

Clinical Epidemiology of Neonatal Sepsis among Neonates Admitted to King Khalid University Hospital in Riyadh During the Year 2016

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Abstract

Background: Neonatal sepsis is a clinical syndrome characterized by systemic signs of infection and accompanied by bacteria infection, Sepsis occurring in the first 7 days of life is defined as early-onset sepsis (EOS) and that occurring beyond 8 - 28 days of neonate age as late-onset sepsis (LOS). Sepsis is the most common cause of neonatal mortality (death in the first 28 days of life); it is responsible for about 30 - 50% of the total neonatal deaths in developing countries. It is estimated that up to 20% of neonates develop sepsis and approximately 1% die of sepsis related causes. Sepsis related mortality is largely preventable with prevention of sepsis itself, timely recognition, rational antimicrobial therapy and aggressive supportive care. The organisms associated with neonatal infection vary significantly in different geographical areas and the treatment vary accordingly. Knowledge of local and regional health problems is a prerequisite for establishing an effective health care delivery system, epidemiological and statistical information regarding neonatal sepsis is the basis for establishing a sound intervention.

Objective: This study was done to determine the clinical epidemiology of neonatal sepsis among neonates admitted to King Khalid university hospital In Riyadh during the year 2016.

Methodology: This is a retrospective descriptive study relied on medical records of the pediatric department of king Khalid university hospital in Riyadh, Capital of Saudi Arabia, included all neonatal sepsis cases registered during the year 2016.

Results: The prevalence rate of neonatal sepsis in king Khalid university hospital in 2016 was (37%), male neonates were exposed more than females (64.5%). Early neonatal sepsis was the common form of the sepsis (73%). Regarding residence of the families, majority were coming from urban areas (65%). Although number of neonates (54.8%) born at hospital and developed sepsis is more compared to neonates born at home, the difference was not statically significant. The common category of antibiotics prescribed by pediatricians in the hospital was the single antibiotics (53.8%) and the frequently prescribed single antibiotic was ampicillin (46%) followed by mixed antibiotics ribed (46.2%) and mostly in the form of ampicillin with cefotaxime (53.49%).

Conclusion: Early neonatal sepsis is the common period of the disease with male neonates are more effected than females. the Neonatal sepsis occurred despite the place or type of delivery raising the questions about the contributing factors to neonatal sepsis.

Recommendations: We recommend the hospital administration prove the process of data compilation and archiving. Antimicrobial culture and sensitivity test must be performed to develop an evidence based practice for management of neonatal sepsis in the University hospital.

Keywords: Neonatal Sepsis; Clinical Epidemiology; Pediatrics; Antibiotics

Introduction

Sepsis is the most common cause of neonatal mortality (death in the first 28 days of life); it is responsible for about 30-50% of the total neonatal deaths in developing countries. It is estimated that up to 20% of neonates develop sepsis and approximately 1% die of sepsis related causes. Sepsis related mortality is largely preventable with prevention of sepsis itself, timely recognition, rational antimicrobial therapy and aggressive supportive care [1,2].

The incidence of neonatal sepsis depends on geographic area and may vary from country to country as well as within the same country. In developing countries, neonatal mortality resulting from all cases of neonatal sepsis is about 34 per 1000 live births, occurring mainly in the first week of life, whilst it is 5 per 1000 live births in developed countries [3].

Neonatal sepsis is defined as a clinical syndrome in an infant 28 days of life or younger, manifested by systemic signs of infection and isolation of a bacterial pathogen from the bloodstream [4]. Neonatal sepsis can be classified into two major categories, early-onset sepsis, and late-onset sepsis. The terms early-onset infection and late-onset infection refer to the different ages at onset of infection in the neonatal period. Although these disorders were originally divided arbitrarily into infections occurring before and after 1st week of life. It is more useful to separate early- and late-onset sepsis according to maternal condition. Early-onset sepsis are acquired before or during delivery (vertical mother-to-child transmission). Late-onset sepsis develop after delivery from organisms acquired in the hospital or the community. The age at onset depends on the timing of exposure and virulence of the infecting organism [5].

The organisms associated with neonatal infection vary significantly in different geographical areas. Group B streptococcus (GBS) continues to be the most important bacterial pathogen associated with early-onset sepsis in many developed countries, for reasons which remain unclear; neonates in some developing nations are rarely infected with GBS, which only accounts for 14% of neonatal infection. Neonatal infections in the developing nations are dominated by Gram-negative (e.g. *Klebsiella species*) and Gram-positive organisms (e.g. *Staphylococcus aureus*). It is therefore essential that antibiotic therapy be tailored to the specific microbial needs of a particular geographical region [6].

