (IQR 6-81) vs 22 months (IQR 6-80) in non SS and non SSh patients (p : 0.39).

The overall prevalence of both SS and SSh was 8.3% (95% CI 8-8.6). The prevalence of SSh was 6.8% (95% CI 6.6 -7.1%) while SS prevalence was 1.5% (1.4-1.6 %).

The trends for combined SS and SSh prevalence on admission and mortality from 2010 to 2018 are shown in figure 1.

The combined prevalence of SS and SSh decreased 33.4 % between 2010 and 2018 (9.9% vs 6.6% respectively).

The prevalence and mortality rate of combined SS and SSh according to HR shown in figure 2. Prevalence rate in public setting was 10.1% (CI 95% 9.8-10.4) vs 2.5% (CI 95% 2.2 -2.8) in PICUs located in private setting.

Poverty was associated with higher prevalence of SS and SSh ($p < 0.001$). Considering Patagonia as reference (HR with lowest percentage of poverty), the association between prevalence of SS, SSh and the HR percentage of poverty increased. The respective OR and CI 95% were: Central: OR 1.36 [95% CI 1.07-1.73]; Cuyo: OR 2.02 [95% CI 1.56-2.62]; NW: OR 2.07 [95% CI 1.61 -2.67]; NE: OR 3.3 [95% CI 2.5-4.38]. The infant mortality rate and the HDI were not included due to collinearity with percentage of poverty and prevalence.

The overall mortality was 25.4% and there were no differences between regions, percentage of poverty or infant mortality rate adjusted for the PIM2 score (p : 0.12). The mortality of patients with SSh, SS and those without sepsis on admission was 27.4%, 16.07% and 6.1% respectively.

Combined mortality decreased almost one third between 2010 and 2018 (mortality rates were 34.5% and 23.5% respectively) (figure 1 and 2). Mortality rate of patients admitted with SS and SSh in public PICUs was 25.46 % (CI 95%: 24.03-26.94) vs 24.09% (CI 95% 19.15 - 29.60) in private setting.

SS and SSh were associated with mortality. The OR of the association and its 95% CI for SSh was 2.4 (95% CI 2.16-2.66) and for SS 1.88 (95% CI 1.46-2.32), adjusted for malignant disease, PIM2 and mechanical ventilation.

Patients with SS and SSh accounted for 27.1% of deaths in the PICU.

The average infant mortality rate, percentage of poverty, percentage of illiteracy and Human Development Index by health region are shown in figures 3 and 4. Vaccination rates did not differ between the regions.

