

## Epidemiology of Neonatal Sepsis in Pediatric Department of Hadramout University Hospital, Mukalla, 2015

Abdulla Salem Bin Ghouth<sup>1\*</sup>, Amal Sharif Ba-Alwi<sup>2</sup>, Amjad Faiz Bin Maraie<sup>2</sup>, Fatma Adel Bawazeer<sup>2</sup>, Fatma Mohssen Alai<sup>2</sup>, Marwa Ahmed Bin Shoba'a<sup>2</sup>, Reem Waleed Al-Aila<sup>2</sup>, Sabreen Mohammed Bin Johar<sup>2</sup>, Sumaia Akrm Bin Taher<sup>2</sup> and Sumaia Mohammed Bazmalha<sup>2</sup>

<sup>1</sup>Professor of community medicine, Hadramout University College of Medicine (HUCOM)

<sup>2</sup>A group of 4<sup>th</sup> medical student, Hadramout University College of Medicine (HUCOM), 2015/2016

\*Corresponding Author: Abdulla Salem Bin Ghouth, Hadramout University College of Medicine (HUCOM), Department of Community Medicine, Fluk, Mukalla, Hadramout, Yemen.

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### Abstract

**Background:** Neonatal sepsis is a clinical syndrome characterized by systemic signs of 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). This study was done to determine the clinical epidemiology of neonatal sepsis among neonates admitted to the Pediatric Department of Hadramout University Hospital in Al-Mukalla during the year 2015.

**Methods:** The study was a retrospective descriptive study relied through medical records in the Pediatric Department of University Hospital in Al-Mukalla, all neonatal sepsis cases registered during Year 2015.

**Findings:** The incidence rate of Neonatal Sepsis in the Hadramout University Hospital in 2015 was 12.8%; male neonate are more exposed than females (64.5%) having early neonatal sepsis (73%) and coming from urban areas of Mukalla (65%). Although numbers of neonates (54.8%) were born in hospital and developed sepsis compared to the neonates born at home but the difference is not significant. The most common antibiotics prescribed by pediatricians in the hospital were single antibiotic (53.8%) and the frequently prescribed single antibiotic was ampicillin (46%) followed by mixed antibiotics prescribed (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 more effected than females. The neonatal sepsis occurred despite the place of and/or type delivery raising the questions about the contributing factors to neonatal sepsis.

**Key words:** Neonate; Sepsis; Mukalla

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## Introduction

Sepsis is the commonest 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 terms early-onset infection and late-onset infection. The terms early-onset infection and late-onset infection refer to the different ages at onset of infection in the neonatal period. These disorders were originally divided arbitrarily into infections occurring before and after 1 week of life. It is more useful to separate early- and late-onset infections according to peripartum pathogens. Early-onset infections are acquired before or during delivery (vertical mother-to-child transmission). Late-onset infections 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 puerperal fever or infection, 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:

1. Hypothermia or fever (former is more common in preterm low birth weight infants)
2. Lethargy, poor cry, refusal to suck
3. Poor perfusion, prolonged capillary refill time
4. Hypotonia, absent neonatal reflexes
5. Brady/tachycardia
6. Respiratory distress, apnea and gasping respiration
7. Hypo/hyperglycemia
8. Metabolic acidosis.

Specific features related to various systems: Central nervous system (CNS): Bulging anterior fontanelle, high-pitched cry, excess irritability, stupor/coma, seizures, neck retraction. Presence of these features should raise a clinical suspicion of meningitis. Cardiac: Hypotension, poor perfusion, shock. Gastrointestinal: Feed intolerance, vomiting, diarrhea, abdominal distension, paralytic ileus, necrotizing enterocolitis (NEC). Hepatic: Hepatomegaly, direct hyperbilirubinemia (especially with urinary tract infections). Renal: Acute renal failure. Hematological: Bleeding, petechiae, 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 be a role for culture and gram staining of tracheal aspirates from intubated neonates shortly after birth. 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 [13]. This information also has significant influence on treatment assessment and subsequent outcome. Therefore the study is designed to describe the clinical epidemiology of neonatal sepsis at Hadramout University hospital in Mukalla, Yemen, during a 12 month period from 1<sup>st</sup> January to 31<sup>st</sup> December 2015, and specifically through determining: a) the incidence of neonatal sepsis among cases admitted to university hospital b) the most common clinical presentation of neonatal sepsis as well as c) identifying the commonly prescribed anti-microbial drugs for treatment of neonatal sepsis in Hadramout University hospital.

### Materials and Methods

**Study design:** This study was retrospective descriptive study carried out by a group of fourth year medical students of Hadramout University in a period between January 1<sup>st</sup> 2015 to December 31<sup>st</sup> 2015.

**The setting:** The study was conducted among neonates in Hadramout University Hospital in Al Mukalla district the capital of Hadramout governorate which located in Arabian Sea in Yemen.