The risk factors of neonatal sepsis include the following : Prematurity, low birth weight, rupture of membrane (ROM) \geq 18 hours, maternal conditions (fever or UTI), resuscitation and male sex [7].

The earliest signs of sepsis are often subtle and nonspecific; Indeed, a high index of suspicion is needed for early diagnosis. Neonates with sepsis may present with one or more of the following symptoms and signs: (a) Hypothermia or fever (former is more common in preterm low birth weight infants), (b) Lethargy, poor cry, refusal to suck, (c) Poor perfusion, prolonged capillary refill time, (d) Hypotonia, absent neonatal reflexes, (e) Brady/tachycardia, (f) Respiratory distress, apnea and gasping respiration, (g) Hypo/hyperglycemia, (h) Metabolic acidosis. Specific features related to various systems: Central nervous system (CNS): Bulging anterior fontanelle, high-pitched Cry, excess irritability, Stupor/coma, seizures, and neck retraction. Presence of these features should raise a clinical suspicion of meningitis. Cardiac: Hypotension, poor perfusion, and shock. Gastrointestinal: Feed intolerance, vomiting, diarrhea, abdominal distension, paralytic ileus, and necrotizing enterocolitis (NEC). Hepatic: Hepatomegaly, and direct hyper-bilirubinemia (especially with urinary tract infections). Renal: Acute renal failure. Hematological: Bleeding, petechiae, and purpura. Skin changes: Multiple pustules, abscess, sclerema, mottling, umbilical redness and discharge [8,9].

The typical complete sepsis workup in a neonate consists of obtaining complete white blood cell count with differential, single blood culture, urine culture, and lumbar puncture for cell count and culture. In addition, there may a role for culture and gram staining of tracheal aspirates from intubated neonates shortly after breath. Acute phase reactants are also frequently used in predicting neonatal sepsis. The most widely used is c-reactive protein, which has a high degree of sensitivity for neonatal sepsis [10].

Clinical diagnosis of presentation is difficult due to nonspecific signs and symptoms. In addition, laboratory diagnosis is time consuming. This matter necessitates the initiation of empirical antibiotic therapy till the suspected sepsis is ruled out. Empirical antibiotic therapy should be unit-specific and determined by the prevalent spectrum of etiological agents and their antibiotic sensitivity pattern. The most commonly used antibiotics include penicillin or ampicillin, cefotaxime, ciprofloxacin, gentamicin and amikacin [11,12].

Knowledge of local and regional health problems is a prerequisite for establishing an effective health care delivery system, epidemiological and statistical information regarding neonatal sepsis is the basis for establishing a sound intervention. These information also has significant influence on treatment assessment and subsequent outcome [13]. Therefore the study is designed to describe the clinical epidemiology of neonatal sepsis in king Khalid university hospital in Riyadh city, Saudi Arabia, during a 12 months period from 1st January to 31st December 2016.

Methodology

Study design and setting

Our study is a retrospective descriptive study carried out by group medical students in the period between (January 1st 2016 to December 31st 2016). The data was collected from university hospital. The study was conducted among neonates attended King Khalid University Hospital for treatment, in Riyadh city, capital of Saudi Arabia.

Study population

Study population included all neonates with neonatal sepsis who registered for treatment in King Khalid university hospital during the period from January 1st 2016 to December 31st 2016.

Data collection tool

The data was collected through medical record and chick list was the only tool used.

The check list included the following data:

- Personal data: (sex - age - area- site of admission).
- The most common risk factors related to neonatal sepsis: place of delivery, type of delivery, gestational age, birth weight, premature rupture of membranes (PROM), (mothers with fever and Urinary Tract Infection UIT).
- The most common clinical picture of neonatal sepsis: poor reflexes, lethargy, respiratory distress, bradycardia, apnea, convulsions, abdominal distension, diarrhea, and cyanosis.
- The most common antibiotic therapy prescribed to neonatal sepsis.
- The prognosis on discharge.

Data analysis

The data was checked for completeness, coded then was entered into the computer and was analyzed by using statistical package for social science program (SPSS version20). Obtained data was analyzed using descriptive statistical tables (frequencies percentages). Data was presented in tables and graphs by using computer applications (Microsoft office word and Microsoft excel).

Ethical considerations

Approval of project was obtained from king Saud university college of medicine, department Of community medicine, and from king Khalid university hospital. We ensured and promised that the information obtained will be used for the research purpose and for the benefits of the community.

Results

There are 252 admitted neonates out of total 1975 admitted children in the hospital during the year 2016, which make the percentage of neonatal admissions among all pediatric admissions in 2016, 12.8%.