Table 2. Characteristics of PICU population

	Global (N = 45480)	With SS/SSh (N = 3777)	Without SS/ SSh (N = 41703)	P	OR (IC95)
<i>General characteristics:</i>					
Male gender; n (%)	26867 (59.1%)	2172 (57.5%)	24695 (54.2%)	0.04	0.93(0.9-1)
Age in months; median (ICR)	21 (6-80)	21 (6-81)	22 (6-80)	0.39	
PIM2; mean (SD)	7,15 (14.4)	18,6 (20.7)	6,1 (13.2)	< 0.001	
Complex Chronic Condition; n (%)	17617 (38.7%)	1446 (38.3%)	16171 (38.8%)	0.55	
Malignant disease; n (%)	1574 (3.5%)	414 (11.0%)	1160 (2.8%)	< 0.001	4.2 (3.8-4.9)
<i>Reason for admission:</i>					
Medical; n (%)	30575 (67.2%)				
Surgical; n (%)	9821 (21.6%)				
Trauma; n (%)	4108 (9.1%)				
Other; n (%)	976 (2.1%)				
<i>Procedence:</i>					
Emergency Department; n (%)	15187 (33.4%)	1157 (30.7%)	14030 (33.6%)		Reference
General Hospitalization Room; n (%)	27230 (59.9%)	2370 (62.7%)	24950 (59.8%)	< 0.001	1.2 (1.1-1.24)
Other; n (%)	3063 (6.7%)	250 (6.6%)	3083 (7.4%)		
<i>PICU Funding:</i>					
Public; n (%)	34652 (76.2%)	3503 (92.7%)	31149 (74.7%)	< 0.001	4.3 (3.8-4.9)
<i>Regions:</i>					
Central; n (%)	35003 (76.9%)	2636 (69.8%)	32367 (77.6%)		Reference
NW; n (%)	4715 (10.4%)	520 (13.8%)	4195 (10.1%)	< 0.001	1.5 (1.4-1.7)
CUYO; n (%)	3273 (7.2%)	353 (9.4%)	2920 (7.0%)	< 0.001	1.5 (1.3-1.7)
PATAGONIA; n (%)	1313 (2.9%)	74 (2.0%)	1239 (3.0%)	< 0.001	0.7 (0.6-0.9)
NE; n (%)	1176 (2.6%)	194 (5.1%)	982 (2.4%)	< 0.001	2.4 (2.1-2.8)
<i>Evolution in PICU:</i>					
Use of MV; n (%)	25079 (55.1%)	3108 (82.3%)	21971 (52.7%)		4.2 (3.8-4.5)
MV days; median (ICR)	5 (2-11)	7 (3-14)	5 (2-11)		
Days of stay in PICU; median (ICR)	5 (2-10)	8 (3-16)	4 (2-10)		
Mortality; n (%)	3530 (7.8%)	958 (25.4%)	2572 (6.2%)		5.2 (4.8-5.6)

(%) based on the N of each group. SS: Severe Sepsis; SSh: Septic Shock; PIM2: Pediatric Index of Mortality-2; MV: mechanical ventilation, NW: Northwestern Argentina; NE: Northeast Argentina; SD: standard deviation; ICR: interquartile range. PICU: Pediatric Intensive Care Unit. PICU: Pediatric Intensive Care Unit.

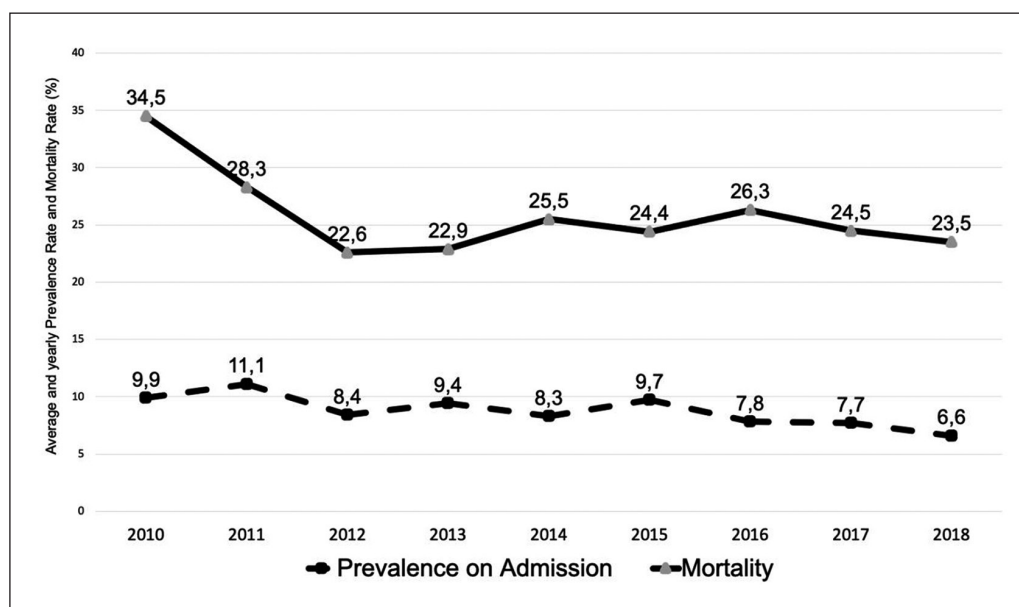


Figure 1. Trends for Severe Sepsis/septic Shock prevalence on admission and mortality from 2010 to 2018 at the participating PICUs. Foot Note: Average yearly prevalence rate on admission (broken line) and mortality (whole line) of patients with SS and SSh from 2010 to 2018.

