



Culture-proven early-onset neonatal sepsis in Arab states in the Gulf region: two-year prospective study



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ARTICLE INFO

Article history:

Received 3 September 2016

Received in revised form 3 December 2016

Accepted 5 December 2016

Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:

Neonatal sepsis

Neonatal infection

Antibiotic resistance

Early-onset sepsis

SUMMARY

Objective: To investigate the incidence and the pattern of causative organisms of culture-proven early-onset sepsis (EOS) in Arab states in the Gulf region.

Methods: Five neonatal care units participated in this 2-year prospective study in Kuwait, the United Arab Emirates, and Saudi Arabia. Data were collected prospectively using a standardized data collection form. EOS was defined as the growth of a single potentially pathogenic organism from blood or cerebrospinal fluid in infants within 72 h of birth, with clinical and laboratory findings consistent with infection.

Results: Out of 67 474 live births, 102 cases of EOS occurred. The overall incidence of EOS was 1.5 (95% confidence interval 1.2–1.8) per 1000 live-births, ranging from 2.64 per 1000 live-births in Kuwait to 0.40 per 1000 live-births in King Abdulaziz Hospital in Saudi Arabia. The most common causative organism of EOS was group B Streptococcus (GBS; 60.0%), followed by *Escherichia coli* (13%). The incidence of invasive GBS disease was 0.90 per 1000 live-births overall and ranged from 1.4 per 1000 live-births in Kuwait to 0.6 per 1000 live-births in Dubai Hospital.

Conclusions: The incidence of EOS and the patterns of the causative organisms in the Arab states in the Gulf region are similar to those in developed countries before the era of intrapartum antibiotic prophylaxis. Efforts should be made to improve intrapartum antibiotic prophylaxis in the Arab state setting, which could avert large numbers of GBS infections.

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1. Introduction

Despite the recent global decline in neonatal mortality, the proportion of deaths among children under the age of 5 years occurring within the neonatal period increased from 37% in 1990 to 44% in 2013.¹ This is because the decline in the neonatal mortality rate has been slow when compared to the decline in mortality rate of children beyond the neonatal period. The decline in under-5 mortality beyond the neonatal period has been accelerated by the strengthening of vaccination programs and

other hygiene measures, while the decline in neonatal mortality has been hindered by neonatal sepsis.^{2,3} Worldwide, sepsis is the single largest cause of neonatal mortality, with 36% of neonatal deaths attributed to infection.^{4,5} Unlike other causes of neonatal death, such as severe congenital anomalies, death from neonatal sepsis is preventable, suggesting that neonatal mortality can be further reduced if preventive and curative measures against neonatal sepsis are properly implemented.

Neonatal sepsis is categorized into early-onset sepsis (EOS) and late-onset sepsis. EOS is variably defined based on the age at onset as infection occurring within 48 h,⁶ within 72 h,⁷ or within 7 days of birth.² In developed countries, the incidence of EOS is estimated to be 0.80–0.98 per 1000 live-births.^{6–9} Despite this low rate, EOS is responsible for approximately 16% of all neonatal mortality,⁷ and

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contributes to significant morbidity. EOS is usually acquired through the vertical transmission of organisms from the mother to the infant; this occurs in the birth canal during the intrapartum period. In developed countries, the leading cause of this type of sepsis is group B *Streptococcus* (GBS). Since the introduction of intrapartum antibiotic prophylaxis, EOS due to GBS infection has declined in some settings;^{10–13} however, the impact of this strategy on other non-GBS sepsis remains unclear. There has been a concern that the use of intrapartum antibiotics may simply replace GBS sepsis with other potentially more severe causes of neonatal sepsis.

Most of the literature has addressed neonatal sepsis separately for developing and developed countries. However, Arab states in the Gulf region are distinct from neighboring low-income countries. The health services are easily accessible and almost all deliveries occur under medical supervision. Data to guide empirical antimicrobial treatment are scarce and are usually based on epidemiological information and antimicrobial susceptibility testing. This study aimed to investigate the incidence of EOS in Arab states in the Gulf region over a 2-year period, describe the main causative organisms causing EOS, and investigate the antibiotic sensitivity and resistance to the most commonly used antibiotics to treat EOS.

2. Methods

Five neonatal care units (NCUs) participated in this observational prospective cohort study; these are located at the following hospitals: Al Sabah Maternity Hospital in Kuwait, Dubai Hospital and Tawam Hospital in the United Arab Emirates, and King Abdulaziz Hospital and the Maternity and Children's Hospital in Saudi Arabia. Data were collected prospectively over a 2-year period (June 2013 to May 2015) using a standardized data collection form. In order to standardize data collection across all units, detailed guidelines for collecting and reporting data were prepared and used throughout the study.