The study focused on the cases of neonatal sepsis; out of the admitted 252 neonates there were 93 neonates diagnosed clinically as having neonatal sepsis, which means the proportion of neonatal sepsis among all admitted neonates in the king Khalid university hospital was 37%. Regarding the gender of the neonates, (64.5%) were males and (35.5%) were females; Regarding the type of neonatal sepsis, (73%) of them were having early neonatal sepsis compared to (27%) were having late neonatal sepsis, and (65%) of the cases were living in the urban areas of Riyadh (Table 1).

Characteristics	No. of neonates	%
Sex		
Male	60	64.5%
Female	33	35.5%
Total	100	100%
Residence		
Urban	61	65.6%
Rural	32	34.4%
Total	93	100%
Gestational age at birth		
Full term	78	83.9%
Preterm	15	16.1%
Total	93	100%
Birth weight		
Low birth weight	34	36.6%
Norma birth weight	59	63.4%
Total	93	100%
Place of birth		
Home	42	45.2%
Hospital	51	54.8%
Total	93	100%
Word		
ICU	31	31.3%
Pediatric	62	68.7%
Total	93	100%
Age at onset of sepsis		
Early	68	73%
Late	25	27%
Total	93	100%

Table 1: Description of the studied neonates with neonatal sepsis, king Khalid university hospital, Riyadh, 2016.

The study showed that, most common clinical manifestations suggestive of sepsis were fever (57%), Poor of feeding (57%), Difficulty of breathing (29%), jaundice (22.6%), cyanosis (12,6%), hypotonia (20%), diarrhea and Abnormal movement (Table 2).

Clinical signs/accompanied diagnoses	No. of cases	%
Fever	53	57%
Poor feeding	53	57%
Difficulty of breathing	27	29%
Jaundice	21	22.6%
Hypotonia	19	20%
Abnormal movements	13	14%
Cyanosis	12	12.9%
Bulging of anterior fontanelle	8	8.5%
Vomiting	7	7.5%
Diarrhea	6	6.5%

Table 2: Clinical manifestations reported in the total 93 neonates diagnosed clinically as having neonatal sepsis, king Khalid university hospital, Riyadh 2016.

Neonatal sepsis is classified by the age of the neonate when the sepsis started, there are two categories: early onset sepsis (EOD) and late onset sepsis (LOD). The EOD is the onset of neonatal sepsis during the first 7 days of life, The LOD is the onset of neonatal sepsis during the period of 8 - 28 days of neonate age. EOD in this study represented in 71% of the studied neonates while LOD is present in 29% of them (Figure 1 and 2).

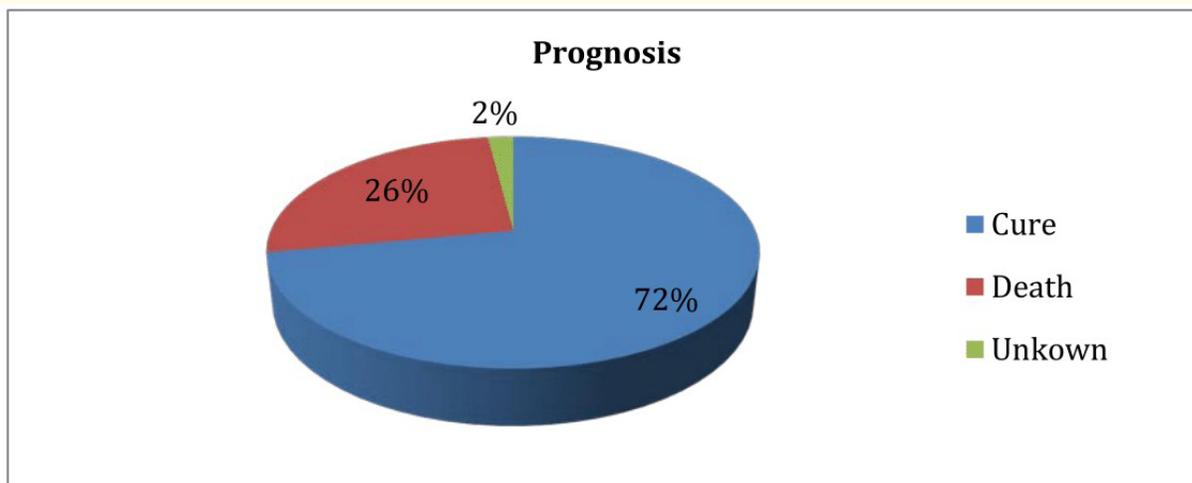


Figure 1: Prognosis of neonatal sepsis patients, king Khalid university hospital , Riyadh 2016.