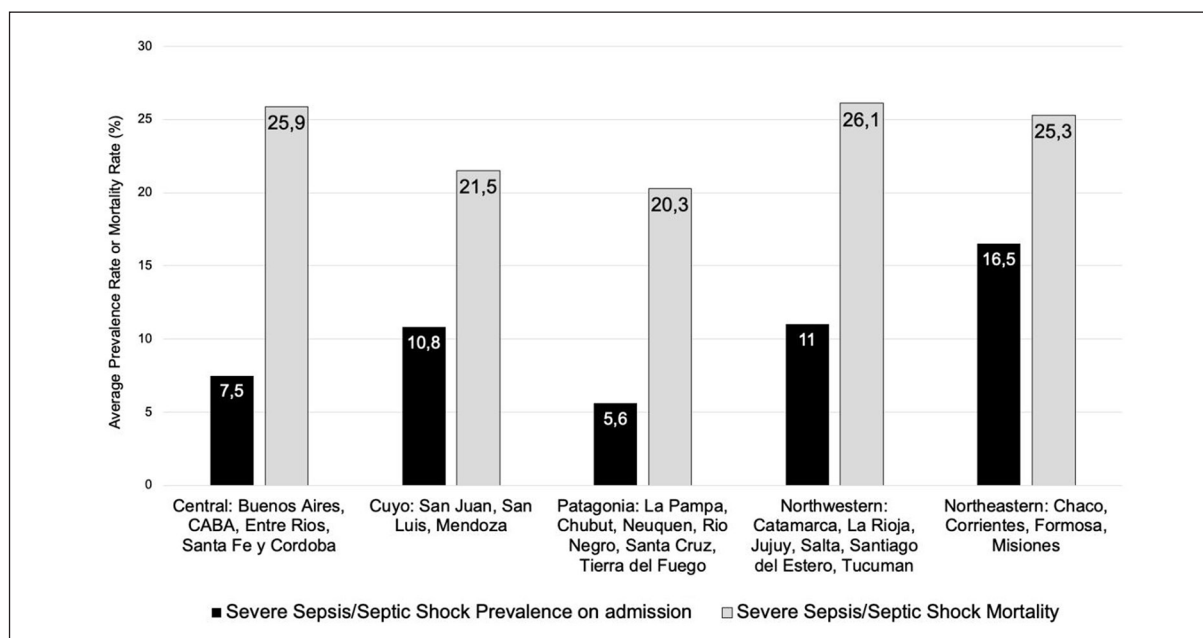


Figure 2. Average prevalence and mortality rate of patients admitted with diagnosis of severe sepsis/septic shock in the participating PICUs, by Argentinean Healthcare Regions. Foot note: Each healthcare region has provinces that belong to it. Average prevalence on admission (black barr) and mortality (grey barr) from every one of the five regions is presented. The name of the provinces that belong to every region is stated. Argentina has five healthcare regions (HR) that are composed by different provinces. The composition of each HR is the following: Central HR: Buenos Aires, CABA, Entre Rios, Santa Fe and Córdoba. Cuyo HR: San Juan, San Luis and Mendoza. Patagonia HR: La Pampa, Chubut, Neuquén, Río Negro, Santa Cruz and Tierra del Fuego. Northwestern HR: Catamarca, La Rioja, Jujuy, Salta, Santiago del Estero and Tucumán. Northeastern HR: Chaco, Corrientes, Formosa and Misiones.