**Study population:** Study population was all neonates with neonatal sepsis who admitted for treatment in Hadramout University hospital during the period from January 1<sup>st</sup> 2015 to December 31<sup>st</sup> 2015.

**Data collection tool:** The data was collected through medical records and the only tool used was the check list.

**This includes: Personal data:** (sex - age - area - date of admission - date of discharge - Hospitalization period - site of admission). The most common risk factors related to neonatal sepsis: (gestational age, birth weight, mode of delivery, and risk factors for sepsis: premature rupture of membranes (PROM), maternal with fever and Urinary Tract Infection (UTI)). The most common clinical picture of neonatal sepsis: (poor reflexes, lethargy, respiratory distress, bradycardia, apnea, convulsions, abdominal distension, and diarrhea). The most common antimicrobial therapy prescribed to neonatal sepsis. The prognosis of discharge.

**Data Analysis:** The data was checked for completeness, coded then was entered in to the computer and was analyzed by using statistical package for social science (SPSS V 20). The obtained data were 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 Consideration:** Approval of project was obtained from Hadramout University College of medicine (HUCOM) department of community medicine. We ensure that the information which will be involved in the study will be used for the benefits of the community.

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## Results

This study is conducted in the pediatric department of the Hadramout University hospital in Mukalla city where there are 252 admitted neonates out of the total 1975 admitted children in the hospital during the study period giving the proportion of neonatal admissions among the total pediatric admission in the hospital to 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 that means the proportion of neonatal sepsis among all admitted neonates in the University hospital of Mukalla was 37%. Most of the neonatal sepsis cases were males (64.5%) having early neonatal sepsis (73%) and coming from urban areas of Mukalla (65%) (Table1).

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%

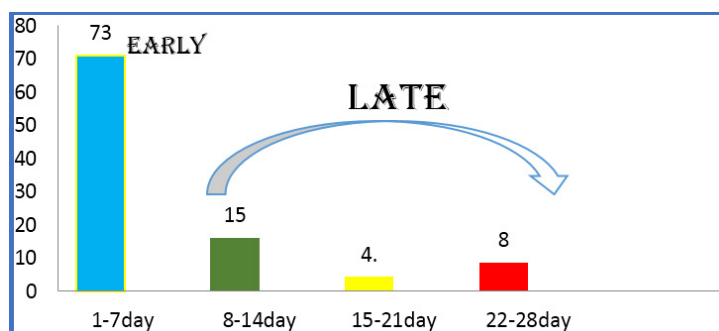
**Table 1:** Description of the studied neonates with neonatal sepsis, University Hospital, Mukalla, 2016.

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 (Table2). Neonatal sepsis is classified by the age at onset of sepsis into two categories: early onset disease (EOD) and late onset disease (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

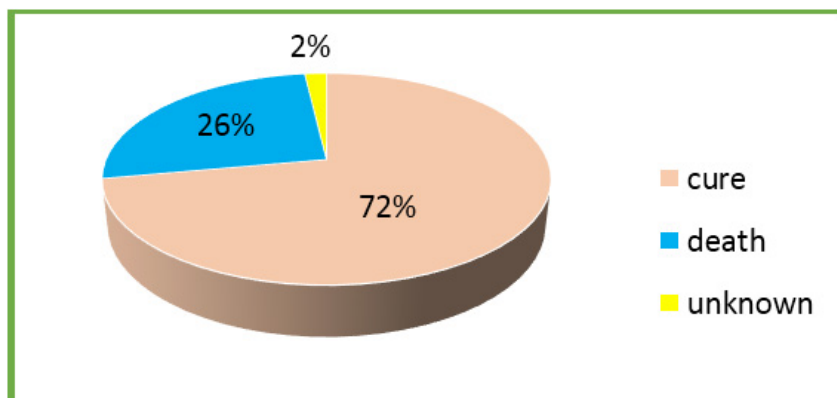
age. EOD in this study represented in 71% of the studied neonates while LOD is present in 29% of them (Figure1). Case fatality rate due to neonatal sepsis is high in Hadramout University hospital (26%), (Figure 2) with significant difference according to the period of onset of sepsis (P-value <0.05) (Table 4).

Clinical signs/accompanied diagnoses	No.%
Fever	53 57
Vomiting	7 7.5
Poor of feeding	53 57
Difficulty of breathing	27 29
Jaundice	21 22.6
Cyanosis	12 12.9
Abnormal movement	13 14
Hypotonia	19 20
Diarrhea	6 6.5
bulging of anterior fontanel	8 8.5
Other*	26 28

**Table 2:** Clinical manifestations reported in the total 93 neonates diagnosed clinically as having neonatal sepsis, The University Hospital, Mukalla 2016.