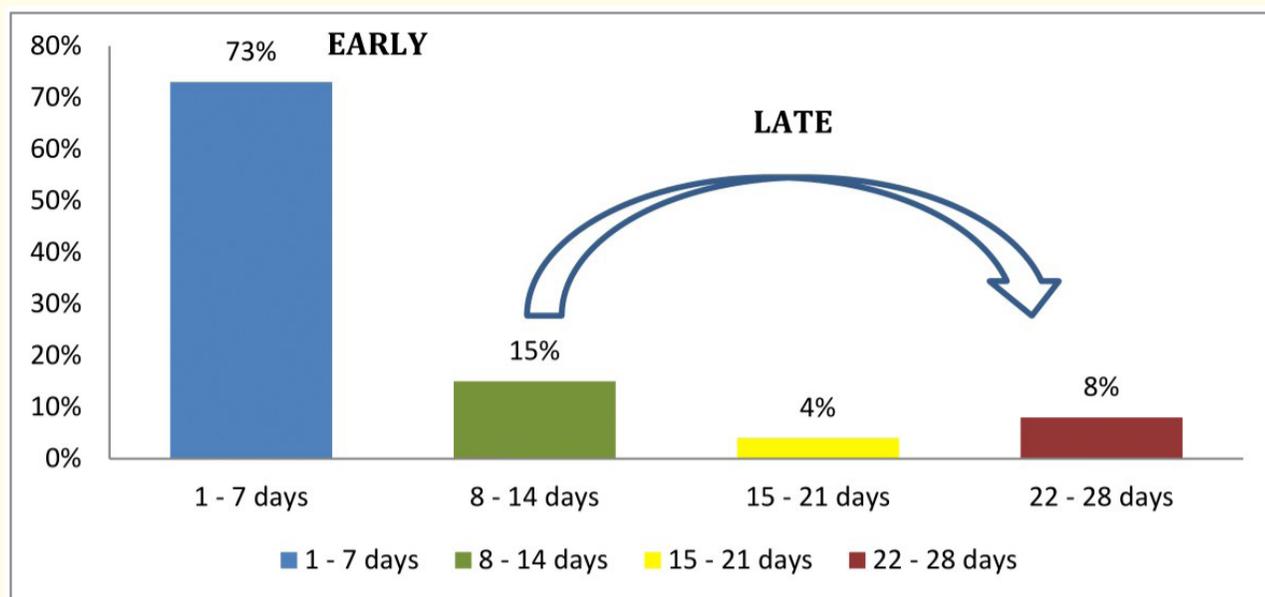


Figure 2: Classification of neonatal sepsis based on forms (Time of onset of sepsis).

In this study; we are able to describe the relation of certain neonatal and maternal characteristics on the age at onset of neonatal sepsis but unfortunately no statistical association were exist (Table 3 and 4).

Characteristics	Early neonatal sepsis (N = 68)	Late neonatal sepsis (N = 25)	Total (N = 93)	P-value*
Sex				0.4
Male	42	18	60	
Female	26	7	33	
Residence				0.2
Urban	47	14	61	
Rural	21	11	32	
Place of delivery				0.2
Home	28	14	42	
Hospital	40	11	51	
Mode of delivery				0.1
Vaginal	59	25	84	
LSCS	9	0	9	
Gestational age at birth				0.5
Full-term	56	22	78	
Preterm	12	3	15	
Birth weigh				0.3
Low birth weight	27	7	34	
Normal birth weight	41	18	59	
Days of hospital stay				0.7
1 - 7 days	53	18	74	
8 - 14 days	11	6	17	
15 - 21 days	4	1	5	
Neonatal outcome				0.07
Cured	34	16	50	
Died	17	1	18	
Unknown	17	8	25	

Table 3: Relationship between age at onset of the neonatal sepsis and certain neonatal characteristics, king Khalid university hospital, Riyadh 2016.

*Chi-square test (P < 0.05 is considered statistical significance)

Maternal factors	Early neonatal sepsis (N = 68)	Late neonatal sepsis (N = 25)	Total (N = 93)	P-value*
Place of delivery				0.2
Home	28	14	42	
Hospital	40	11	51	
Mode of delivery				0.1
Vaginal	59	25	84	
LSCS	9	0	9	
Premature rupture membrane				0.9
Yes	3	1	4	
No	65	24	89	
Maternal condition fever or UTI				0.5
Yes	18	5	23	
No	50	20	70	

Table 4: Relationship between age at onset of the neonatal sepsis and certain maternal factors king Khalid university hospital, Riyadh 2016.