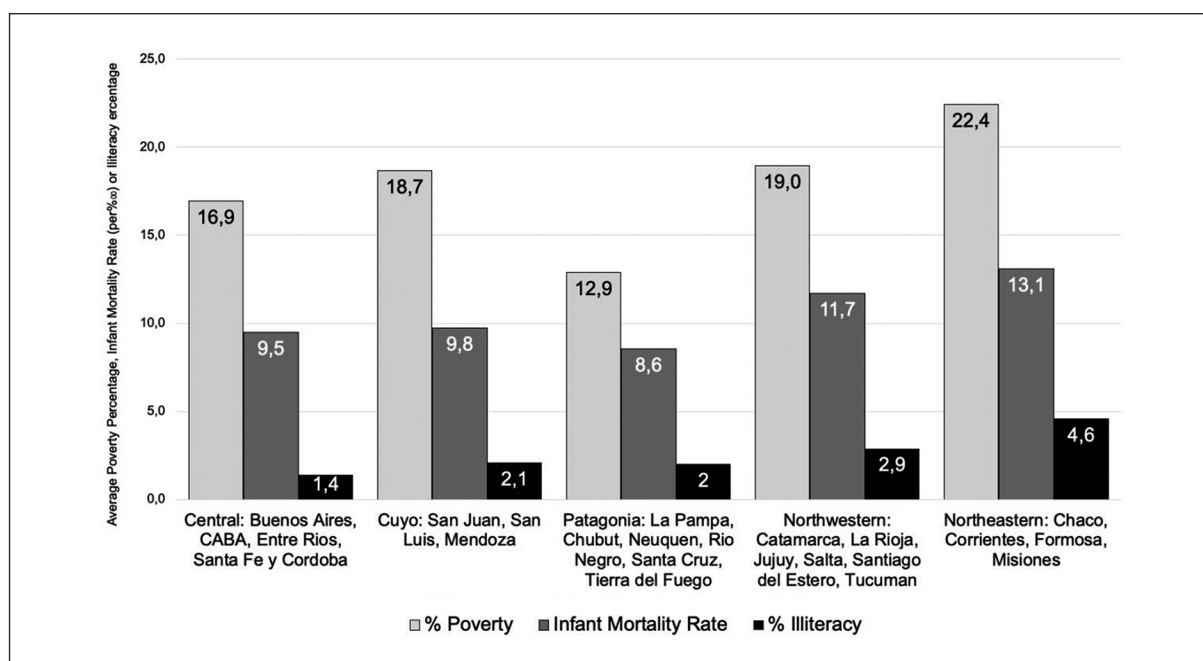


Figure 3. Average Infant Mortality Rate, Poverty Percentage and Illiteracy Percentage by health regions of Argentina. Foot Note: Regional average percentage of poverty (%P) -light grey-, Infant Mortality Rate (IMR) -dark grey- and illiteracy (black) from every healthcare region. The name of the provinces that belong to every region is stated. Central HR: Buenos Aires, CABA, Entre Rios, Santa Fe and Córdoba. Cuyo HR: San Juan, San Luis and Mendoza. Patagonia HR: La Pampa, Chubut, Neuquén, Río Negro, Santa Cruz and Tierra del Fuego. Northwestern HR: Catamarca, La Rioja, Jujuy, Salta, Santiago del Estero and Tucumán. Northeastern HR: Chaco, Corrientes, Formosa and Misiones.