**Figure 1:** Classification of the studied neonates by their ages at onset of sepsis.



**Figure 2:** Prognosis of neonatal sepsis among neonates admitted to Hadramout University Hospital, 2015.

Regarding management of neonatal sepsis in University hospital of Mukalla; the most commonly antibiotics prescribed by pediatricians in the hospital were single antibiotic (50/93, 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, 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 3). 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 (Tables 4 & 5).

Antibiotic	No of neonates	%
Ampicillin	53	57%
Amikacin	20	21.5%
Cefotaxime	53	57%
Cefuroxime	4	4.3%
Vancomycin	12	12.9%

**Table 3:** Types and Frequency of antibiotics prescribed for treatment of neonatal sepsis either as a single or mixed, The University hospital of Mukalla 2016

Characteristics	Early neonatal sepsis n = 68 (%)	Late neonatal sepsis n = 25 (%)	Total N = 93	P-value*
Sex				
- Male	42 (70%)	18 (30%)	60	0.4
- Female	26 (78.9%)	7 (21.1%)	33	
Residence				
- Urban	47 (77%)	14 (23%)	61	0.2
- Rural	21 (65.6%)	11 (34.4%)	32	
Place of delivery				
- Home	28 (66.6%)	14 (33.4%)	42	0.2
- Hospital	40 (78.4%)	11 (21.6%)	51	
Mode of delivery				
- Vaginal	59 (70.2%)	25 (29.8%)	84	0.1
- LSCS	9 (100%)	0 (0%)	9	
Gestational age at birth				
- Full-term	56 (71.8%)	22 (28.2%)	78	0.5
-Preterm	12 (80%)	3 (20%)	15	
Birth weight				
- Low birth weight	27 (79.4%)	7 (20.6%)	34	0.3
- Normal birth weight	41 (69.5%)	18 (30.5%)	59	
Days of hospital stay				
1-7days	53 (71.6%)	18 (28.4%)	74	0.7
8-14 days	11 (64.7%)	6 (35.3%)	17	
15-21 days	4 (80%)	1 (20%)	5	

Neo (n = 68) † natal outcome				
- Cured	34 (68%)	16 (32%)	50	0.03‡
- Died	17 (94.4%)	1 (5.6%)	18	

\*chi square test was used with 0.05 significance level‡ Fischer exact test is used

†15 cases not included in this analysis because no data documented about the outcome of treatment

**Table 4:** Relationship between age at onset of the neonatal sepsis and certain neonatal characteristics, University Hospital, Mukalla, 2015

Maternal factors	Early neonatal sepsis N = 68 (%)	Late neonatal sepsis N = 25 (%)	Total N = 93	P-value*
Place of delivery				
- Home	28 (66.6%)	14 (33.4%)	42	0.2
- Hospital	40 (78.4%)	11 (21.6%)	51	
Mode of delivery				
- Vaginal	59 (70.2%)	25 (29.8%)	84	0.1
- LSCS	9 (100%)	0 (0%)	9	
Premature rupture membrane				
- Yes	3 (75%)	1 (25%)	4	0.9
- No	65 (73%)	24 (27%)	89	
Maternal puerperium fever or infection				
-Yes	18 (78.3%)	5 (21.7%)	23	0.5
-No	50 (71.4%)	20 (28.6%)	70	

\*chi square test was used with 0.05 significance level

**Table 5:** Relationship between age at onset of the neonatal sepsis and certain maternal factors, University Hospital, Mukalla, 2015

## Discussion

Sepsis remains one of the most important causes of morbidity and mortality in the newborn. The results of this study showed that the incidence of neonatal sepsis among neonates in the University hospital of Mukalla in 2015 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 Hadramout University hospital is based on clinical diagnosis that may overestimate the true incidence. Eman., *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 neonate (EOS) which constitutes 73% of cases while 27% of the disease occurred in the late neonate (LOS). The result indicated that the incidence of EOS septicemia was more common than LOS which is consistent with other reports from Nepal, Iran, Iraq, Bangladesh, and Yemen [14]. This 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 neonate (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%), and 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 south Eastern 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 is 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, psudomonas aerogiosa, 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 Hadramout University hospital.

Regarding the outcome of the neonatal sepsis our study show that the case fatality rate of neonatal sepsis was high (26%) with statistically significant difference between early- and late-onset sepsis. In consistence 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].

**Limitation of the study:** This study collected data from hospital archive that were not completely filed because the specialists not requires the blood culture this issue limited our study only on the clinical diagnosis.

## Conclusions

Early neonatal sepsis is the common period of the disease with male neonates more effected than females. The Neonatal sepsis occurred despite the place of or type delivery raising the questions about the contributing factors to neonatal sepsis. Neonates with sepsis in early period are prone to risk of death more than those developing sepsis in the late period.

## Recommendations

- We recommend the hospital administration to improve 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.

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