*Chi-square test (P < 0.05 is considered statistical significance)

Regarding management of neonatal sepsis in king Khalid university hospital; the most commonly antibiotics prescribed by pediatricians in the hospital were single antibiotic (50 out of 93 neonates, 53.8%) and the frequently prescribed single antibiotic was ampicillin (23/50, 46%) and it found that it is effective. In the case of mixed antibiotics prescribed (43 out of 93 neonates, 46.2%); and mostly in the form of ampicillin with cefotaxime (23/43, 53.49%). Other antibiotics prescribed were: Amikacin, cefotaxime, Cefuroxime and Vancomycin (Table 5 and 6).

Category	Number of neonates	Percentage
Single	50	53.8%
Mixed	43	46.2%
Total	93	100%

Table 5: Categories of antibiotics used to treat neonatal sepsis.

Antibiotic	No. of neonates
Ampicillin	53
Amikacin	20
Cefotaxime	53
Cefuroxime	4
Vancomycin	12

Table 6: Types and Frequency of antibiotics prescribed for treatment of neonatal sepsis either as a single or mixed, king Khalid university hospital , Riyadh 2016.

Discussion

The result of This study showed that the incidence of neonatal sepsis among neonates in king Khalid university hospital in 2016 was 37%. This figure is higher than that were reported from Nepal (12.4%) [14] and India (7.6%) [15]. The difference here due to that the diagnosis in king Khalid university hospital is based on clinical diagnosis that may overestimate the true incidence. Eman M., *et al.* (2015) reported a high incidence of neonatal sepsis in three hospitals in Egypt [16], the study focused on admitted neonates in intensive care units in which most of the cases were critically ill and with high probability of sepsis than those admitted to other the general pediatric department as the case of our study.

The disease occurred mostly in the early period (EOS) which constitutes 73% of cases while 27% of the disease occurred in the late period (LOS), The result indicated that the incidence of EOS septicemia was more common than LOS which is consistent with other reports from Nepal [14], Iran, Iraq, Bangladesh, and Yemen. result in contrast with study of Egypt where 44% of neonatal sepsis occurred in the early period while most of cases (56%) occurred in the late period(LOS) [16].

The result of this study showed that most clinical presentations of neonatal sepsis are fever (57%), poor feeding (57%), Difficulty of breathing (29%), and jaundice (22%) which is consistent with other studies; a study in Sudan showed that the most common clinical pictures were fever (63%), Difficulty of breathing (44%), poor feeding (32.5%), jaundice (31%) [17], while in a study conducted in Sanaa (Yemen) showed that the most common clinical pictures were Difficulty of breathing (72.2%), jaundice (62.2%), cyanosis (51.1%), lethargy (47.8%) [18]. Similar findings were reported in India; lethargy (77.4%), hypothermia (47.5%) and respiratory distress (44%) [19].

This study focused on some neonatal, maternal factors that may precipitate the development of neonatal sepsis like place of delivery gestational age at birth, birth weight and premature rupture of membrane and maternal fever, unfortunately no association being exist between any of these factors and the neonatal sepsis while a study in southeastern Mexico at 2012 [20], revealed that, prematurity, premature rupture of membrane and low birth weight are significant contributing factors to the neonatal sepsis. Failure to confirm any association in this study due difference in study designs, since this is limited to one year period.

Antibiotic prescription for neonatal sepsis are not based on antimicrobial sensitivity tests. The most prescribed antibiotics are Ampicillin, Cefotaxime and Amikacin in contrast with study conducted in Nepal where the prescriptions are laboratory based with the most pathogens in neonatal sepsis are *Staphylococcus aureus*, *Klebsiella*, *Pseudomonas aeruginosa*, all the pathogens were sensitive to amikacin and highly resistance to ampicillin [21]. This discrepancy raising the concern about clinical diagnosis and the need for laboratory based management in king Khalid university hospital.

Regarding the outcome of the neonatal sepsis our study show that the case fatality rate of neonatal sepsis was high (26%) without significant difference between early and late-onset sepsis. In contrast to study that done in southeastern Mexico, which show a marked difference in between early- and late-onset sepsis, as well as case fatality rates are in Mexico (9.5%) [20].

Conclusions

- Early neonatal sepsis is the common period of the disease with male neonates are more affected than females.
- The Neonatal sepsis occurred despite the place or type of delivery raising the questions about the contributing factors to neonatal sepsis.

Recommedations

- Early neonatal sepsis is the common period of the disease with male neonates are more affected than females.
- The Neonatal sepsis occurred despite the place or type of delivery raising the questions about the contributing factors to neonatal sepsis.

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