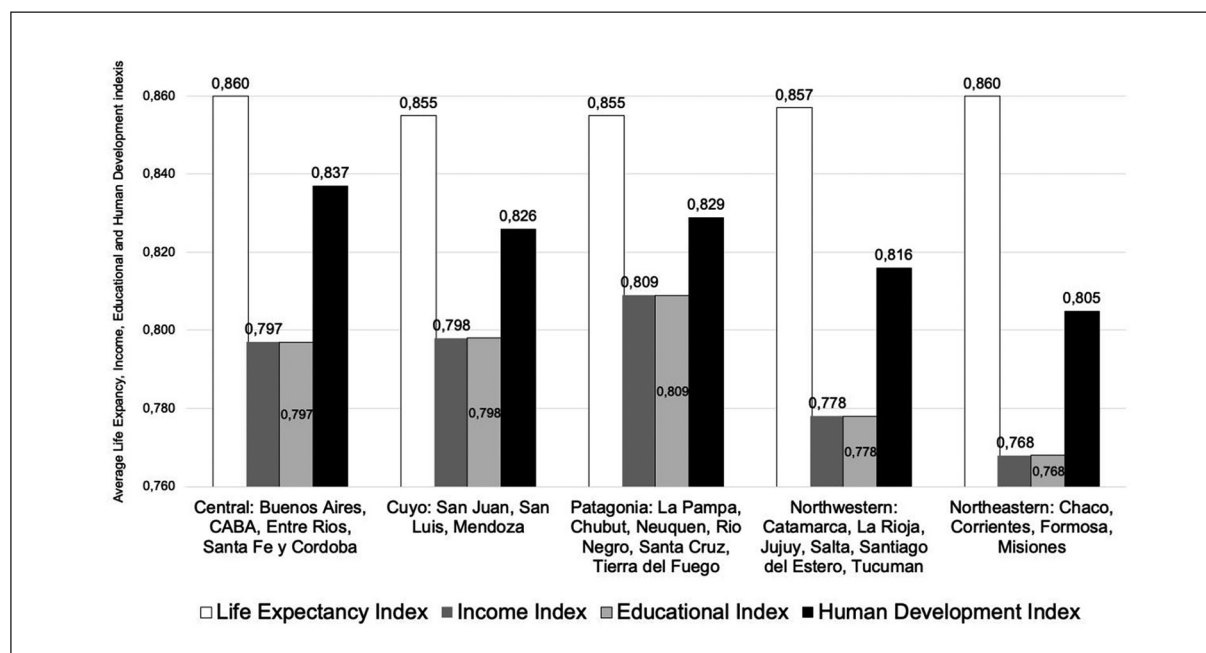


Figure 4. Average Human Development Index by health regions of Argentina. Foot Note: *Regional average percentage of Human Development Index -black barr- from every healthcare region. There are also the HDI dimensions (life expectancy at birth -white barr-, income index -dark grey barr-, education index -light grey barr-, and GNI per capita or income index).*

Discussion

To our knowledge, this is the first epidemiological report of pediatric sepsis carried out over several years in Argentina and the first that compares SS and SSh prevalence and mortality with socioeconomic features like IMR, % P, % I and % of vaccination by healthcare regions.

Our significant findings are that prevalence and mortality has decreased by one third between 2010 and 2018, and prevalence varies between regions. There was an association between higher prevalence and worse socioeconomic factors (poverty, illiteracy, infant mortality rate, human development index) but no difference in mortality between regions nor between private and public PICUs.

Our overall prevalence 8,3%, was similar with the global prevalence (8.2%) reported in the international study SPROUT (Sepsis Prevalence, Outcomes, and Therapies) but less than the 16.3% reported for South American PICUs in the same study⁸. The differences could be due to a PICU selection bias in SPROUT that included general hospitals and private institutions in Latin America, an issue that may not be representative. Ruth et al also reported a prevalence of 7.7% for SS in U.S. children's hospitals²¹. In Argentina, the Study of Severe Sepsis in Pediatrics (Estudio Epidemiológico de Sepsis Severa Pediátrica -ESSPED-) reported a prevalence of 13% for SS and SSh in 61 PICUs²², but

that study included patients who presented with sepsis both at admission and during their stay in the PICU. If only those with SS and SSh at the time of admission are analyzed, the prevalence in the ESSPED was 7%.