The International Sepsis Definition Conference has defined sepsis as a pathological process caused by invasion of a normally sterile tissue or fluid or body cavity by pathogenic or potentially pathogenic microorganisms.¹⁴ Accordingly, EOS in the present study was defined as the growth of a single potentially pathogenic organism (bacterium or fungus) from blood or cerebrospinal fluid (CSF) in infants ≤ 3 days of age (0–72 h of life) with clinical and laboratory findings consistent with infection.^{15,16} Likely contaminants were excluded by clinical judgment. Coagulase-negative staphylococci (CoNS) were considered as representing true infection if two repeat blood samples were positive and there were laboratory findings suggesting infection. The isolation of organisms from blood or CSF and their susceptibility or resistance to antibiotics were recorded using recognized methods of antibiotic susceptibility testing, but were not standardized across the different sites.

Data were also collected on the nationality of the mother, type of delivery, gestational age, complications during pregnancy, and use of intrapartum antibiotics. Data related to infants such as birth

Table 1

Characteristics of 102 mothers and neonates with early-onset sepsis in Arab states in the Gulf region over a 2-year period

Characteristics		n (%)
Nationality	GCC countries	64 (62.75)
	Other countries	38 (37.25)
Gravidity	Primigravida	49 (48.03)
	Multigravida	53 (51.96)
Type of pregnancy	Singleton pregnancy	88 (86.27)
	Multiple pregnancy	14 (13.73)
Mode of delivery	Normal	67 (65.69)
	Cesarean section	31 (30.39)
	Other	4 (3.92)
	Extreme preterm <28 weeks	14 (13.73)
	Very preterm 28 to <32 weeks	13 (12.75)
	Moderate to late preterm 32 to <37 weeks	15 (14.71)
Intra-partum antibiotic	Yes	60 (58.82)
	No	28 (27.45)
Sex ^a	Male	50 (50.50)
Birth weight, kg, median (IQR)	2.69 (1.60–3.40)	

GCC, Gulf Cooperation Council.

^a Missing for one case.

weight, sex, the age (in days) at which the positive blood culture was obtained, and whether the baby was born in the hospital (intramural admission) or outside the hospital (extramural admission) were also collected. Finally, data on the number of admissions to the neonatal units and the number of live births in the hospitals were also collected.

This study was approved by the ethics committee of the Health Science Centre, Kuwait University. Individual study sites also obtained approval from the respective authority when deemed necessary.

Data were entered into a database using EpiData Entry software and then transferred to Stata 12.0 (StataCorp, College Station, TX, USA) for data analysis. The incidences of EOS were calculated by dividing the number of inborn infants with EOS by the number of live births in the hospitals. The 95% confidence intervals (95% CI) were calculated using the binomial distribution.

3. Results

By the end of the study period, 67 474 live births had occurred in the study hospitals; among these, there were 102 cases of EOS. The characteristics of the neonates with EOS and their mothers are depicted in [Table 1](#). [Table 2](#) shows the incidence of EOS out of live births and out of admissions at each study site. There was a significant difference in the incidence of EOS between the different study sites ($p < 0.001$). The highest incidence of EOS was in Kuwait at 2.64 (95% CI 2.02–3.38) per 1000 live-births, while the lowest incidence was in King Abdulaziz Hospital in Saudi Arabia at 0.40 (95% CI 0.05–1.45) per 1000 live-births.

[Table 3](#) illustrates the causative organisms of EOS in all study hospitals. GBS was the main causative organism and was identified in 60% of EOS; this was consistent across all study sites except King

Table 2
Incidence of early-onset sepsis out of live births and out of admissions in Arab states in the Gulf region over the 2-year period

Study site	Number of live births	Number of admissions	Number of EOS	Incidence EOS per 1000 live-births	Incidence EOS per 1000 admissions
Al Sabah Maternity Hospital/KW	23 501	6019	62	2.64	10.30
Tawam Hospital/UAE	7261	1672	8	1.10	4.78
Dubai Hospital/UAE	6323	856	3	0.47	3.51
King Abdulaziz Hospital/SA	4973	1452	2	0.40	1.38
Maternity and Children's Hospital/SA	25 416	3985	27	1.06	6.78
Total	67 474	13 984	102	1.51	7.29

EOS, early-onset sepsis; KW, Kuwait; UAE, United Arab Emirates; SA, Saudi Arabia.

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