De Souza et al reported a prevalence of SS of 25.9% on 21 PICUs located in Argentina, Brazil, Chile, Ecuador and Paraguay.²³ Most recently, De Souza et al reported a SS and SSh prevalence of 25% (95% CI 21.6-28.8) in 144 PICUs in Brazil, with slight variation among the regions²⁴. A factor that may explain the observed differences in overall prevalence between these studies is the heterogeneity of used definitions, study design, and socioeconomic conditions (malnutrition, low level of education, low vaccination coverage, and lack of knowledge among health care professionals).

Our study used admitting physician criteria for SS and SSh, therefore, there are probably differences in the way the cases were classified. At the same time the process for assigning ICD codes or the use of consensus has not been standardized between institutions, and therefore misclassification of sepsis is another possible source²². Hence, the use of clinical criteria versus administrative (ICD codes) versus consensus criteria can lead to discrepancies in classification^{21,25-27}.

The non-uniformity prevalence of SS and SSh that we report across regions may be explained by socioeconomic disparities. This is similar to the finding of Rudd et al whereby the highest age-standardized inci-

dence of sepsis occurred in countries with the lowest Socio-demographic Index (SDI)¹. In Argentina the NE and NW health region present the most vulnerable populations, with lower socioeconomic conditions (the highest levels of infant mortality rate, poverty and illiteracy in the country, and the lowest Human Development Index)^{11,13,14,16}. Amartya Sen called for a strong look on the perception of illness in a social context, one of the “social capabilities” as he named it.³ Kang et al reported about parental inability to recognize the signs of sepsis as one of the most common barriers in sepsis therapy²⁸. Indeed, Gavidia et al reported that parental illiteracy was associated with delays when seeking care for fever²⁹.

De Souza describes that maternal illiteracy was independent risk factors associated with the occurrence of sepsis in young population²³.

Another issue that contributes to these differences in prevalence can be associated with health system dysfunction. The Argentine health system is a particular case due to its high fragmentation and poor coordination between subsectors, which offer very heterogeneous quality of care³⁰. Moreover, there are disparities in healthcare workforce, financing and infrastructure between regions^{30,31}. The lack of an optimal access to the services due to time constraints at Outpatient Department, something that happens in Argentina, as Gasparini et al has reported, can delay the optimal management³². Identifying a country's worst-performing region lead to awareness of the extent of geographical inequality pinpointing that some of the resources in these healthcare region are left behind consistently over time³³. Also, as other world regions, inside Argentina there is persisting substantial heterogeneity in terms of PICU's availability and resourcing, quality of services, and medical transportation of critically ill children³⁴. In some Argentinian regions children must be transported more than 500 km by ground to reach a PICU. Jabornisky et al reported a statistically significant association between rural origin and severe sepsis mortality in Argentina²². In Latin America a referral from a non-urban area is independently associated with mortality³⁵.

As other low-resource regions of the world, poverty, health inequity, and under-resourced and low-resilience public health and acute health care delivery systems are fundamental contributors to the burden of sepsis^{36,37}. Poor preventive health care, substandard living conditions, bed sharing, and exposure to environmental and animal vectors increase risk for acute infection³⁷.

The higher prevalence of SS and SSh we have observed in public PICUs could represent a characteristic of the country's Health System, where the public sector continues to be a fundamental base in the care of chil-

dren³⁰. Indeed 76.2% of the patients were admitted to the PICUs in the Public Health System.

The decrease in prevalence over the studied period observed by us mirrors that reported by Rudd et al whereby the global age-standardized incidence of sepsis fell between 1990 and 2017 in nearly every location worldwide¹.

Mangia et al observed a reduction in SS prevalence in Brazil between 1992 to 2006 and they assumed has largely due to immunization, sanitation, trash collection, water treatment and a national nutrition and oral rehydration³⁸⁻⁴⁰. Although vaccination rates were similar between regions in Argentina, it's possible that others public health measures may unevenly distributed and less available in poorer regions. In addition, adherence with a SSh care bundle of care may vary and be lower in poorly resourced areas but this was not reflected in outcomes, as Rudd et al reported¹.

Although mortality has decreased over the years, this decrease has been slowing down, remaining between 22 and 26% since 2012, with peaks of 25.5% (2014) and 26.3% (2016). At the beginning of the study period, 2010, it was 34.5%. The ESSPED, which was carried out in 2008, reports a mortality of 32%²². In 2008, the Global Sepsis Initiative of the World Federation of Intensive and Critical Care Societies (WF-PICCS) published a report indicating that for developing countries, such as ours, the estimated mortality was 29.8%⁴¹. Despite this, the SPROUT study reports an 11% mortality for South America. This last figure should be interpreted with caution since only one PICU from Argentina, allocated in a high resource HR, participated in this study and hence the figure may represent a high resource setting⁸.

Despite the differences seen in prevalence, mortality does not show differences between the different regions not between public and private PICUs. No pediatric studies in Latin America were found that reported differences between private and public PICUs. Conde et al, based on data from Brazilian adult units, reported statistically significant differences regarding mortality between the private and public sectors⁴². However, Machado et al, indicated that they found no differences in mortality between adults seen in private or public units in Brazil⁴³. They reported that their pseudo-random sample could have selected both high-quality and low-quality private hospitals, which might better represent Brazilian private health system than Conde's convenient sample which probably led to a selection bias^{42,43}. Jaramillo-Bustamante et al reported higher mortality in Colombian children with sepsis coming from lowest socioeconomic levels but no difference regarding been managed in public or private PICUs⁴⁴.

There could be some explanations about the lack

of difference in mortality between private and public PICUs that we observed. The PICUs belonging to the SATI-Q program generally represents pediatric intensivists practicing contemporary care and is concerned with improvements in daily practice. Schultz et al referred that access to adequate information has improved massively in this cyber age³⁷. From 2008 to 2010, the diffusion of virtual training programs has increased in Argentina. There have been courses like SATI's Specialization Course in Pediatric Critical Care Medicine for pediatric intensivists and the Emergencies and Critical Care Program -ECCri- from the Argentine Society of Pediatrics for general pediatrician and pediatric emergency and intensive care physicians. These programs made a greater diffusion of the Pediatric Sepsis Clinical Practice Guidelines. Even though the education on sepsis management is still mainly focused on pediatric ICU and emergency physicians, there are attempts to include it in medical schools, nursing schools and the training of other healthcare workers. Thus, the lack of difference in mortality can be explained for a similar quality of care among the analyzed PICUs.

Patients across all regions in our study have a moderate to high risk of severity as measured by PIM2. The ESSPED reported a similar PIM2 severity, mirroring the characteristics of our study and likely the characteristics of our health system²². The Standardized Mortality Rate (relation between observed and expected mortality), remained homogeneous between the different regions except in the NE where it was higher than the rest. The causes of this deserve an in-depth analysis.

There are some limitations in our study. First of all, the SATI-Q program is not mandatory and therefore not all the country's PICUs are represented, with a predominance of the central healthcare region units. Second, due to national protocols, the socioeconomic information data is not collected every year. For example, illiteracy is collected every ten years. Third, we did not explore the influence of late presentation, the quality of care rendered, lack of adherence to sepsis clinical practice guidelines, as well as lack of access to preventive care, and early diagnostic and screening services, all of which could be implicated in high prevalence and the overall high national mortality²⁹.

By making these data visible will let policy makers and providers to guide efforts to change reality and trying to help families, patients and health worker to better visualize the sepsis.

Conclusion

SS and SSh are common in children in the Argentine Healthcare System, representing a significant num-

ber of patients hospitalized in the country's PICUs. Although mortality has decreased, the gains have levelled off in recent years. Poverty and lower socio-economic conditions were associated with higher prevalence of sepsis but not worse outcomes.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: This study was approved by the respective Research Ethics Committee. The authors state that the information has been obtained anonymously from previous data.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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